OCCASION

This publication has been made available to the public on the occasion of the 50th anniversary of the United Nations Industrial Development Organisation.

DISCLAIMER

FAIR USE POLICY

CONTACT

Please contact publications@unido.org for further information concerning UNIDO publications.

For more information about UNIDO, please visit us at www.unido.org

UNITED NATIONS INDUSTRIAL DEVELOPMENT ORGANIZATION
Vienna International Centre, P.O. Box 300, 1400 Vienna, Austria
Tel: (+43-1) 26026-0 · www.unido.org · unido@unido.org

1634-S

UNITED NATIONS INDUSTRIAL DEVELOPMENT ORGANIZATION

Genetic Engineering and Biotechnology Monitor

Issue No. 17

July-September 1986

Dear Reader,

Since the last issue of the Monitor reached you, progress as regards the physical establishment of the ICGEB is well advanced and the first laboratories of the ICGEB at Trieste are ready to have the equipment installed, while the temporary accommodation provided for the Centre at New Delhi has been constructed and is likewise waiting for installation. As a result the ICGEB is now searching for dedicated research scientists and associates to begin the work for which the Centre was established.

For the benefit of new readers, let me briefly outline the aims of the ICGEB and then indicate the possibilities available:

The International Centre for Genetic Engineering and Biotechnology (ICGEB) is an intergovernmental organization being established by 39 countries as a centre of excellence devoted to the application of genetic engineering and biotechnology to accelerate economic development. The United Nations Industrial Development Organization (UNIDO) assists the member countries of the ICGEB in establishing the Centre and is currently implementing an interim programme for a period of three years by which time the Centre is expected to function as an autonomous intergovernmental organization.

The Centre has two Components, Trieste, Italy, and New Delhi, India. Early work in Trieste concerns molecular aspects of DNA replication in human cells and the molecular, immunological and pharmacological aspects of human papilloma and rotavirus infections. At New Delhi the initial focus is on the molecular aspects of plant biology, hepatitits virus and parasitology with special emphasis on protozoan infections.

The GENETIC ENGINEERING AND BIOTECHNOLOGY MONITOR is issued free of charge.

Compiled by Development and Transfer of Technology Division, Department for Industrial Promotion, Consultations and Technology, UNIDO, P.O. Box 300, A-1400 Vienna, Austria.

The Centre is under the directorship of Prof. Irwin C. Gunsalus. The Trieste Component is headed by Prof. Arturo Falaschi. Prof. K. K. Tewari, proposed by the Director as head designate, is advising him on the development of the New Delhi Component. Positions are now available as follows:

Reasearch Scientists are being recruited at levels from Assistant to Senior Research Scientist, with equivalance to academic attainment of Assistant to full Professor at major internationally recognized universities. Ph.D. candidates with recent post-doctoral experience, to be appointed at the Assistant Research Scientist level, can, after in-depth review according to the Centre's guidelines, receive promotion. For candidates with established recognition in their scientific field and demonstrated experience and leadership, senior appointments are available. Fluency in English is essential.

Research Associate appointments will be available for participation, in Trieste and New Delhi, with Research Scientists in the areas listed above. Recent Ph.D. graduates in the physical and biological sciences with emphasis on chemistry, biochemistry, molecular and cell biology. Immediate research interests include molecular genetics, plant and animal molecular biology, molecular virology, parasitology, bacterial physiology and fermentation. Preference will be given to candidates with publications in peer reviewed journals with strong training in chemistry and biology.

In general, initial appointments will be for one to three years depending on the experience and qualifications with salaries and allowances according to United Nations system scales and conditions of employment. The assignment of successful candidates will be based on the Component of applicant's preference and the availability of the requisite research topic.

Those of our readers who may be interested in applying for these positions should send a resumé with three letters of recommendation to Prof. I.C. Gunsalus, c/o UNIDO.

I wish to thank again all readers who reacted to our mailing list survey by commenting on the content and format of the Monitor; please be assured that each comment is considered and, if possible, taken into account, even if we cannot reply individually to our readers. One complaint we receive frequently is that the print is now too small; however, since we depend on the joint printing facilities of the Vienna International Centre all documents are now created in the same format, and this is beyond our control. One serious complaint is that the Monitor arrives with great delay at some overseas destinations since it is mailed by surface post. We will therefore be looking into the possibility of subscribers who wish to do so making a contribution to pay for airmail and handling charges. We would be grateful for an early indication of interest from those wishing to participate in any such scheme.

K. Venkataraman
Senior Technical Adviser
Department for Industrial Promotion,
Consultations and Technology

		Page
A.	POLICY, NEWS AND OTHER EVENTS	1
	UNIDO News	
	International Centre for Genetic Engineering and Biotechnology	1
	Regulatory issues	
	European failure to agree on biotechnology regulations	1
	USA reveals biotechnology rules	1
	Revision of Japan's rDNA experiment guidelines	2
	Social implications	
	Gene therapy	2
	General	
	Exchanging of biological material	2
	Unique system for freeze-dried micro-organisms	3
	Centre for Plant Conservation to save endangered species	?
	New biology/chemistry institute	?
	Human Leukaemia Centre	?
	Marine biotechnology laboratory to be built	4
	Consortium to design gene tool kit for four crops	4
	Biotechnology firms plan insurance pool	4
	Micro-organism sales gain	4
	Biotechnology stock market	5
	How to evaluate a biotechnology acquisition	5
B.	COUNTRY NEWS	6
	EEC	6
	EUREKA proposals in biotechnology	6
	Australia	7
	Malaria vaccine joint venture	7
	Calgene launches Australia affiliate	7
	Austria	7
	Drug to treat AIDS under development	7
	New laboratories for cancer research	7
	Belgium	7
	Belgian Bioindustries Association	7
	Brazil	7
	Extension of patent protection to high-technology sectors	7
	Canada	8
	Major biotechnology company turns to other areas	8
	Colombia	8
	Vaccine development	8
	Czechoslovakia	8
	Long-term development of biotechnology	8
	Denmark	8
	Denmark first to legislate gene manipulation	8
	Company receives approval to produce insulin via genetic engineering	9
	Danish science park expands	9
	Novo Industri forms new bio-industrial group	9
	Federal Republic of Germany	9
	Guidelines for genetic experiments issued	9
	Government measures to promote biotechnology	9
	New infrastructure for genetic research set up	10
	Bonn allocates biotechnology budget	10
	Finland	10
	Fir trees cloned by Finnish researchers	10
	France	10
	Club will encourage French biotechnology firms	10
	India	11
	Temporary infertility vaccine	11
	Israel	11
	Growth factors and cell development	11
	Italy	11
	New initiative called for	11
	Sorin Biomedica US diagnostics push	11
	Japan	11
	Protein engineering system	11
	Beta-TNF	11
	Joint research with China	12
	Silk used to fix enzymes	12
	New rice strain	12
	Interferon producers obtain approvals	12
	Microbes as energy source to be studied	12
	Computerized market gardening	12
	Norway	12
	National action plan for biotechnology established	12
	Sweden	13
	Alfa Laval and Pharmacia to set up and sell complete factories	13
	Switzerland	13
	Biogen may sell Geneva facilities	13
	Taiwan	13
	Government biotechnology development plan	13
	United Kingdom	13
	Biopolymers unit starts production	13
	Gene releases investigated	13
	Bio-reactor scale-up	13
	SERC confirms biotechnology's importance	14
	Plant research	14
	Agricultural biotechnology	14
	Wellcome links up with US firm	14
	United States of America	14
	New biology/chemistry institute	14
	US to screen marine organisms for drugs	14
	New centres for clinical trials	15
	Fingerprint deal	15

	Page
Test of gene-altered bacteria postponed	15
EPA approves biotechnology field test	15
Union of Soviet Socialist Republics	16
Vaccination catalyst	16
Firms compete for biotechnology projects	16
Yugoslavia	16
The Fourth International Symposium on Microbial Ecology	16
C. RESEARCH	17
Research on human genes	17
More versatility from RNA	17
Oncogene amplification	17
Research on common cold virus	17
The reasons for malignancy	17
Factor VII cloned	17
Genetic predisposition to high blood pressure	17
Scientists find viral infection triggers arthritis	17
Single-chain antibodies developed	18
New herpes-like virus discovered	18
Possible prediction of carcinogenicity	18
New cancer treatment	18
New T-cell receptor discovered	18
Cancer-spreading genes	18
Mapping the human genome	19
More AIDS research	19
Enzymes repair damaged DNA	19
Single gene may predispose to heart disase	19
New fertility-regulating hormone discovered	20
Dystrophy gene proves mysterious	20
New vaccine technology	20
Cloning and expression	20
Advances reported on cystic fibrosis	21
Monoclonals block graft rejection	21
Cot deaths linked to faulty enzyme	21
Research on animal genes	21
Pea genes help increase wool production in sheep	21
Luciferase gene cloned	22
Crabs may improve a biosensor	22
Simple animals lack body blueprint	22
Extra genes reveal the route to resistance	23
Monoclonal antibodies developed to combat fish diseases	23
A DNA fingerprint for killer bees	23
Insect virus as super-vector	24
Research on plant genes	24
RNA plasmid discovered in maize mitochondria	24
Luminous gene tags	24
Gene inserted into sunflowers	25
Vanadium-containing nitrogenase isolated	25
Gymnosperm tissue culture	25
Direct gene transfer	25
Research on yeast and fungus genes	25
Enzymes for pulping wood	25
Research on viral genes	26
Hepatitis virus binding site identified	26
Researchers discover new AIDS virus gene	26
Research instrumentation	26
DNA sequencing goes automatic	26
New biosensor	26
General	26
Spotlight on biocommunication	26
Perfecting polymers to release drugs	27
Liposome research: new paths for drug delivery	27
Biotechnology Conference on Biosensors sponsored by The Royal Society, London, UK	28
D. APPLICATIONS	28
Pharmaceutical and medical applications	28
Tissue type matching	28
MABs used to prevent kidney rejection	29
Monoclonal antibody test developed for diagnosing Alzheimer's disease	29
Potential uses of monoclonal antibodies	29
Human trials under way to test effectiveness of recombinant malaria vaccines	29
Recombinant vaccine against cholera and typhoid soon to be tested	30
New hepatitis B vaccine	31
Further progress with prototype AIDS vaccine	31
Vaccine for simian AIDS developed	31
Vaccines without side-effects	32
Drug sensitivity testing with potential for cancer chemotherapy on patient tumour cells may soon be available through Chemoscreen	32
Biodegradable polymer to treat brain cancer	32
New approach to combat tumours	32
Alpha-2b interferon used against basal cell carcinoma	32
Biotherapeutics Inc. and Scripps Clinic and Research Foundation establish cancer research programme	33
Cancer markers	33
Alpha interferon product has UK marketing approval	33
Test to detect genetic susceptibility to diseases	33
A DNA probe that detects tuberculosis	33
Monoclonal antibodies are used in a gonorrhea test	34
DNA probes	34
A DNA probe for the detection of Campylobacter	37
AIDS infection detection kit	37
Another possible target for interferon	37
Gamma interferon reported active in treating rheumatoid arthritis	37
Beta-interferon effective against hepatitis B	37
Cetus plans European subsidiary	37
Promising drugs for treatment of AIDS	37
Growth hormone trials to begin	38
Müllerian inhibiting substance to be tested	38
Clinical trials to begin for GM-CSF	38
Biotechnology to find cosmetic applications	38
Livestock applications	39
DNA coding for vaccine virus	39
Vaccine against foot-and-mouth disease	39
Transgenic sheep and foot rot vaccine	39
New biotechnology facility for livestock	39
Vaccine for poultry	39

	Page
French develop rabies vaccine	39
Monoclonals for early detection of canine heartworm	40
Kits to diagnose fish disease	40
Agricultural applications	40
New developments in biotechnology will have major effect on future of biopesticides	40
Disease resistant peach plants cultured	42
Improved tomato	42
Permission granted to field test pesticide and herbicide resistant tobacco	42
Hormones to sweeten navel oranges	42
New grass strain	43
Seeds coated with freeze-dried bacteria	43
Supergrasses with tropical tendencies	43
New uses for algae	43
Tree for poor soils	43
'Fingerprinting' technology to protect silage additives	43
Food production and processing	43
Bioreactor for whey processing	43
Cattle feed from biomass plant to be built	44
Australian hydrolyzed milk to curb lactose problems	44
Enzymes recovery on the way	44
Biotechnology in food production and processing	45
Chemical applications	47
Adhesive production gene isolated	47
Biotechnology company has micro-algae source for a higher fatty acid	47
Energy and environmental applications	47
Coal tar clean-up	47
Technology: in situ bioreclamation	47
Industrial microbiology	48
Detergent enzyme plant start-up	48
Industrial equipment	48
Biotechnology takes its place in schools	48
Equipment for large-scale biotechnology production	48
E. PATENTS AND INTELLECTUAL PROPERTY ISSUES ..	48
Genentech faces hGH patent suit	48
Genex patents novel antibodies	48
Gamma interferon patented in Germany	48
Patent sought for alga that secretes hydrocarbons	49
Interleukin-2 patent	49
Two biotechnology companies in dispute over an anticancer drug patent	49
Enzo Biochem licenses technology from Yale	49
F. BIO-INFORMATICS	49
A new OECD report on biotechnology: "Recombinant DNA safety considerations"	49
Biotechnology market opportunities	50
EC Concertation Unit for Biotechnology in Europe	50
"Biotechnology and Microbiology in Australia"	50
Recombinant DNA methods for teachers	50
The biotechnology of malting and brewing	50
Biotechnology and wastewater treatment	51
Economic aspects of biotechnology	51
ACS helps swell the tide of on-line data bases	51
EEC bio-informatics programme	51
New computer programme	52
DNA databases are swamped	52
Grant awarded to develop computer system for protein engineering	52
New molecular simulation programme	52
GENEUS computer programme	52
Princeton scientist speeds up gene identification process	52
G. MEETINGS	53

A. POLICY, NEWS AND OTHER EVENTS

UNIDO News

International Centre for Genetic Engineering and Biotechnology

The Preparatory Committee on the Establishment of the International Centre for Genetic Engineering and Biotechnology (ICGEB) held its eighth session in Vienna, Austria, from 18-20 June 1986, at which Professor I.C. Gunsalus was elected Director of the ICGEB and Dr. Arturo Falaschi, Director of the Institute of Genetics at Pavia, Italy, as the Head of the component at Trieste.

The representatives of Algeria, Argentina, Brazil, Bulgaria, China, Cuba, Kuwait, Mexico and Yugoslavia reported the progress in regard to ratification in their respective countries and the Committee took note that in several of those countries the process of ratification had advanced considerably.

The Committee noted that the recruitment of scientists was one of the responsibilities of the Director and hoped that, once the Director assumes his duties, the process of recruitment would be initiated. Concerning voluntary contributions by member States, a number of countries announced the decision of their Governments to make contributions to the budget of the ICGEB, and to consider further contributions in the light of the research programmes to be undertaken.

Regulatory issues

European failure to agree on biotechnology regulations

Attempts to standardize European regulations governing biotechnology have failed, and a number of countries are developing their own regulations. The Federal Republic of Germany and Denmark have already passed laws, and the Netherlands and other countries are working on their own versions. Meanwhile, the European Parliament is now expressing some interest in the problem and the OECD is expected to publish its own proposed regulations. A consortium of 15 biotechnology firms has recommended that no new laws be passed to govern biotechnology, since laws governing pharmaceuticals and chemicals are already sufficient, although some adaptation may be needed. If any new laws are passed, they must be equally binding on commercial and non-commercial biotechnology applications. The Committee set up by European industry felt that any new law on the release of organisms must be based on a system assessing risks applied uniformly, to commercial and non-commercial organizations, throughout Europe. The companies said laws on assessing risks should be flexible enough to recognize the different risks with each step between the first experiments and commercial application.

The Committee said that industry accepts the need to make available information on possible risks, but that it would do so only if the authorities agree to keep it secret. In the US, the Government's Recombinant DNA Advisory Committee considers applications in open session.

The European Commission has criticized the industry report as being incomplete, but has not offered any regulations of its own, partly because 15 of its 20 directorates are in some way affected by biotechnology, leading to many conflicts. Individual countries are therefore developing their own regulations, a situation that the industry commission was formed to prevent. The United Kingdom has only a set of voluntary guidelines published by the Health and Safety Executive. Meanwhile, the Federal Republic of Germany is relaxing its laws on production of substances, but is tightening rules on research. (Extracted from New Scientist, 10 July 1986)

USA reveals biotechnology rules

Guidelines that will provide the blueprint for a US federal policy regulating biotechnology have received presidential approval. The framework is designed to ease strict controls to promote commercialization of biotechnology products and organisms.

Under development for the past two years, the new framework aims to help and guide US firms seeking to obtain licences to market new products. These include new vaccines, drugs, pesticides and others made by gene-splicing.

Officials at the White House claim the policy is designed to be "neither unduly burdensome nor carelessly incomplete". The policy also includes a system for protecting the public and the environment from potential hazards posed by the new technology.

The Food and Drug Administration (FDA) will regulate human and animal drugs, foods and food additives, medical devices and vaccines.

The Environmental Protection Agency (EPA) will regulate pesticidal micro-organisms and products of intergeneric combination.

The US Department of Agriculture's (USDA) Animal and Plant Health Inspection Service (APHIS) will regulate bioengineered plants, animals and pathogenic micro-organisms.

The Department of Agriculture and Occupational Safety and Health Administration will have authority to regulate genetically-manipulated products with their respective remits, and the National Institutes of Health will continue to oversee and monitor research.

However, critics felt there were gaps in the programme and that public concerns must be addressed concerning the release of genetically engineered microbes into the environment.

For example, scientists said the regulations did not deal with new design requirements for greenhouses and other facilities that would be used to house tests of genetically altered microbes on plants or in other agricultural applications.

The legislators said the regulations also did not adequately cover the use of microbes genetically engineered for dissolving oil spills or for use as living fertilizers.

The Environmental Protection Agency intends to regulate these organisms under the Toxic Substances Control Act.

But the law exempts companies with annual sales of less than $4 million from having to notify the Government about research or development projects. The annual sales of most of the 220 US biotechnology companies are less than $4 million.

The agency is said to be developing new rules to close the gap, and until it finishes this work next year, it has asked small companies to notify it voluntarily of experiments involving industrial applications of gene-altered organisms.

Several scientists and legislators were concerned that ecologists did not take part in the

two-year process of formulating the new rules. (Extracted from Chemical Week, 2 July 1986, European Chemical News, 7 July 1986 and International Herald Tribune, 25 July 1986)

Revision of Japan's rDNA experiment guidelines

The Japanese Science and Technology Agency (STA) has revealed its policy of carrying out a major revision of rDNA experiment guidelines, finally switching from a positive to a negative list. The Ministry of Education is expected to revise its own guidelines for experiments. In connection with the revision, as yet unwritten guidelines will be drafted for release of recombinant bodies into the environment, inoculation of plants and animals with genes and handling of recombinant bodies. Consideration will be given for the inclusion of cell fusion and RNA recombination within the coverage, as is the case with US and British guidelines. The STA's experiment guidelines were revised for the seventh time in June. That revision eased restrictions on experiments on large-scale cultures of recombinant bodies and added 13 new types of hosts and vectors.

The Japanese Ministry of Health and Welfare (MHW) made it known that in July it would start up a special research team composed of persons with academic experience, with the tentative name "Special Research Team on Evaluation of Safety of Biotechnology in Food Products", and the purpose of considering safety guidelines for food produced using biotechnology. Research costs are already figured into the 1986 budget. The research period is three years, but considering the rapid development of biotechnology, a wide range of views will be heard and an interim report is to be made by the end of 1986.

Meanwhile, the Japanese Ministry of Agriculture, Forestry and Fisheries (MAFF) finished a report of the research committee on encouraging recombinant DNA (rDNA) technology in the fields of agriculture, forestry and fisheries, and announced ministry policy on drafting guidelines for industrialization of rDNA technology.

The report concentrated on the release into the environment, in agricultural applications, of recombinant gene plants and micro-organisms. The key points were that in all cases, manufactured organisms would be individually examined by a newly established investigatory committee, and that releases would be in stages as safety was established.

The report set up three categories for use of plants: closed, GILSP and open. It included restrictions on plants created with recombinant genes and those bred or derived from such plants. The ministry also announced a policy studying micro-organisms in a model environment during transfer from the laboratory to the environment. As for animals with recombinant genes, consideration was first given to the idea of handling them the same as plants, but there was no answer and study will continue. (Extracted from Nikkei Biotechnology, 30 June 1986)

Social implications

Gene therapy

The first experimental test of human gene therapy is on the horizon. It is possible that the first protocol will be submitted to the US National Institutes of Health for approval within the next few months; it may turn out to be longer in coming. But it is certain that medical researchers are close to being ready for a pioneering study and, in anticipation, an elaborate system of reviews has been put in place.

Policy-makers, ethicists, researchers and others have been debating the social and technical facets of human gene therapy for several years. The US Congress has held hearings; the congressional Office of Technology Assessment (OTA) has conducted a thorough, wide-ranging study; the NAC and its gene therapy subcommittee have examined the issues in open meetings. Both the NAC and the subcommittee contain members who represent the public.

Before the first experimental attempt at human gene therapy can legally begin, it will have to be cleared at the local level by the research centre's Institutional Biosafety Committee, which looks at procedures for the safe handling of recombinant organisms, and by the Institutional Review Board, which concerns itself with the protection of the patient and such matters as informed consent. At the national level, the experiment will be reviewed in open session by the gene therapy subcommittee, which has spelled out a host of technical and ethical considerations in a document called "Points to Consider", which is itself constantly being reviewed. The experimental therapy protocol will have to be described in lay language and published in the Federal Register so any member of the public can comment. The full NIH Recombinant DNA Advisory Committee must approve the protocol. And, finally, it must be approved by the director of NIH.

Gene therapy can be thought of in two main categories: somatic and germline. Somatic (or body) cell therapy, which will be the goal of initial experiments, is aimed at correcting a serious medical disease by repairing the defective gene that is the cause of the disorder. The genetic therapy of certain severe immune deficiency diseases is an example. Because of a faulty gene, the body fails to produce a protein that is essential for normal immune system function. In theory, by altering or repairing the gene, one could cure the disease. Technical problems and the need for further animal testing must be resolved before the first test of somatic cell therapy, but almost no one objects to it on ethical grounds. Somatic cell therapy is directed only at body cells that are not part of the germline.

Germline therapy, by contrast, would correct defects in reproductive cells, thereby not only alleviating disease but doing it in a way that means the corrected genes would be passed on to an individual's children.

Another category of potential future gene therapy is so-called "enhancement therapy", whose aim would be to alter a gene in order to affect some feature such as eye colour or height. (It can be seen as a form of somatic cell therapy.) The prospect of tampering with the gene for growth hormone, in order to custom-grow basketball players, for instance, is often cited as an undesirable potential use of gene therapy. (Extracted from Science, Vol. 233, 26 September 1986)

General

Exchanging of biological material

To address the issues surrounding the growing exchange of biological material, Stephanie Doores, microbiologist and assistant professor of food science at Penn State College of Agriculture and also chairman of the Committee on Culture Collections of the Board of Public and Scientific Affairs, recently organized and convened a round

table on the subject at the 86th annual meeting of the American Society for Microbiology (ASM) in Washington, D.C.

As there were numerous laws and regulations governing the transfer of disease-carrying and even beneficial organisms, Doores felt that there was some concern that the average scientist, who only occasionally needs to transfer material, might not fully understand the ins and outs of transporting biological material.

Many biological cultures must be transported in specially-sealed double containers with required warning and descriptive labels. Scientists often need to apply for an import/export licence if they are shipping materials in or out of the country. Regulations allow some organisms to be sent via the postal service, others must go another route. Certain countries restrict certain substances from entering their borders. Even when packaging, licences and destinations are legitimate, transportation problems can arise because airline pilots and other carriers may use their discretion to refuse to carry a package.

"The simple act of moving a vial of serum from one lab to another can get quite complicated, especially when two countries are involved", says Doores. "The session we offered at the conference alerted scientists to just what requirements they face, and which agencies issue permits and licences". She thought there was going to be more and more emphasis on shipping and international exchange of biotechnological materials, and wished to ensure that everyone understood the regulations and acts responsibly, so the free exchange of scientific ideas and materials can continue safely. (Source: News Release, 7 May 1986)

Unique system for freeze-dried micro-organisms

The American Type Culture Collection has developed what it claims to be a unique culturing system for freeze-dried micro-organisms, eliminating the need for fresh medium. Especially useful for classroom demonstrations, Uniplus cultures are freeze-dried preparations consisting of a micro-organism in its appropriate growth medium. To establish a growing broth culture, all that needs to be added is sterile water. Further details may be obtained from American Type Culture Collection, 12301 Parklawn Drive, Rockville, MD 20852, USA. (Source: Biotechnology Bulletin, Vol. 55, No. 8, September 1986)

Centre for Plant Conservation to save endangered species

The Centre for Plant Conservation (CPC), based at the Arnold Arboretum of Harvard University has recruited 18 botanical gardens from across the nation into a programme to save endangered species of US plants. For two years those gardens have been surveying their assigned areas for plants in trouble.

This summer the programme's member gardens will be digging into the task in earnest, learning how to cultivate rare plants from continental USA and Hawaii.

Without intervention by conservationists, nearly 3,000 - 15 per cent - of all plant species in the USA may become extinct. Hawaiian vegetation is particularly vulnerable; nearly half of Hawaii's 1,800 native plants may be lost. CPC has adopted a strategy that is novel in the field of plant conservation to counter this threat.

Up to now, public and private groups have concentrated on protecting the lands where rare species are found. CPC, applauding these efforts, goes one step further by bringing endangered plants into cultivation under the protection of botanical gardens.

Two of the centre's senior officers - Dr. Linda R. McMahan and Dr. Kerry S. Walter - visited member gardens this spring to review plans to cultivate endangered plants.

Endangered species of plants are often found in unusual, inhospitable habitats, but botanical gardens may find most of them easy to grow under more benign conditions.

A key part of CPC's work is to generate a central list of endangered species and where they are being cultivated. Zoos have long had access to this kind of information, but botanical gardens have not. This inventory will help researchers, and endangered plants put into cultivation will be made available for study. The centre's staff hopes that some of this research might eventually aid efforts to preserve endangered plants in the wild.

The Centre for Plant Conservation is filling a gap left by commercial efforts to conserve germplasm. Commercial and federal seed banks are concentrating upon plant species with obvious commercial importance in their conservation efforts. (Extracted from Genetic Engineering News, July/August 1986)

New biology/chemistry institute

A gift of $50 million from the Arnold and Mabel Beckman Foundation has enabled the establishment of a new institute at the California Institute of Technology. The Beckmann Institute will try to solve problems at the interface between biology and chemistry. Research areas that the institute may support include chemical synthesis of new proteins, development of advanced genetic engineering concepts and instrumentation, preparation and testing of new types of catalytic and ceramic materials, and development of computer and instrumentation techniques for protein engineering and human chromosomal mapping. (Source: Genetic Engineering News, September 1986)

Human Leukaemia Centre

A Human Leukaemia Virus Centre, the first of its kind in the world, is to be established at the University of Glasgow, Scotland. Supported by funds of almost £2 million over the next five years, it will be located in the Department of Veterinary Pathology, where William Jarrett carried out his pioneering work over the past two decades on feline leukaemia.

Following the demonstration by Jarrett and his colleagues that leukaemia in cats is usually associated with a retrovirus, the researchers found that the same virus is a major cause of an immunosuppressive AIDS-like syndrome in cats. The centre's formation comes soon after the incrimination of a related agent in one form of human leukaemia, the pinpointing of HTLV-III/LAV as the agent of human AIDS, and suspicions that further retroviruses may be responsible for multiple sclerosis and other conditions. Directed by David Onions, the centre's research programme will bring together epidemiology and molecular biology. The Glasgow University Leukaemia Research Group, the largest in Britain working on oncogenic viruses, has

already produced a successful vaccine against feline leukaemia virus (FeLV), and is collaborating with the US National Cancer Institute (Bethesda, MD) on the development of a vaccine against human AIDS.

Construction to accommodate the new centre should be completed next spring, at which time a team of ten people will be recruited. One of the first aims is to apply genetic engineering techniques to investigate human leukaemias that occur in clusters, the significance of which is unknown to epidemiologists. (Extracted from Bio/Technology, Vol. 4, July 1986)

Marine biotechnology laboratory to be built

University of California regents have approved an $8 million marine biotechnology laboratory to be installed at the university's Santa Barbara campus. The marine biotechnology laboratory will serve as a bridge between the marine and biotechnology industries and will make use of the existing ultrapure seawater collection system on campus to provide conditions for the cultivation of marine organisms that can be manipulated using genetic engineering techniques for enhanced food production. Isolation and characterization of potential new pharmaceuticals are other objectives. Scientists will also use the facilities to carry out applied research in areas such as encrustation of ship bottoms by marine organisms and basic research in areas such as the mechanisms by which deep ocean communities subsist on chemical rather than solar energy. (Source: Reprinted with permission from Chemical and Engineering News, 28 July 1986. Copyright 1986 American Chemical Society)

Consortium to design gene tool kit for four crops

A European consortium of 15 academic and industrial organizations has just launched an ambitious pre-competitive research programme which could dramatically affect the price and quality of food in the mid-1990s. Over the next three years they hope to design a plant gene "tool-kit" and user's manual, permitting the user to make radical changes in the genetic make-up of some of Europe's more valuable crops.

The 11 companies include such multinationals as Royal Dutch-Shell, Unilever and Ciba-Geigy. The four academic institutions are the Plant Breeding Institute and the John Innes Institute, both of the Agricultural and Food Research Council, and the Universities of Durham and Warwick.

Companies pay the same, regardless of size; about £50,000 a year. The Government doubles the money, providing a total of £3 million for the three-year programme. Still more to the point, the companies have harnessed the expertise of about 40 British academics - perhaps 70 per cent of the national expertise in this area of plant science.

The research will be done in the four academic institutions, overseen by a programme manager.

If the programme eventually succeeds it will have established "enabling technology" to allow any user of the plant gene tool-kit to make gene transfers within crop plants a routine procedure. The 11 companies will then be free to exploit this enabling technology in any way they wish - perhaps to grow peas more resistant to weather or pests in the case of a big food company, or to develop into a specific technique which can be licensed to third parties in the case of a start-up.

The programme focuses on four crops of particular interest in Europe: wheat, barley, peas and oil seed rape.

The first and biggest of the three projects aims to establish transformation and regeneration systems for all four chosen crops. The second project concerns genetic engineering. It aims to isolate the gene of interest - one that controls the storage of energy or the process of photosynthesis, for example - and test such plant genes to ensure that the isolated and reconstructed genes can be expressed (replicated) by biotechnology methods.

The idea is to use the "gene cassettes" produced by this project to transform the four crops, using the technology developed in project 1. It will focus particularly on the genetic engineering of seeds, because it is seeds or grains which are normally harvested. But it may turn out that in order to modify plant growth the new gene products have to be localized in specific parts of the plant's cell, such as the chloroplasts, where photosynthesis takes place. (Extracted from The Financial Times, 15 May 1986)

Biotechnology firms plan insurance pool

A group of 21 biotechnology-based companies intends to form an off-shore captive insurance company to provide them with hard-to-find liability coverage. The firms, all members of the Association of Biotechnology Companies (ABC), expect to establish the company by September 1986.

ABC hired insurance brokerage firm Johnson & Higgins, which has organized similar captive insurance carriers, to conduct an actuarial evaluation of biotechnology product risks and to plan the company. The insurance programme will probably allow members to select, according to their needs, either primary coverage or protection for claim amounts over a set minimum. The programme will emphasize risk management, with compulsory training and safety audits.

Insurance is becoming a matter of increasing concern for biotechnology-based firms, many of which have no liability policies. Many firms will be introducing their first products in the near future, which will greatly increase their liability exposure at a time when the insurance industry is reluctant to provide product coverage.

Johnson & Higgins' actuarial project will be complicated by the lack of risk history for most biotechnology-based products, a vacuum that makes traditional insurance carriers doubly wary. In order to rate biotechnology product risks, the company will examine the results of a member survey, consult with underwriters, and where possible make analogies to comparable products made by traditional means.

Once Johnson & Higgins presents its findings, ABC members will have to decide which risks they will insure mutually and how much each company must pay for coverge.

The Industrial Biotechnology Association, a different trade group, hopes to solve the coverage problem by familiarizing the insurance industry with biotechnology. (Extracted with permission from Chemical and Engineering News, 14 July 1986. Copyright 1986 American Chemical Society)

Micro-organism sales gain

According to a new study by Stamford, Conn., market analysts Business Communications, Inc., sales of micro-organism-based products, now pegged at $100 billion worldwide will grow steadily during the next few years.

Overall growth will average 2 per cent a year, although some market areas, such as living cultures,

will grow much faster than average. About half the market for microbial products is in the US.

Living cultures, which now generate revenues of about $770 million at the manufacturer or supplier level, will grow at an average annual rate of about 3.1 per cent and reach $898 million by 1990. This growth will be largely due to companies' shifting from in-house cultures to outside suppliers of the cultures.

Sales of microbially-derived substances will grow at a steady 3 per cent during the rest of the 1980s. 1985 revenues from these products were $4.16 billion, which will climb to $4.83 billion by 1990. (Extracted from Chemical Marketing Reporter, 28 July 1986)

Biotechnology stock market

The biotechnology stock market, scene of red-hot growth throughout the first three months of the year, has now cooled off considerably. Several factors have worked to slow the rate of growth of biotechnology stock values. For one thing, the elements that combined to create the great surge in stock prices last autumn - two high-priced acquisitions of biotechnology companies, government approval of Genentech's recombinant DNA human growth hormone, and encouraging results from human trials of interleukin-2 - in general have now been factored into company stock prices by investors.

The most positive commercial development this spring was the US Food and Drug Administration's approval of -interferon for the treatment of hairy cell leukaemia. The bringing to market of the first recombinant interferon - once expected to be the confirmation of genetic engineering's commercial promise - was a major achievement and helped raise stock prices. The approval, in particular, dusted off the prestige of Biogen, which developed the version of -interferon being marketed by Schering-Plough.

The other major factor has been the drain on investment capital. Rushing to exploit the tremendous popularity of biotechnology stocks, many public companies issued secondary stock offerings while many other private firms, some of which had moved too slowly to benefit from the 1983 boom market and others of which are just a few years old, made initial public offerings.

At this point, investors are believed to be awaiting a new series of positive developments, particularly in terms of product approvals. All eyes are on the hepatitis B vaccine developed by Chiron for Merck. Analysts expect FDA approval for the vaccine, which would be the first commercialized genetically engineered human vaccine, will come later this year. Approval undoubtedly would boost interest in stock in Chiron and companies with related projects - Biogen and Amgen, for instance - as well.

Even more eagerly awaited is approval of Genentech's tissue-type plasminogen activator (TPA), generally expected to be the first blockbuster-sized biotechnology product. Approval is generally expected in 1987, although optimists think FDA could send the heart attack treatment, eagerly sought by physicians, to market as early as this December. Other companies with TPA projects, such as Genetics Institute and Integrated Genetics, would also probably benefit in the stock market as a result.

Other major product approvals, such as for other interferons, could come next year. In the mean time, some stocks could gain from good progress reports on the continued testing of interleukin-2 in cancer patients.

Investors are still focusing on product development, earnings, and management structure in their deliberations. Those are constant elements in the investment decision, of course, but the beginning trickle of genetically engineered products entering the marketplace means that, for the first time, investors will be able to judge companies on how well their products sell as well. (Extracted with permission from Chemical and Engineering News, 14 July 1986. Copyright 1986 American Chemical Society)

How to evaluate a biotechnology acquisition

Investors and companies planning to diversify into the biotechnology arena must methodically assess the attendant risks of this lucrative high-growth sector. Among the factors to be weighed up are research and equity. Other parameters must also be considered, as Robert Riley, an analyst with Massachusetts-based consultants Arthur D. Little, explains.

The valuation of a small, specialized biotechnology company, which is composed mainly of scientists undertaking early stage research, requires models that are linked to the strategic potential of the firm. Several key considerations in the rapidly developing biotechnology industry point to the need to include strategic requirements in biotechnology valuation.

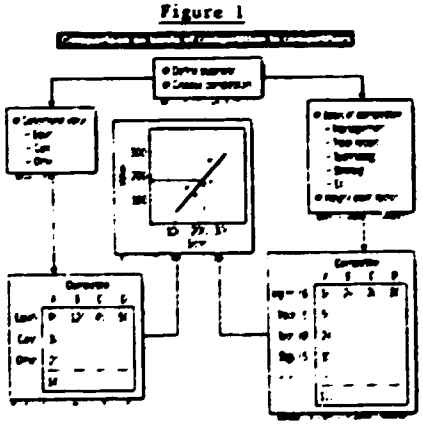
First, as a growth industry, biotechnology requires planning for the allocation of limited resources and marketing for the development of product revenues. In addition, this technology-intensive industry requires R&D planning for new-product flow and strategic management for the identification of optimal strategic thrusts.

In order to compete, biotechnology relies on corporate planning for strategic direction and marketing strategy for product-to-product sector penetration. Taking a global perspective, biotechnology needs co-ordinated planning for international and domestic activities and offshore development planning for international product sales.

Given the foregoing considerations, the next step is to examine two models that include strategy as part of the evaluation process. One model compares a company's strategy to those used by a set of similar competitors. The second establishes a value based on the worth of cumulative research. When comparing similar competitors, the model bases evaluation on characteristics against the value placed by the market.

Several steps must be undertaken to use this model. Figure 1 illustrates the flow of steps and the equation which can then be used to establish a value for the biotechnology company under consideration.

Figure 1



Planners should clearly define the biotechnology company's business in terms of the technologies employed and the markets to be entered. Examples are monoclonal antibodies for site-directed tumour imaging or mammalian cell cloning and expression for production of peptide therapeutics targeted towards cardiovascular disease treatment.

Next, executives should select a range of representative competitors in this same business using similar technologies directed at similar market segments. It is critical that a range of companies be chosen because these companies will determine the horizontal axis of the evaluation graph.

At the same time management should establish the strategic factors which form the basis of competition. They can look at companies currently competing in management ability, the track record of product development or clearing technical and regulatory hurdles, technology strengths, strategic/tactical movements, such as joint ventures or movements towards full integration.

They should weigh up the factors to determine their relative importance and contribution to a total score, using, say, a 10-point system with higher numbers indicating greater relative importance. Each strategic factor would be scored for each competitor and then recorded before the next is scored because the scoring is based on comparison to the entire set of competitors.

Next, one would determine the score for the company, being evaluated by deciding which elements of capitalization, or other measure of value, are important for the investment objectives. Examples are equity, cash and future cash commitments from development partners. Determining the capitalization, or other value measure, for each competitor, would be the next step.

Finally, users would plot the total score for each competitor's basis-of-competition factors against the capitalization of each competitor and the straight line determined by the points on the valuation graph. Then the total basis-of-competition score for the company could be evaluated, compared with the chosen set of competitors. (Source: ECN Specialities Supplement, October 1985)

B. COUNTRY NEWS

EEC

EUREKA proposals in biotechnology

Early in June the third EUREKA Ministerial Conference took place in the UK to work out the final decisions for this initiative of European co-operation in technology.

The last EUREKA conference, held at Hannover in 1985 adopted a declaration of principles and a first set of ten projects to be launched immediately.

Two projects cover biotechnology:

- The development of diagnostic kits for sexually transmitted diseases with partners in UK (P.A. Technology) and in Spain (Biokit); and
- The development of membranes for ultrafiltration with partners in Denmark (Dansk Sukkerfabrikker) and in France (Société Lyonnaise des Eaux and Degremont).

Industrial proposals collected at the national level for possible co-operation under the EUREKA label include:

The Netherlands: developing biotechnology for production of vaccines; augmentation of added value of agricultural products in the fields of dairy products, hydrocarbons, feedstuff and sugars, using biotechnological processes such as fermentation and precipitation; furthermore development of technology for processing residuals.

Denmark: Plant cell culture (A/S Dansk Gaerings-Industri); protein engineering (Novo Industri A/S); high-level technology in plant and animal production and related industries (Carlsberg Research Laboratory).

Finland: root growth inducers and hormones in plant engineering (Orion Corporation Ltd.); application of DNA probe technology to animal and plant disease diagnostics and improvement and commercialization (Orion Corporation Ltd.); automation of liquid manipulation operation in genetic engineering, biotechnology, biomedical and medical fields (Fluilogic Systems Oy); genetic engineering methods for plants (Kemira Oy); development of a method to produce anticancer anthracycline antibiotics with a streptomyces strain modified by genetic engineering (Huhtamäki Oy); environmental gas monitoring by biosensors (Vaisala Oy); antigen-antibody sensors for rapid diagnosis of infectious diseases (Orion Corporation Ltd.).

Greece: production of metabolic products and energy (cell immobilization and bioreactors); production of monoclonal antibodies by means of hybridoma immobilization in bioreactors for medical purposes; production of peptides for synthetic vaccines and as novel reagents; production of hybrids by means of genetic engineering for agricultural applications; development of fermentation technologies for utilization of by-products (BIOHELLAS); second generation bioreactors for biosynthesis and biotransformation; pheromones (isolation, identification, synthesis); plant growth factors, production of high added secondary metabolites (pharmaceuticals, flavours, fragrances); fusion of protoplasts; dormancy in plants and optimization of plant production (VIORYL S.A.).

Ireland: Synthetic seeds; control and regulation systems (University Colleges at Dublin and Cork).

Portugal: development of seeds by genetic or synthetic processes; development of biofertilizers; utilization of new vegetal protein sources (FAVORITA-Industria Agro-Alimentar Lda.); process development for enzymatic products and immuno-modulator agents; process development for extraction under supercritical conditions to be applied for aromatics and essences (Franco Farmaceutica).

Belgium: control systems applied to the field of medicine (SABCA); development of biospecific detection systems for biological compounds (Arbios); industrialization and automation of in vitro cultivation (Belgonucleaire); development of genetic engineering technology to improve sugar beet cultivation and characteristics such as resistance to diseases (virus, mould) and to herbicides (Plant Genetic Systems); genetics of plant varieties in view of a selective reforestation (BIAGRAL); artificial seeds (Plant Genetic Systems); biomass utilization (Plant Genetic Systems); development of a computer-aided protein design system (Plant

Genetic Systems); separation processes (Oleofina); production of food products by micro-organisms (ARBIOS); continuous fermentation reactor technologies (including fungi culture technologies) (ARBIOS).

France: artifical seeds (Rhône-Poulenc); animal cell mass culture (Bertin et Cie); fine regulation of inoculation in medicine (ELF); construction of 'host-vector' pairs leading to micro-organisms or genetically modified animal cells (ORGANIBIO).

Finally, the EC Commission proposes co-operation in biotechnology, in particular genetic and biomolecular engineering and their applications to health and agro-industry. (Source: Journal of Biotechnica '86, Hannover)

Australia

Malaria vaccine joint venture

The Australian Industry Development Corp (Aidc) is to invest Aus$9.2 million to assist the development of a malaria vaccine. A joint-venture company, 40 per cent owned by Aidc, is working on a vaccine by cloning genes of the malaria blood agent. A prototype is currently being tested at the Centre for Disease Control in Atlanta, Georgia, in the USA. A commercial product is not expected until 1991. (Source: European Chemical News, 21 July 1986)

Calgene launches Australia affiliate

Calgene, Inc. of Davis, Calif., announced the formation of Calgene Pacific Pty. Ltd., a 33 per cent owned affiliate to be based in Melbourne, Australia. Calgene Pacific will become the world-wide base for Calgene's production and distribution of ornamental, forestry and plantation crop species. Financing for Calgene Pacific is being provided by three prominent Australian venture capital firms by Amcor Limited (the leading packaging and forest production company in Australia) and by the government of the State of Victoria, through the Victorian Investment Corporation Limited. (Source: News Release, 4 September 1986)

Austria

Drug to treat AIDS under development

Cerisco International will continue joint development of a drug to treat AIDS with Klaus Keplinger (Innsbruck, Austria) using compounds prepared from the root of a plant found in the Andes mountains of Peru. The principal product from the compounds will be marketed under the ImmunAct name. Cerisco will offer the drug for evaluation by the US Government's new programme for nationwide testing of experimental drugs for the treatment of AIDS. Holomed (Sweden) will distribute ImmunAct in Scandinavian countries. (Extracted from Chemical Week, 9 July 1986)

New laboratories for cancer research

Fundamental cancer research in Europe is about to be strengthened by several new privately financed laboratories. One will be in Vienna and is jointly owned by Genentech, the Californian biotechnology company, and the Federal Republic of Germany's chemical and pharmaceutical company Boehringer Ingelheim. The other four, and probably five, laboratories are new branches of the Ludwig Institute of Cancer Research, administered from Zurich.

Despite its commercial backing, the Vienna institute will be concerned only with basic research in the general area of molecular pathology, with a particular focus on oncogenes. First rights on any discovery of commerical interest stemming from the research are shared by Genentech and Boehringer Ingelheim.

Building work on what is likely to be called the Institute of Molecular Pathology began this summer. Various relevant university institutes, at present scattered around the city, are likely to be re-sited alongside the new institute. The director will be Dr. Max Birnstiel, presently at the University of Zurich.

Of the new branches of the Ludwig Institute of Cancer Research two have begun operation in Sweden (in Stockholm, under Dr. Ulf Pettersson and in Uppsala, under Dr. Carl-Henrik Heldin) and two will start soon in London (at Middlesex Hospital Medical School, under Dr. Michael Waterfield, and at St. Mary's Hospital Medical School, under Dr. Paul Farrell). Negotiations are under way for another London branch and Dr. Webster Cavenee has just begun to direct a new Ludwig Institute in Montreal's McGill University. (Extracted from Nature, Vol. 321, 19 June 1986)

Belgium

Belgian Bioindustries Association

Five Belgian companies active in the bioindustrial sector have joined to form the Belgian Bioindustries Association (BBA). Their goal is, on the one hand, to intensify their co-operation with Japan and on the other to encourage European and national authorities to adapt biotechnology regulations to the needs of research and industry. The association, founded in March 1985 by Arbios (ACEC [Electrical Construction Works of Charleroi]), Oleofina, Foridienne, the Raffinerie Tirlemontoise, and UCB [Belgian Chemical Union], wants to expand and has opened its doors to any Belgian company involved in biotechnology that would like to share its objectives. BBA has had a representative in Tokyo since last January to develop contacts between Japanese businessmen and representatives of the association's member companies.
(Source: Industrie, June 1986)

Brazil

Extension of patent protection to high-technology sectors

Brazil may extend its protection of the informatics industry - computer technology and manufacture - to other high-technology sectors, including biotechnology, fine chemicals and pharmaceuticals. The law excludes foreign firms from participating in major segments of the computer market until 1992 and similar legislation is being considered for other sectors. The US is studying the law to see if it constitutes an unfair trade practice, subject to US reprisals. Brazil still refuses to recognize international drug patents. Even in other industries, royalty payments for international patents are required for only five years and may not exceed 3 per cent of sales. The patent office reserves the right to sell to third parties patents of any product used in Brazil. The situation is similar to that in Mexico where foreign participation is limited to 40 per cent in the downstream chemical sector, resulting in outmoded technologies. However, it is considered by Brazil's Secretariat for Biotechnology that foreign multinationals will be drawn to Brazil's potentially rich market for biotechnology altered seeds,

fertilizers and pesticides, and to its huge output of sugar cane, molasses and cellulose for use as feedstocks. (Extracted from Chemical Week, 6 August 1986)

Canada

Major biotechnology company turns to other areas

One of Canada's leading biotechnology companies, Bio Logicals Inc. is moving into other business areas, including telecommunications and information technology. Although the company's biotechnology activities have been substantially scaled down, however, it retains an interest in a number of bio-projects. Under a management agreement with Bio Logicals and First Mississippi Corp., Bio Logicals' vice-president Dr. Samuel Asculai runs international Genetic Sciences Partnership, a biotechnology operation in Israel, which is developing proprietary techniques for gene transfer into plant and animal cells.

Projects with Bristol-Myers and the Alberta Research Council have been terminated, although Bristol-Myers was apparently reconsidering its decision to stop funding anti-viral R&D in mid-July. Bio Logicals has put its bacterial leaching work on hold, until it can find another joint venture partner. The most active of its bio-programmes now is its work on exotic edible mushrooms. This project, under the direction of Dr. André Fortin at Laval University, is being supported by the company and by a grant from Canada's National Science and Engineering Research Council. Results on a test system for these mycorrhizal mushrooms, which only grow in association with trees, suggests that the project could develop a reproducible way of causing fruit body formation. (Source: Biotechnology Bulletin, Vol. 5, No. 7, August 1986)

Colombia

Vaccine development

The Institute of Immunology at San Juan Dios Hospital in Bogota is developing a candidate malaria vaccine. In tests animal models (the Aotus monkeys) could be protected against infection with the protozoan Plasmodium falciparum by immunization with a combination of three synthetic peptides, corresponding to partial sequences to one of the major proteins on the surface of the malarial red blood cells. The hospital is also working on gene cloning and vaccines against leprosy and tuberculosis. (Extracted from Nature, Vol. 321, 19 June 1986)

Czechoslovakia

Long-term development of biotechnology

The Main Objectives for the Economic and Social Development of the CSSR for 1986-1990 and the Outlook for the Year 2000, which was approved by the 17th CPCZ Congress, establishes that, as part of the basic objectives of R&D as a critical factor in economic intensification, basic science, research and development will be concentrated on the development of biotechnologies, fermentational and microbiological products, and their utilization in the agro-food complex and the health care sector. This task is fully in line with objective trends in the evolution of R&D. It is therefore also assumed that the development of biotechnologies and their extensive application will represent one of the critical areas of scientific and technical progress which will significantly influence future socio-economic development.

In the CSSR increased attention began to be paid to the development of biotechnologies at the end of the 1970s and the early 1980s. This involved mainly tasks related to the biochemicalization and chemicalization of livestock production, where CSSR's research is relatively advanced and where it was possible to draw upon positive results achieved in the agro-food complex. The rapid worldwide development of biotechnologies and the necessity to be in the main worldwide developmental trends motivated a decision to replace individual programmes and measures with a single programmatic document that could serve as the basis for the purposeful management of the biotechnology development in the CSSR.

Under the supervision of the State Commission for R&D and Investment Development [SKVTIR], a group of leading experts was organized which drafted a comprehensive document on the development of biotechnologies. After discussion, the CSSR Government adopted the Long-Term Comprehensive Scientific and Technical Programme for the Development and Implementation of Biotechnologies in the CSSR. The programme also formulated the basic precondition for active participation of Czechoslovak organizations in the fifth priority programme of the Comprehensive Programme of R&D Progress for CMEA Member Countries through the Year 2000. This programme makes it possible for the Czechoslovak R&D base to participate in the resolution of tasks and to use the results of other projects for which it does not have facilities. The important results of the international division of labour in the development and use of biotechnologies have formed the basis for extensive application of this promising field of industry. The direct participation of the Czechoslovak programme in the priority programme of the Comprehensive Programme for Scientific and Technical Progress for CEMA Member Countries through the Year 2000 is the most basic guarantee that the Czechoslovak programme and its goals will be handled with great efficiency using state-of-the-art knowledge.

The Long-Term Comprehensive Scientific and Technical Programme for the Development and Implementation of Biotechnologies in the CSSR is divided into the following six areas:

(a) The application of selected biotechnologies to livestock production;

(b) The development of a microbiology industry;

(c) The application of biologically active substances and tissue cultures;

(d) The application of biotechnologies in agriculture, primarily in plant production;

(e) Developing production capability and application for enzymes; and

(f) The application of developing biotechnologies in food processing industries.

(Extracted from Hospodarske Noviny (Supplement) No. 22, 30 May 1986)

Denmark

Denmark first to legislate gene manipulation

The world's first law concerning genetic engineering was adopted recently by the Danish parliament, the Folketing.

The law prohibits the use of genetically manipulated organisms in nature. Bacteria which

resist frost, and plants with built-in insecticides are the current results of new findings in the field of biotechnology. This kind of use of genetic engineering is prohibited by the Danish law. The authorities can grant an exemption, but not until the principle has been approved by parliament.

The law looks more leniently at genetic manipulations with the aim of creating new biological tools in a closed environment.

All applications must be approved. Bacteria, yeast, fungi, and other organisms which are coded for secreting desirable products such as medications, represent genetic engineering which is permitted in principle. According to the new law, different applications must, however, be approved from a health and environmental point of view. All experiments, also those carried out in teaching laboratories, must be concurrently registered with the authorities. The Danish Food Administration will be the monitoring agency. Later this responsibility will be shifted to the individual county councils (counties). (Extracted from Ny Teknik, 19 June 1986)

Company receives approval to produce insulin via genetic engineering

The Danish drugs and enzymes firm Novo Industri is set to start production of gene-spliced human insulin following a go-ahead from the regulatory authorities. Approval has been granted for production of human insulin by fermentation at its new facility at Kalundborg, west of Copenhagen.

Construction of the facility and installation of process equipment has been under way since the company received environmental approval for the plant, which will produce human insulin using genetically altered yeast cells. (Source: European Chemical News, 25 August 1986)

Danish science park expands

The research centre in Horsholm, which is part of the Danish Ministry of Education, will be expanded during the course of the next eighteen months. The biotechnology firm of Chr. Hansens Laboratorium A/S has leased space in the research park and develops, among other things, products for treating allergies. The general contracting firm of Hojgaard & Schultz is behind the construction of the four new buildings which are to be ready for occupancy in late 1987. (Extracted from Aktuelt, 4 March 1986)

Novo Industri forms new bio-industrial group

Novo Industri A/S of Denmark is reorganizing its Enzyme Division into Novo Bio-Industrial Group, to be comprised of four divisions under the direction of Erik Soerensen, executive vice-president of Novo. Each division will be responsible for production, research and development and marketing.

The new biochemicals division will concentrate on bulk industrial products, the detergent enzymes division will focus on world market opportunities, the enzyme process division will focus on markets where enzymes are integral to manufacturing processes, and the fruit juice and wine division will maintain the activities of Novo Ferment AG. (Extracted from Chemical Marketing Reporter, 2 June 1986)

Federal Republic of Germany

Guidelines for genetic experiments issued

The FRG's Federal Cabinet is planning to relax restrictions on some industrial genetic experiments including production of insulin and interferon. But restrictions on other forms of gene manipulation are to be imposed for the first time.

Under the new safety guidelines for genetic experiments drawn up by the Federal Ministry for Research and Technology (BMFT) and passed by the Cabinet, firms producing insulin and interferons in vats of more than 10 litres will no longer be required to obtain special permits. Nevertheless, all genetic laboratories will have to be registered with the federal health authority's Commission on Biological Safety, ZKBS. The Cabinet said it sees registration as the only method of enforcing safety regulations for genetic experiments.

The Government's plans foresee division of what it considers to be "risk-laden experiments" into four categories. Research with "harmless" organisms such as bacteria may be conducted in all registered laboratories without prior notification. Trials with infectious germs or organisms that produce toxins must be approved by ZKBS. For experiments involving gene transfer in human organisms, an opinion by an ethics committee will also have to be obtained.

The fourth category includes experiments considered by the Safety Commission to be permissible only under exceptional conditions, including plant cell manipulation on agricultural lands. Manipulation of human genetic material will continue to be prohibited. The Cabinet has also called on the Federal Health Ministry to study whether additional restrictions on gene manipulation are necessary. (Source: European Chemical News, 9 June 1986)

Government measures to promote biotechnology

The Federal Government attaches growing importance and a high innovation potential to biotechnology as a key technology with a "broad effect", influencing many technical areas. In the future, the Federal Government's promotion measures for biotechnology and gene technology will be concentrated on four objectives:

- Peak scientific and technical performance is to be encouraged and demanded. It is desired to establish a friendly climate for research through appropriate general conditions. The general conditions include the preferential support of persons and installations capable of outstanding performance, the securing of the necessary latitude for the competition of ideas and discoveries, and the distinction and recognition of such performance by the State.

- The pace of innovation in the FRG economy is to be accelerated. The most important promotion instruments are central key projects and projects of integrated research. These direct supporting measures are supplemented through indirect measures with rather broad objectives that are intended to promote mainly middle-class industry and the rising generation of scientists. Supporting resources are made available for middle-class industry through a measure that is very much simplified administratively.

- Research and development projects in special areas of state provision for the present and future. It is important to make use of the chances that are being opened up by the new methods in gene technology and cell biology, especially for the development of drugs or plant breeding.

- The future chances of the rising scientific-technical generation are to be improved through qualified training. In the medium term, it is to be expected that the

expansion of the research capacities in economic enterprises and public institutions will lead to a greater number of jobs for appropriately trained young people.

(Extracted from Handelsblatt, 17 July 1986)

New infrastructure for genetic research set up

A new infrastructure has been set up for research and development in the area of biotechnology and genetic engineering. One year after the corresponding programme of the Federal Government was presented, three genetic engineering centres are operating in Heidelberg, Cologne and Munich in which universities, research installations outside of the universities, and industry are co-operating. They will be supported by the Federal Ministry for Research and Technology for 12 years. The fourth such centre will be set up in Berlin as a permanent facility.

In an interim analysis of the programme, the Federal Ministry for Research and Technology pointed out the high innovation potential of biotechnology. Biological process engineering has turned out to be a weak point. Two focal points are to be established in this research discipline. This subject is to be developed at the University of Hanover in close co-operation with the microbiological institute of the University of Goettingen. Researchers in Stuttgart are to deal with biological decomposition under the exclusion of air (anaerobic). They are joined in this work by the Fraunhofer Institute for Interface and Biological Process Engineering.

There are some difficulties in the changeover from the direct project promotion previously practiced to special promotion of biotechnology, in which the scientists have relative freedom in disposing of state grants. The close association between university and industrial research is considered a way out. In addition, small and medium-sized enterprises can develop their research capacities in especially promising areas of cell culture and enzyme engineering within the scope of a special concept for which about DM100 million will be available until 1989. (Source: Frankfurter Allgemeine Zeitung, 19 July 1986)

Bonn allocates biotechnology budget

The FRG Government has earmarked a key part of its 1987 budget allocation for biotechnology R&D. Bonn plans to spend DM 1.14 billion ($556 million) during 1987-1989. Most of this sum will be spent in three areas. Corporate biotechnology research, together with European molecular biology research and European molecular biology conferences, will receive a total of DM 336 million over the next two years. Gene centres and projects will receive DM 152 million while some DM 121 million will be spent on personnel and equipment.

Microbiological and genetic R&D is to get DM 101 million; cell culture DM 98 million; enzyme R&D and bioprocedures DM 140 million; novel areas DM 45 million; plants and renewable resources, DM 34 million; and alternatives to vivisection and safety in biotechnology, DM 97 million.

In addition a US/FRG anticancer joint venture involving 18 institutes and companies is to benefit from state funds to the tune of DM 8 million. The venture is already said to have come up with some "interesting substances". (Source: European Chemical News, 1 September 1986)

Finland

Fir trees cloned by Finnish researchers

Ways of cloning or replicating evergreens are being sought in Finland. The Forest Management Foundation has begun micro-cutting experiments through which an attempt will be made to find out whether it would be possible to quickly grow many identical shoots from artificially generated spruce and pine buds. If the experiment succeeds, increased production can be expected from previously improved trees and the best improvements can be put to use quicker than before.

The Foundation began studies this year to determine whether evergreens could be reproduced from micro-cuttings. Similar experiments are being carried out in New Zealand, the United States, France and Sweden. If the experiment is successful, spruce and pine could quickly provide many identical shoots, although they would cost more than those grown from seeds.

Ornamental plants are already being cloned throughout the world and the same technique also produces the parent plants required for the seed production of many garden and field plants. But evergreens have not yet succumbed to the will of the biologist. They are difficult to replicate and many questions are still without firm answers. Nevertheless many dare believe that mass cloning of pines and spruces will soon take place in Finland.

The Forest Management Foundation experiment is part of the pine cell tissue cultivation research performed at Oulu University. The cell tissue cultivation of forest trees has already been known throughout the world for about 20 years. It has been applied primarily to tropical trees, but also birches can be generated with this method. (Extracted from Helsingin Sanomat, 13 July 1986)

France

Club will encourage French biotechnology firms

Small French companies with an interest in entering potential biotechnology markets will be able to call upon the services of a new group. Club Agri, a risk venture to be established by a number of companies and organizations from the industrial, scientific and finance sectors, will be the vehicle for providing professional advice.

Rhône-Poulenc Agrochimie and Pernod-Ricard will supply industrial expertise while CNRS and INRA, government-sponsored research laboratories, will provide scientific know-how in biotechnology applied to agricultural and food production.

Club Agri will orient its aid to bridge the development gap between fundamental research and the earliest stages of commercial application. It will finance selected projects, which will be subject to bids, and possibly provide assistance at all levels for commercial application.

The secretariat of the Agri Club will be in charge of the collection of projects and their subsequent transmission to the club members. The project selection will be made according to several criteria, including the field of activity, the realism of the project, its duration and the common industrial benefits. Bids will be selected by an evaluation committee. The final decision, made by a managerial committee, may be swayed by the presence of relevant experts. Once selected, however, the

club proposes to liaise with three named experts: a scientist, an industrialist and a banker, who will assess the likelihood of success and the necessary means to ensure it.

This will include the evaluation of relevant markets, investments, need for research, installation of a pilot plant and industrial development. The time for industrial completion, the validity of patents and the willingness of the project holder to collaborate will also be considered. New projects will be followed up by a report every six months and all projects will be supported up to the developmental stage. (Source: European Chemical News, 9 June 1986)

India

Temporary infertility vaccine

A vaccine is undergoing clinical trials to create temporary infertility by targeting antibodies against a hormone crucial to pregnancy, according to Doctor G.P. Talwar of the National Institute of Immunology at Jawaharal Nehru University. Vaccines are under development for eight of the points where the reproductive cycle can be intercepted. The most extensive work involves vaccines made of a subunit of human chorionic gonadotropin (beta-hCG). Four hCG vaccines are now in clinical trials. The hCG hormone may signal the ovaries to sustain the corpus luteum gland during pregnancy. In some of Talwar's work, beta-hCG is linked to tetanus toxoid in order to increase its overall immunity-stimulating potency while producing immunity to tetanus.

Biotechnology procedures are being used to isolate the beta-hCG gene and insert the gene into viruses already used as vaccines. In phase I safety trials of the hCG vaccine, no side effects, including menstrual abnormalities, were observed. Antibody levels gradually fell in 7-16 months, and normal fertility returned. However, subjects showed a wide disparity in the levels of hCG antibodies produced. Scientists are trying to create birth control vaccines using each of four other reproductive hormones. They are also searching for components of the sperm and egg surface that may be good targets for antibody attack. In animals, monoclonal antibodies to reproductive hormones have been used to terminate pregnancies without interfering with fertility. (Extracted from Science News, 7 June 1986)

Israel

Growth factors and cell development

Growth factors may nick DNA to affect its expression during cell development, according to research being carried out at the Weizmann Institute of Science. The macrophage and granulocyte inducers, type 2 (MGI-2), govern whether a myeloid cell in bone marrow will develop into a macrophage or granulocyte by binding to the DNA and nicking or breaking it. In tests with leukemic mice, MGI-2 inhibits the development of myeloid leukemia because it causes the cells to mature. Different differentiation- regulating proteins might nick DNA at different points, thus determining which genes are activated and so allowing development of the various types of cells that make up an organism. (Extracted from New Scientist, 3 July 1986)

Italy

New initiative called for

Italy needs to spend roughly £420 million on a massive biotechnology programme over the next five years, according to a new report from the Italian National Committee for Biotechnologies in order to give the Government a tool to make Italy competitive in previously neglected sectors such as chemicals and agriculture.

Four areas are earmarked for funds: fundamental research in public centres and universities including three special projects from the Consiglio Nazionale della Ricerca (CNR), the national research council (25 per cent of funds), national research involving both scientific bodies and industry (40 per cent), the finance of research societies and stimulation of industrial activity (25 per cent) and training of researchers (10 per cent).

Established in July 1985, the Committee includes 14 representatives from universities and public research centres and eight from industry. Co-ordinated by Professor Arturo Falaschi, director of the CNR Institute of Genetic Engineering in Pavia and the newly appointed director of the Trieste component of the International Centre for Genetic Engineering and Biotechnology, the report looks largely at the short term. The biomedical field, says the report, is likely to yield returns in the short term, while agriculture, the food industry and fine chemicals have good medium-term prospects. So the report suggests doubling in five years the number of researchers in biotechnology in public centres such as CNR and ENEA (the National Centre for Alternative Energy), as well as in the universities and health ministry, rather than in industry.

To co-ordinate the programme, it is suggested that either the present committee be institutionalized or a National Institute of Biotechnology should be set up like that for nuclear physics. (Extracted from Nature, Vol. 322, 3 July 1986)

Sorin Biomedica US diagnostics push

Sorin Biomedica, an Italian biomedical concern belonging to Bioengineering International, is bent on entering the US diagnostics market.

The parent group has just initialled an accord for the acquisition of a 51 per cent stake in Clinical Sciences, a US concern operating in the field of diagnostics and serum reagents, based in Wippany, New Jersey.

Meanwhile, Sorin is to proceed with a share issue to raise its capital equity. In a complex share swap deal, Fiat is to hand over Bioengineering International to Snia, the chemicals and defence concern, but Fiat is to boost its own stake in Snia. (Source: European Chemical News, 7 July 1986)

Japan

Protein engineering system

Five Japanese companies led by Sumitomo Chemical and NEC Corp. have developed a biochemical expert system called BIOCES for protein engineering and pharmaceuticals and agricultural chemicals design. The system, which sells for $125,000, incorporates drug receptor theory. It operates on a $625,000 ACOS general-purpose computer, and is designed to create or modify existing proteins and investigate drug receptor relations. Colour graphics terminals can produce three-dimensional models of proteins from their single-dimension structures. (Source: Chemical Week, 23 July 1986)

Beta-TNF

Fujisawa Pharmaceuticals has decided to concentrate its clinical efforts on the evaluation of beta tumour necrosis factor (TNF). The Japanese

drugs company, under licence from Genentech, has been evaluating both the alpha and beta forms of the potential anti-cancer agent for the past two years.

Fujisawa decided to pursue beta-TNF as two other Japanese firms, Asahi Chemical and Dainippon Pharmaceutical, are engaged in developing the alpha form. Genentech has TNF in phase 1 clinical trials in the US. Tests indicate that TNF shows good anti-tumour activity. The US biotechnology concern is also testing TNF in parallel with gamma interferon. In Europe Boehringer Ingelheim, under licence from Genentech, is about to enter clinical trials. (Extracted from European Chemical News, 28 July 1986)

Joint research with China

In April, Gakken Co., Ltd., in co-operation with Itagaki Nursery, will establish a joint venture in China with the Plant Research Institute of China's Academy of Sciences. The new company will begin by exchanging researchers and information on agricultural biotechnology between the two countries. In China there are plants not readily found in Japan, and the Chinese Academy of Sciences is rich in plant information. It is said that through this joint venture there is a strong possibility that Japan will very likely be able to procure what it could till now only obtain with difficulty and that such a procurement could eventually lead to acquisition of needed genetic resources. The new joint venture is named Shinka Plant Resources New Technology Development Co., with headquarters in Beijing. The company will be headed by Qian Ying Qian, director of the Plant Research Institute. As the Japanese counterpart to this new venture, Gakken Chinese Plant Development Co., Ltd. was established in Japan last March. This company will begin by importing medicinal plants, natural pigments, spices, and health foods from China. (Extracted from Nikkei Biotechnology, 7 April 1986)

Silk used to fix enzymes

Silk can be used to fix enzymes in bioreactors and so prolong their catalytic activity, according to the University of Agriculture and Technology in Tokyo. Enzyme fixation is a major factor in determining bioreactor performance. Immobilizing enzyme proteins by attaching them to or wrapping them in a polymer base improves their catalytic activity and extends their lifetime. Gelatin is usually used to fix enzymes for such applications, but researchers working with glucose oxidase determined that silk is in many ways a better immobilizing agent. When it was used hardly any of the oxidase escaped. Enzymes fixed by silk also showed much higher activity and better resistance to variations in temperature and the acidity of the culture medium. (Extracted from Japan Economic Journal, 16 August 1986)

New rice strain

A new strain of rice with grains the size of peanuts has been developed by the Ministry of Agriculture, Forestry and Fisheries' research laboratory in Kyushu. The grains are two-and-a-half times longer and one-and-a-half times wider than ordinary Japanese rice. Each weighs 60-70 mg, versus the usual 20-22 mg. One problem with the new strain is that the grains are so heavy they cause the plant to topple over. It has not yet been perfected, but will probably be used for animal feed. (Extracted from Wall Street Journal, 7 July 1986)

Interferon producers obtain approvals

The Ministry of Health and Welfare's Central Pharmaceutical Affairs Council has approved the use of an interferon drug to treat hepatitis B. Toray Industries' Feron will be used against two strains of B-type chronic heptatitis. It is the first drug thought to be able to attack the virus in patients and Toray is the first company to market the drug for this indication. Approval was granted following clinical studies which showed that three out of 10 seriously ill patients recovered after a two-week course of the drug. Mochida Pharmaceutical is concluding its tests on hepatitis B patients with its beta interferon drug. The firm has now applied for permission to market its product for certain cancer indications. (Extracted from European Chemical News, 15 September 1986)

Microbes as energy source to be studied

Japan's Agency of Industrial Science and Technology is to study microbes as an energy source. Within the framework of the Ministry of International Trade and Industry's Sunshine project, the bio-energy programme will take up four research themes including a hydrogen production system utilizing photosynthetic microbes and a new synthetic fuel production method by making use of biotechnology. Government laboratories participating in the project include the National Chemical Laboratory for Industry and the Research Institute for Polymers and Textiles. (Source: European Chemical News, 29 September 1986)

Computerized market gardening

Research Development (Japan) has developed a computerized system that can grow vegetables without soil or sunlight. It was orginally developed for Japanese farmers in cold regions who wished to grow vegetables found only in warmer areas. During tests on Hokkaido Island, vegetable seeds were sown on a bed of urethane foam and exposed to high-pressure sodium light. Moisture, temperature and other conditions were controlled by computer. Under these conditions some vegetables actually grew four times faster than under natural conditions, but they cost up to 50 per cent more at the wholesale level. A test plant in Hokkaido will soon begin shipping vegetables to grocery stores. (Extracted from Wall Street Journal, 28 July 1986)

Norway

National action plan for biotechnology established

Implementation of the national action plan for biotechnology began almost a year ago. This research field has been designated by the Government as one of five principal areas to receive priority in the coming years. The four research councils together have primary responsibility for the plan and intend to invest 98 million kroner during the coming three-year period. Four areas of research have been singled out as important: genetic engineering, human and veterinary medicine, plant and animal breeding, technical and industrial biotechnology.

Even though Norway lags behind in many areas of biotechnology, interesting work is being done, particularly in the breeding of fish. With the help of recombinant DNA technology, attempts are being made in Bergen and Trondheim to clone growth hormones in salmon. What is possible with salmon is also possible with other animals. Bigger, stronger, and healthier are key adjectives in the national action plan for biotechnology. There is also a high degree of application in agriculture. And here the goal is, of course, the same: the biggest possible profit in the shortest possible time.

One of the areas which may be interesting is the manufacture of fodder. Oil and gas from the

North Sea could be used in the production of unicellular proteins. The latter would be good fodder, especially for fish breeding.

Mining is another catchword. Maybe old mounds of ore can be made into something valuable again with the help of bacteria which extract metals from the ore.

Another interesting sector where biotechnological methods can be applied is the chemical industry. Many of the synthetic chemicals which are used today can be replaced by biochemical substances which serve the same purpose. (Extracted from Aftenposten, 3 April 1986)

Sweden

Alfa Laval and Pharmacia to set up and sell complete factories

Alfa Laval and Pharmacia have joined forces in a new biotechnology enterprise. The enterprise, located in Uppsala, began operating in June, and will be the only one in the world to sell complete biotechnology factories.

Pharmacia is today the leading enterprise in purification, the separation of biotechnological products on a laboratory scale while Alfa Laval is in a position to manufacture equipment for separation and also has long experience in purification on a large scale.

In the new enterprise, Pharmacia will be in charge of the basic processes and Alfa Laval of the construction of entire plants. (Extracted from Ny Teknik, 10 April 1986)

Switzerland

Biogen may sell Geneva facilities

Biogen looks set to rationalize its operations. The biotechnology company is currently split between R&D and fermentation facilities on both sides of the Atlantic - in Geneva, Switzerland and Cambridge, Massachusetts. It is understood that it is looking for a corporate partner to share or take over completely its Geneva facilities.

The closure of the facility has been on the cards for well over a year in the face of mounting losses. But in spite of these losses the company has a sound financial position following its recent $35 million share issue. The company anticipates significant revenues from its gene-spliced gamma interferon and hepatitis B vaccine which are expected to reach the market within the next year or so. (Extracted from European Chemical News, 8 September 1986)

Taiwan

Government biotechnology development plan

The Government has instituted an ambitious plan to develop biotechnology-related production. Under the plan, Taiwan expects to move from zero to $1 billion in sales of biotechnology products by 1990, for a 2 per cent world market share. Even this small market share would allow Taiwan to create a major new industry, coinciding with its aim to move from labour-intensive businesses to a high-technology base. Other developing countries in Asia have also targeted biotechnology as a priority industry for development, but Taiwan enjoys several advantages that puts it a step ahead of its rivals. These include a broad base of university graduates in the life sciences, a pool of experienced senior scientists of Taiwanese origin who could be lured back to their home country and a government policy that seeks to support and encourage the private sector while guarding against stifling it with bureaucracy.

The Government is offering about $13 million/year of funding for biotechnology research at academic institutions and medical centres. The establishment of the non-profit Development Center for Biotechnology, with $3 million capital, is designed to carry out product development projects for private companies under contract, invest as a minority shareholder in promising new products and establish technology transfers with foreign companies. (Extracted from International Management, June 1986)

United Kingdom

Biopolymers unit starts production

A joint project for the commercial production of water-soluble biopolymers between Sturge Biochemicals and Shell Research is under way. The unit is described as commercial-scale and will produce tons of product from a 220 cubic metre fermenter.

The project represents a major R&D thrust by Shell to produce high-quality polymers. To be marketed as Shellflo, the biopolymer will have the ability to thicken aqueous systems and can be used in a wide variety of commerical applications. Typical applications range from use in agrochemical formulations, the paint and textile industries and, more important in Shell's marketing strategy, in the oil industry for enhanced oil recovery.

To date, the collaboration has produced two distinct microbial biopolymers. The more established xanthan polysaccharide is made by the bacterium Zanthomonas while a new polysaccharide containing glucose and galactose sugars is also available. The new type of biopolymer has a number of interesting properties designed to improve the performance of specialist clear-brine drilling systems. (Extracted from European Chemical News, 8 September 1986)

Gene releases investigated

The Royal Commission on Environmental Pollution is to investigate the risks from the release of genetically engineered organisms into the environment. The Royal Commission will look at whether there are important differences between releasing genetically engineered organisms (to protect against plant disease, for instance) and routine genetic selection by cross-pollination, or mutation and selection of micro-organisms. It will also examine whether studies in the laboratory can predict the likely consequences of a release outdoors, and how easily an organism could be destroyed if an experiment in the open air began to disrupt the environment. (Source: New Scientist, 24 July 1986)

Bio-reactor scale-up

The first major club project in the UK specializing in the design and utilization of bio-reactors has been established by the Department of Trade and Industry at the National Engineering Laboratory in East Kilbride, Scotland. Launched in January, the club has a present membership of 20 industrial companies and research organizations. It not only acts as a forum for contact between manufacturers, users, contractors and research institutes, but also carries out research, surveys

and consultancy projects. The associated research programme, funded by the DTI is being carried out by the NEL and the Universities of Birmingham, Bradford and Strathclyde.

The present research programme on bio-reactor scale-up is of a pre-competitive nature. Future research work is formulated by the sponsors and universities through a number of review panels whose areas of interest are 'Fluid Dynamics and Transport Processes', 'Process Control and Fermentation' and 'Novel Reactors'. (Source: Biotechnology Bulletin, Vol. 5, No. 7, August 1986)

SERC confirms biotechnology's importance

The Science and Engineering Research Council (SERC) has announced the results of the inquiry into biotechnology, chaired by Imperial Chemical Industries' research director Dr. Charles Reece. The inquiry panel concluded that biotechnology has great importance for the UK and that SERC has an important role to play in supporting research in this field. The panel also concluded that the SERC Biotechnology Directorate has been a success, so the Council of SERC has agreed to maintain its substantial funding of the Directorate to the end of the present five-year period. The Directorate is being encouraged to develop its existing strategic research role, while strengthening links with the Department of Trade and Industry. The panel identified a need for enhancing the existing co-operation between the Research Councils in the biotechnology field and the heads of the Research Councils are discussing how best to achieve this. (Source: Biotechnology Bulletin, Vol. 5, No. 7, August 1986)

Plant research

The British Government is to go ahead with its plan to sell off its institutes for the development and marketing of new varieties of plants. The two organizations to be sold, the National Seed Development Organization and the Plant Breeding Institute (PBI), might seem to form a natural couple. PBI, belonging to the Agricultural and Food Research Council (AFRC), runs large-scale programmes in plant breeding which have produced nearly all the new varieties sold by the National Seed Development Organization. This has been a profitable business, generating £4.65 million for the Government last year. Given that support for plant breeding research at PBI cost just £2.5 million last year, the institutions are bound to seem an attractive buy.

Before privatization, PBI's molecular genetics and cytogenetics sections will be split off and combined with other AFRC institutes to form a new Plant Sciences Institute.

The new Plant Science Institute will be completed by the addition of the John Innes Institute, the Unit of Nitrogen Fixation at the University of Sussex and a small part of the Rothamsted Experimental Station. But no provision has been made to bring the various parts together at one site: the "institute" will be more of an administrative convenience. (Extracted from Nature, Vol. 322, 7 August 1986)

Agricultural biotechnology

Britain's last major independent seed company, Sinclair McGill, has been absorbed by Imperial Chemical Industries (ICI, London) at a cost of £5.1 million. This occurs at a time when the National Seed Development Organization (NSDO) and part of the associated Plant Breeding Institute (PBI, Cambridge) await news of their fate. Sinclair McGill specializes in vegetable and cereal varieties and forage crops. Having successfully surrendered all of its fertilizer and seed interests, the parent company, William Sinclair Holdings, will now concentrate solely on the garden leisure sector, where it feels better able to compete. (Extracted from Biotechnology, Vol. 4, September 1986)

Wellcome links up with US firm

Wellcome Biotechnology of the UK and Genetics Institute of the US have established a joint venture to manufacture biotechnology-derived pharmaceuticals. The new company, Wellcome Manufacturing, will operate a planned facility based in New England in the US. The plant is expected to come on-stream by 1989. A precise location will be announced before the end of the year.

Products from both partners will be made at the facility and a board with equal representation will decide on production priorities. Products from Genetics Institute, including some developed in collaboration with other firms, will be manufactured at the plant. Burroughs-Wellcome, the US subsidiary of Wellcome Biotechnology's parent company, plans to make all its biotechnology products at the plant.

Within the agreement there is a provision to cope with conflicts of proprietary interest. The formation of the venture is subject to receiving appropriate US government regulatory approvals. (Extracted from European Chemical News, 15 September 1986)

United States of America

New biology/chemistry institute

A new institute to "attack problems at the interface between biology and chemistry" will be set up at California Institute of Technology through a grant donated by the Beckman Foundation.

Some research areas that the institute might support include chemical synthesis of new polymers, development of advanced genetic engineering concepts and instrumentation, preparation and testing of new types of catalytic and ceramic materials, and development of computer and instrumentation techniques for protein engineering and human chromosomal mapping. The institute eventually will be housed in a new building on campus, which will have, in addition to research facilities for institute-sponsored projects, major research instrumentation that will be available to the entire Caltech community.

The Beckman grant, which is the largest single gift the Foundation has ever made, comes in two parts: an initial $40 million, which is contingent on the school's raising $10 million in capital funds from private sources, and an additional $10 million if Caltech raises an equal amount for the institute's general endowment from the members of its board of trustees. (Extracted with permission from Chemical and Engineering News, 23 June 1986. Copyright 1986 American Chemical Society)

US to screen marine organisms for drugs

The National Cancer Institute (NCI) at Bethesda, Maryland will award two important contracts directed toward the discovery of potential anti-tumour products from marine organisms. One of the two contracts will call for the screening of organisms from shallow water (under 100 feet). The other applies to deep water (over 100 feet). Both call for the acquisition of a total of 1,000 organisms a year for five years. The shallow-water contract will concentrate on the Indo-Pacific

region; the geographic area to be covered by the deep-water contract will be less specified. Actual collections should begin by the end of the year.

According to NCI, compounds with anti-tumour activity have already been isolated from sponges, tunicates, bryozoans, nudibranch egg-masses, corals, and algae. The collections will focus on these invertebrates, as well as molluscs.

It is estimated that NCI will have preliminary results on crude extracts from the collections within a year or two; isolation of pure products from which to make potential drugs could take 5-10 years. Compounds will be tested at NCI's Frederick Cancer Research Facility near Bethesda on a "disease oriented" in vitro panel of more than 20 human cancer cell lines. Trials will initially focus on lung cancer, but will include other solid tumours like colon and breast cancers. The colorimetric, growth-inhibition assay, to be performed in microculture plates, is based on reduction of a tetrazolium salt to a coloured formazan inside viable cells. When a substance is demonstrated effective on one or more cell types, in vivo animal studies will be done.

Currently, only one product derived from a marine organism is in US clinical trials: didemnin B. Now in late stages of phase I testing, the drug is derived from an unclassified tunicate from the genus Trididemnum, originally collected in the Western Caribbean sea in 1978 by Kenneth Rinehart (University of Illinois, Urbana-Champaign). Didemnin B has shown anti-viral and immunosuppressant activity in addition to in vitro activity against leukaemia and melanoma cells.

NCI regards large-scale collection and screening as an important complementary strategy to "rational" drug development. Consequently, NCI's Developmental Therapeutics Programme is not limited to scouring the sea for potential drugs. It plans to extract chemicals from some 20,000 plants that will be collected in rain forests over the next five years; over the same period it also intends to isolate and cultivate 1,000 blue-green algae from marine and terrestrial environments. (Extracted from Biotechnology, Vol. 4, August 1986)

New centres for clinical trials

As the number of cases of acquired immune deficiency syndrome (AIDS) continues to snowball, finding an effective therapy becomes increasingly urgent. The US National Institute of Allergy and Infectious Diseases (NIAID) announced in July that it was committing $100 million over the next five years to speed the search for a therapy.

Fourteen AIDS treatment evaluation units will be set up around the United States to test drugs that have shown some promise, either by blocking replication of the virus that causes AIDS, or by strengthening immune system function. In announcing the new units, Anthony Fauci, director of NIAID, said a successful treatment would probably combine an anti-viral drug with a immune modulator, but combination therapies will be tested only after each single agent is tested.

A Data Safety Monitoring Board will evaluate the progress at each centre recommending new directions on initial results. To streamline exchange of information among the 14 units, NIAID plans to award a contract this September for a trial co-ordinating centre.

The fourteen institutions receiving NIAID funds are: Harvard University; John Hopkins University; Memorial Sloan-Kettering Cancer Center; New York University; Stanford University; University of California, Los Angeles; University of California, San Diego; University of California, San Francisco; University of Miami; University of Pittsburgh; University of Rochester; University of Southern California; University of Texas M.D. Anderson Hospital and Tumor Institute; and University of Washington. (Extracted from Nature, Vol. 322, 10 July 1986)

Fingerprint deal

BioTechnica Ltd., Cambridge, Mass., and Cardiff, Wales, has agreed to apply its patented "fingerprinting" technology to Pioneer Hi-Bred International Inc.'s proprietary organisms used in a silage additive.

In fingerprinting the DNA of Pioneer's organisms, BioTechnica Ltd. will provide Pioneer with a characteristic pattern for the proprietary strain, which can be used in enforcing patent protection as well as quality control purposes. The particular strains involved are in the Lactobacillus plantarum family and are in Pioneer's silage additive products.

BioTechnica Ltd.'s fingerprinting technique exploits the minute natural variations that occur in chromosomes of living organisms from which a characteristic fingerprint can be obtained.

The technique includes a method for obtaining the highly discriminating patterns and the ability to quantify the certainty of an organism's identity. In addition the technique can be applied to identification of organisms previously released in nature and then re-isolated for identification. It can also be used for quality control of organisms that may mutate or otherwise change during production or use. (Extracted from Chemical Marketing Reporter, 4 August 1986)

Test of gene-altered bacteria postponed

The field test by University of California, Berkeley researchers of bacteria that have been genetically altered to protect crops from frost damage is probably not to be conducted until late next spring at the earliest. The long-delayed field test of ice-minus Pseudomonas syringae produced by recombinant DNA techniques was planned to begin at the university's field station in Tulelake, Calif., in August. However, opponents of the tests obtained a court order delaying the test. They claimed that the university had failed to produce an environmental impact report, which is required by California law. In an out-of-court settlement, the university agreed to postpone the test, meet with the opponents to discuss their concerns, and conduct an assessment to determine whether a full environmental impact report is needed. According to a university spokesman, a factor in reaching the settlement was that it is already too late in the season to conduct the test because, by the time the plants started to grow, heavy frosts would have set in. (Source: Reprinted with permission from Chemical and Engineering News, 25 August 1986. Copyright 1986 American Chemical Society)

EPA approves biotechnology field test

EPA will not require an experimental use permit for field testing a fungus genetically altered by ultraviolet radiation. The work by David Sands of Montana State University uses Sclerotinia

sclerotiorum, a fungus common throughout Montana. Sands is trying to derive a strain of the fungus that will be herbicidal to the weeds Canada thistle and spotted knapweed. An EPA review of the experiment proposed by Sands concludes that the potential risk from the small-scale field test is minimal because UV radiation tends to inactivate gene functions and laboratory tests of the irradiated fungus show reduced ability to survive compared with the parent strain. (Source: Reprinted with permission from Chemical Engineering News, 18 August 1986. Copyright 1986 American Chemical Society)

Union of Soviet Socialist Republics

Vaccination catalyst

Scientists have discovered a vaccination 'catalyst' which increases the response of the body's defense system to a vaccine by 100 per cent. The catalyst could eliminate harmful side effects associated with some vaccinations, protect against a number of diseases which presently resist vaccine treatment, and possibly provide a universal vaccine. It should also make vaccination against allergies possible. Soviet researchers identified a minute part of the viral DNA, a mere 20 amino acids long, which was common to all influenza viruses, no matter how much the organism mutated. Western scientists who had also identified similar common factors among these viruses could not understand how to prepare a vaccine from so minute a part to provoke a protective response. For the Russians, the answer is the catalyst. Combined with the 20 amino acid part of the virus, it provokes a full immune response. A second vaccine using the principle is being developed against salmonellosis. The catalyst will make it possible to use synthetic copies of viral DNA and so avoid passing viruses through hens' eggs and monkey embryo livers which can also result in harmful side-effects. (Extracted from The Times, 19 June 1986)

Firms compete for biotechnology projects

Acting on behalf of the Soviet Academy of Science, the foreign trade organization Techmashimport has invited companies to tender for several biotechnology projects. The most advanced (expected to be signed in November this year) is a project at the Chemyakin Biotechnology Research Institute in Moscow. The others are at the Biolar Biochemical Institute at Olayne, south of Riga in Latvia; at an institute in Taroussa, south of Moscow; and two at Ufa in Bashkiria. In total these projects involve the production of over 1,000 items and open up a fascinating new Soviet market.

Three consortia are competing for the prestigious Chemyakin project. They are headed by Orion Yhtyma Oy of Finland, Oweg GmbH of Austria and Pec Engineering of France.

The Chemyakin scheme is to set up development laboratories and pilot plants for the production of growth regulators for the development of plants and animals; peptides; pure solvents; monoclonal antibodies; low molecular weight protein; chemical reagents; polymer for biotechnology for sorbent use in chromatography.

The USSR wants the laboratories to develop good processes before it moves on to full-scale commercial production.

The Orion-headed consortium also includes YIT (Yleinen Insinooritoimisto), a Finnish engineering company. The Oweg group is believed to also include Terrabetoni of Finland and Biogenetics of the Federal Republic of Germany.

The French group includes Perusyhtyma, an important Finnish civil engineering firm, and the University of Compiegne, France's best-known biotechnology university.

The Finnish connection in each of the bids is designed to help out with the financial aspects as Finland has a clearing arrangement with the USSR.

While the Chemyakin project is clearly defined, the remaining schemes are still vague.

Valued at more than double the Chemyakin project's price, the Biolar plan calls for the setting up on a turnkey basis of seven buildings to include research laboratories and pilot production of high technology products. These will include about 150 derivatives of amino acids, more than 50 peptides, over 25 oligo-polynucletiodes, about 30 nucleic acids, 150 proteins and ferments, about 25 lipids, 50 glucosides and many reagents.

Information on the Taroussa and Ufa projects is still sketchy. It is known, however, that the Taroussa project will involve a mixture of chemical and biochemical units. The two Ufa projects (one research and one production) call for the setting up of a multipurpose "universal plant for the production of organic products".

The Ufa projects are being followed by Heurtey Industries of France and Technipetrol of Italy. The Oweg team is pursuing the Ufa and Biolar projects and a team comprising Technip and Litwin is offering Biolar.

Meanwhile, in an unrelated development, Technip is proposing to build a large plant to produce cattle feed from biomass in the Soviet Union. It is offering technology developed by the Toronto-based Stake Technology of which it is an exclusive licensor. The plant will use 50,000 - 100,000 ton/year of biomass. Companies are also bidding to build a high fructose corn syrup plant in the USSR. (Extracted from European Chemical News, 29 September 1986)

Yugoslavia

The Fourth International Symposium on Microbial Ecology

The Fourth International Symposium on Microbial Ecology held at the end of August in Ljubljana attracted 760 participants from 40 countries.

The programme featured 20 morning sessions of invited speakers on selected focal topics that included extreme environments; trends in microbiological theory; unusual micro-organisms; anaerobic interactions; ecology of fermented foods; human pathogens in the environment, and microbial activity and influence in the gastrointestinal tract. There were also sessions on more traditional subjects such as marine microbiology, cycling of elements, and microbiology of soil fertility. Round table discussions designed to promote exchanges of information and opinion were conducted on microbial interactions in acid stressed aquatic environments; life associated with hydrothermal vents, and the fate of genetically engineered elements in the environment. Professor Ralph Wolfe of the USA presented the opening plenary address on the "Biochemical ecology of anaerobes", and Professor Hans Schlegel of the FRG concluded the event by discussing "Microbial ecology and the prepared mind". A volume of abstracts of presented papers was distributed at the Symposium, and the proceedings will be published by early spring of 1987.

C. RESEARCH

Research on human genes

More versatility from RNA

Scientists in the United States and Denmark have discovered an RNA molecule that can act as a "cofactor" - a molecule that helps an enzyme to carry out its job of catalyzing some chemical reaction within cells. The discovery adds a further twist to the continuing story of the chemical versatility of RNA.

RNA's best-known role in the life of a cell is as an intermediate form of genetic material - the "messenger RNA" that carries a copy of a gene's information from the nucleus into the cytoplasm. RNA can also serve various structural or "scaffolding" roles. Astrid Schön and her colleagues in the Department of Molecular Biophysics and Biochemistry at Yale University, and Simon Gough and colleagues at the Carlsberg Laboratory's Physiology Department in Copenhagen, found that a transfer RNA carrying the amino acid glutamate acts as a cofactor by allowing an enzyme involved in the manufacture of chlorophyll in green plants to act on the glutamate. The transfer RNA appears to supply glutamate to the enzyme responsible for converting glutamate into glutamate-1-semialdehyde, a vital step during the manufacture of chlorophyll.

Although some transfer RNAs have been implicated in similar processes in the past, this is the first example of one in which transfer RNA clearly acts as a cofactor in a reaction that has nothing to do with the manufacture of protein. (Extracted from New Scientist, 14 August 1986)

Oncogene amplification

Oncogene amplification corresponds to the clinical status of small-cell lung cancer, according to M. Bishop of the University of California (San Francisco). Patients with a high degree of gene amplification are being assigned to more aggressive therapy and researchers are attempting to determine if amplification correlates with prognosis of lung cancer. A study at Washington University (St. Louis) indicated that N-myc amplification affected 18-month survival rates in neuroblastoma patients. Patients with a single copy of the gene had a 70 per cent survival rate, versus a 30 per cent survival in patients with 3-10 copies of the gene and 5 per cent for those with more than 10 copies. (Extracted from Medical World, 9 June 1986)

Research on common cold virus

Viruses of the common cold could be thwarted by blocking receptors on cells, according to researchers at the University of Virginia School of Medicine (Charlottesville). Antibodies are designed to attach to the receptors, which are needed by the virus to allow their entry into cells. The receptor blockade technique has been tested on human cells in culture, in chimpanzees and in human volunteers. Nose drops containing the antibodies protect cells in the nasal passages from rhinoviruses, which must attach to the receptors before they can enter the cells, where they can then reproduce. So far, the viruses have been unable to circumvent the blockade technique.

Researchers at Purdue University recently described the complete 3D structure of a rhinovirus, and have been testing two drugs that prevent a virus from shedding its protein coat in order to enter and infect a cell.

Although there are over 100 rhinoviruses, which cause 30-50 per cent of all colds, the blockade technique takes advantage of the fact that the virus attaches to a cell using a region of the virus which does not mutate. Thus, the virus cannot adapt to circumvent the blockade. The rhinoviruses use only two types of receptors on human cells, and the major receptor is used by 80 per cent of rhinoviruses. Smaller antibodies must be developed so they will not elicit an immune response. More long-lasting protection against rhinoviruses is also needed. (Extracted from New York Times, 16 September 1986)

The reasons for malignancy

In the chromosomes of almost any cell are sequences nearly identical to those associated with cancers. Two major theories exist as to what causes these sequences to initiate malignancies. One is that the sequences become overactive, thereby creating high levels of growth-controlling proteins. The other is that a point mutation turns a normal cell into a cell-transforming agent. Research being carried out by Dr. P.H. Duesberg of the University of California at Berkeley leads him to say that a major restructuring of the gene must occur in order to initiate cancer. Reversing the single nucleotide changes in cancer-causing DNA segments does not prevent them from transforming cells. Duesberg says a DNA region upstream of the ras gene is actually a crucial part of the normal cellular gene that corresponds to ras, and that a fifth exon exists before the four coding regions which are already known. When this region is truncated by some agent, the cancer gene becomes active. (Extracted from Science News, 3 May 1986)

Factor VII cloned

The gene coding for the blood coagulation protein factor VII has been cloned by ZymoGenetics (Seattle, WA), in collaboration with the University of Washington and Novo Industri A/S (Bagsvaerd, Denmark). The company believes that factor VII could be more useful than factor VIII in treating haemophilia because factor VII plays its part in the blood coagulation pathway alone, whereas factor VIII need factor IX to be effective. (Source: Bio/Technology, June 1986)

Genetic predisposition to high blood pressure

A novel theory has been put forward that negroes may be predisposed to high blood pressure because their genes evolved with a low-salt diet, according to T. Wilson of Bowling Green State University (Ohio). Blood pressure differences among West African tribes can be correlated with historical accounts of salt availability. Salt was always available in Senegal and the Gambia, where blood pressures are low, based on studies of the Mandinka and Serer tribes. Present-day blood pressures are much higher among the Yoruba, a Nigerian tribe in an area with virtually no salt. A large proportion of today's inhabitants of West Africa are descended from tribes with a historical lack of salt, making increased salt consumption a serious public health hazard. (Extracted from Science News, 3 May 1986)

Scientists find viral infection triggers arthritis

Doctors at Exeter University have found that infection with a recently discovered virus, the parvovirus, which causes a flu-like illness, may trigger rheumatoid arthritis in genetically predisposed people. About 80 per cent of people with this disease carry a gene called DR4 (as compared with 30 per cent of the general population)

and the researchers' work suggests that infections may trigger rheumatoid arthritis in those people with the relevant genes. The team is now looking for evidence that other infections can trigger arthritis in the same way. (Source: Genetic Engineering News, September 1986)

Single-chain antibodies developed

Genex Corp., Gaithersburg, Md., has filed for patents on its single-chain antibodies for diagnosis and therapy of disease and for use in sensing devices and separations of biological substances. Use of single chains may avoid both immunological reactions by patients to conventional antibodies and non-specific binding. The greater stability and lower costs of single-chain antibodies may enhance their use in biosensors and protein purification processes. The company may design a carrier group for the other end of the linker to complex with a radioisotope for use in cancer diagnosis and therapy. Celltech of Slough, UK, and American Cyanamid Co., Wayne, N.J., are co-operating to develop similar single-chain antibodies. (Extracted with permission from Chemical and Engineering News, 15 September 1986. Copyright 1986 American Chemical Society)

New herpes-like virus discovered

Scientists at the US National Cancer Institute have discovered a herpes-like human virus that could open up new avenues of research into a number of diseases, from blood and lymph system cancers to immune system disorders.

Dr. Robert C. Gallo, head of the institute team that found the virus, said it infected a type of white blood cell that played a key role in the body's immune system. It was a member of the herpes family of viruses. All of the known human herpes viruses cause disease and this may be true for the new one as well.

Dr. Gallo said that he did not yet know how infectious the new virus was but that it might require "close contact but not necessarily intimate contact". (Extracted from International Herald Tribune, 24 October 1986)

Possible prediction of carcinogenicity

Tests for a nuclear protein associated with chromatin might be a better predictor of carcinogenicity than simply waiting for tumours to appear, according to Z. Medvedev of the National Institute of Medical Research (London). The protein might be involved in repairing chromosome damage or in detoxifying carcinogens. Elevated levels of the protein appear long before the cancer is evident. Liver cells can have multiple copies of each chromosome, so the liver (the main organ of detoxification) can withstand a great deal of damage without affecting cell function. In humans, there can be up to eight copies of each chromosome, although mice often have 32 copies of chromosomes in liver cells. This means that mice might be less susceptible to carcinogens than humans. The newly-discovered protein, however, appears long before a tumour starts to develop, so mice can still be good indicators of carcinogenicity. (Extracted from New Scientist, 29 May 1986)

New cancer treatment

During the past decade, cancer specialists have experimented on adoptive immunotherapy. The object of this type of treatment is to boost the patient's own defences to attack his or her own tumour. White blood cells are taken from the patient's blood, cultured in large quantities and returned to fight the cancer.

A small number of patients with advanced cancer have benefited from such treatment with lymphokine-activated killer (LAK) cells, a form of lymphocyte associated with tumours. In 1980, Steven Rosenberg, of the National Cancer Institute (NCI) in Bethesda, Maryland, found that a combination of LAK cells incubated in interleukin-2 (IL-2), a protein of the immune system, and given with IL-2, reversed the spread of cancer in 21 of 55 patients. Five of those patients were cured of malignant cancer.

Unfortunately, large doses of LAK cells and IL-2 are needed for treatment. Both substances are in short supply, and IL-2 has serious side effects. Now, however, Rosenberg has found another type of killer cell that is 50 to 100 times more potent and requires very little IL-2 to be effective. Rosenberg has tested his new breed of killer cell, called tumour-infiltrating lymphocytes (TIL), on mice.

Pure TIL cells eliminated 96 per cent of small metastasised tumours - those that had spread from the original tumour - in doses of a few million cells. Their LAK competitors required 50 to 100 times that number to do as well. On larger tumours, TIL cells worked as well when the immune systems of the mice were first temporarily shut down with either cyclophosphamide or radiation. Similarly advanced tumours were immune to treatment with LAK cells. Furthermore, the TIL cells worked with very little help from IL-2, which Rosenberg believes will reduce the threat of toxic side-effects.

Rosenberg and colleagues can draw TIL cells from a variety of human tumours, including melanoma and kidney tumours, and various adenocarcinomas. They have grown human TIL cells for as long as two months to generate the large populations needed for experimental treatment. So far, TIL cells taken from human melanoma have been able to kill the same type of human melanoma in vitro. Rosenberg hopes to obtain approval from the Food and Drug Administration to start trials of his treatment within the next two months. (Extracted from New Scientist, 25 September 1986)

New T-cell receptor discovered

T-cell tumours may arise through a mechanism similar to that which causes B-cell malignancies, according to research being carried out at Wistar Institute. T-cell lymphocytic leukaemia involves the repositioning of a portion of a T-cell receptor gene next to a cellular oncogene. Immunoglobulin gene translocations have already been demonstrated in B-cell tumours. The translocations are not random, but result from a mechanism that normally rearranges the T-cell receptor genes. The new finding may help clarify the role of HTLV-I in causing adult T-cell leukaemia. (Extracted from Medical World, 11 August 1986)

Cancer-spreading genes

Japanese scientists have made a new breakthrough in the search for the origin of secondary cancers, or metastases. Kiyoshi Taniguchi and colleagues at the Chiba University Medical School have isolated a gene coding for a chemical which they believe is responsible for the formation of metastases.

The researchers prepared four monoclonal antibodies capable of binding to cancerous rather than normal cells in mice. They tested the ability of the antibodies to suppress formation of secondary cancers by injecting each one in turn into mice infected with malignant cells. One of the

monoclonal antibodies limited the spread of lung cancer by a factor of ten. Reasoning that the antigen (binding site) on the surface of the cancer must have been responsible for the formation of metastases, the team isolated a gene coding for that antigen. Taniguchi and his colleagues are now working out the DNA sequence of the gene in the hope that they might be able to clarify its role in the development of secondary cancer. (Source: New Scientist, 12 June 1986)

Mapping the human genome

Until recently, sequencing the human genome seemed an impossibly large project, but the US Department of Energy (DoE) is giving serious consideration to a project to sequence all of the estimated 3,500 million base pairs making up the human genetic material. Initial estimates put the cost of the entire project at $1,800-$3,600 million or about $1 per base pair.

DoE has historically had an interest in the human genome, and has been supporting research into genetic damage from energy sources for some time. Together with Lawrence Livermore National Laboratory, the Los Alamos National Laboratory has been involved in the National Laboratory Gene Library Project, an effort to construct a chromosome-specific gene library. So far, the small insert library - containing fragments of 5,000-10,000 base pairs - is complete, and work on the large insert library for fragments of up to 50,000 base pairs has begun. Los Alamos has also developed flow cytometry technology capable of rapidly separating large amounts of DNA by chromosome.

In addition to the gene library project, DoE has the computational facilities necessary for such a large-scale project and the DoE believes it has the know-how to undertake large-scale scientific projects.

Current plans call for a decentralized programme, with one co-ordinating facility organizing the work of many centres around the country. The organizers hope the sequence can be a multinational effort. European interest in the project is already high. Critics of the sequencing project do not deny that the information would be useful. Rather they worry that spending so much money on such a large project may be an inefficient use of funds.

Still unresolved is what to use as a starting material for the sequence project. One possibility is the DNA from a hydatiform mole. Such DNA can be produced in large quantities, but may be inappropriate as it has aberrant genetic properties. A second possibility would be to use material from a variety of different sources, perhaps a different individual for each chromosome. But critics worry that any choice will necessarily exclude information on the diversity of human genetic material. (Extracted from Nature, Vol. 321, 22 May 1986)

More AIDS research

Pieces of DNA might be designed to bind to viral DNA to prevent genes from being expressed. Dr. P. Zamecnik of the Worcester Foundation for Experimental Biology thought the technique might be useful in combating AIDS. Researchers made a variety of DNA fragments to known AIDS DNA and added the fragments to cultures of human cells infected with the virus. Some fragments produced 95 per cent inhibition. The degree of effectiveness depends on which gene the fragment binds to. The most effective antigene binds to the tat-3 gene, which is unique to the AIDS virus and which plays a role in activating all other viral genes.

Malnutrition may be a cause of the rapid spread of AIDS in Africa. Vitamin deficiency and other aspects of a poor diet seem to lower the resistance of people in Africa to the virus. This might explain why both men and women there are equally infected.

So far, there are few signs that the AIDS virus has spread into areas of Africa where people are severely malnourished, such as Ethiopia and Sudan. If the virus does spread to these countries, however, the disease could move within the population far faster than in other parts of Africa, which have already seen a tenfold increase in the prevalence of the virus in some groups of people over the past three years.

Scientists have postulated that there is an as yet unknown factor which is helping the virus to spread equally in both men and women in Africa. This factor might simply be that the immune systems of both men and women in Africa are less able to fight infection because of their poor diet.

Epidemiologists in Paris presented new data on the spread of AIDS in some parts of Africa. Among Kenyan prostitutes living in Nairobi, the incidence of antibodies to the AIDS virus has risen from 4 per cent in 1981 to 59 per cent in 1985.

In another study, at the Mama Yemo Hospital in Kinshasa, the capital of Zaire, epidemiologists looked at 368 young children in hospital. The scientists found that 11 per cent of the children had been infected with the AIDS virus, compared with just 1 per cent in a control group.

The researchers say that the infected children had all had blood transfusions or medical injections in the previous two years. (Extracted from New Scientist, 3 July 1986 and 28 August 1986)

Enzymes repair damaged DNA

DNA is repaired in an orderly priority system, according to researchers at Standford University. When DNA is damaged, enzymes in all cells undertake repairs. In mouse cells, active genes damaged by exposure to ultra-violet light are repaired before inactive genes. Over 24 hours, 85 per cent of the active DNA was repaired, versus 22 per cent of the inactive genes. It may be that the repair enzymes can physically get to active DNA more easily than to the inactive DNA. Both genes studied are proto-oncogenes. (Extracted from New Scientist, 19 June 1986)

Single gene may predispose to heart disease

A single gene, present in about 15 per cent of the population, may carry a tendency towards development of heart disease. Ronald M. Krauss and Melissa Austin of the Lawrence Berkeley Laboratory, USA, base their hypothesis on a study of lipoproteins in the blood of 79 people who are members of eight extended, multigenerational families. The blood from those people show two distinct patterns of low-density lipoproteins. The less common pattern, occurring in about 15 per cent of the subjects, has a predominance of small, dense lipoproteins. People with that pattern also had levels of triglycerides and other blood lipids normally associated with high heart disease risk, although none of the people in this particular study had any overt symptoms of heart disease. The risk pattern seemed to run clearly in families, but only

in individuals over 40, suggesting to the researchers that it is caused by the presence of a gene that is not active until later in life. They plan a follow-up study of 200 families. (Source: Reprinted with permission from Chemical and Engineering News, 23 June 1986. Copyright 1986 American Chemical Society)

New fertility-regulating hormone discovered

A new hormone that helps regulate fertility in mammals has been discovered independently by two groups of researchers at Salk Institute, La Jolla, Calif. Research teams led by Wylie Vale and Roger Guillemin have each isolated and purified from pig ovaries a protein very similar in size and structure to the ovarian protein inhibin. The functions of the two proteins, however, seem to be exactly opposite: inhibin suppresses the secretion of follicle-stimulating hormone, or FSH, and the new protein stimulates it.

Inhibin itself was identified and characterized by Guillemin's group only last year. It has been found in two forms, called A and B, which share a common α-subunit.

Inhibin has been found in the gonadal fluids of several species of mammals. Its function seems to be to inhibit the pituitary gland from secreting FSH. When it is secreted, FSH causes the follicle to grow and mature.

Both Guillemin and Vale noticed in purifying inhibin a related substance that stimulated, rather than inhibited, FSH secretion. Guillemin's group calls this second substance activin and Vale's calls it follicle-stimulating hormone releasing protein or FRP. Both groups also find that the subunit in their newly isolated protein is the β_A-subunit of inhibin.

Earlier work in Guillemin's laboratory has shown that each of the subunits - α, β_A, and β_B - is produced at the direction of its own messenger RNA.

The new protein should be a prime candidate for treating infertility in women. FSH production can also be stimulated by another hormone, gonadotrophin-releasing hormone, or GnRH, produced by the hypothalamus. The new protein is more specific in its action than GnRH, which stimulates production of a second hormone, luteinizing hormone, as well as FSH. Such specificity makes it a better candidate for treating certain types of infertility. (Extracted with permission from Chemical and Engineering News, 7 July 1986. Copyright 1986 American Chemical Society)

Dystrophy gene proves mysterious

Many molecular biologists, working in more than 20 laboratories throughout the world, are working on the genetic defect that yields Duchenne muscular dystrophy (DMD). They have pinpointed the region of DNA on the X chromosome that creates - when disrupted - the progressive and ultimately fatal wasting of muscle that characterizes this disease. Even so, cure or even treatment is still remote. Researchers still know nothing about the nature of the gene (or genes) that causes the disease, and the new research suggests that attempts to discover what the gene does - and so understand the biochemical basis of the disease - will be difficult.

The exact nature of the mutations causing many hereditary diseases is still obscure. The common Duchenne form of dystrophy is a sex-linked disease and affects one in every 4,000 newborn boys, causing muscular weakness. The boys ultimately die, usually from heart failure, by the second or third decade of life. Classical genetic observations revealed that the mutation was carried on the X chromosome. The defect was then mapped to a relatively small region of the X chromosome by the chance discovery of a handful of cases of muscular dystrophy in girls. These girls acquire the defect by a freak translocation of DNA between one X chromosome and an autosome (non-sex chromosome). With their normal X chromosome inactivated, the girls succumb to DMD as the translocation disrupts the DMD gene.

In recent years researchers have cloned segments of the normal X chromosome to see how they map to the X chromosomes of boys with DMD. The chromosomes of most of these boys are missing segments of DNA. The deletions may be large or small, but the areas of overlap between them should help to reveal exactly what bit of DNA is responsible for the disease. Scientists are also trying to move in on the area of the suspected mutation by isolating overlapping sequences of DNA. Instead of finding well-localized deletions or alterations of the DNA in boys with DMD, the researchers have entered a peculiarly shady stretch of the genome, which so far has refused to give up its secrets.

From the evidence to date, it looks as if the muscular dystrophy gene is very large, and that mutations anywhere along its length can lead to DMD. To locate the critical region more precisely, researchers have now cloned a large piece of DNA thought to be near the middle of the gene. They used this DNA to map parts of DNA missing in hundreds of affected boys.

The results show a confused picture of deletions, often enormous in size, cropping up at sites sometimes close together, sometimes spaced up to a gene's length apart. These results might mean that the dystrophy gene behaves in unpredictable ways, experiencing greater rates of mutation, or even rearrangements and inversions of long stretches of DNA. Alternatively the dystrophy locus may actually be several genes. Whatever the explanation, dystrophy seems to be a hereditary disease quite unlike others, and the solution to its cause may remain shrouded in mystery for some time. (Source: New Scientist, 17 July 1986)

New vaccine technology

Viral envelopes secreted from cells infected with hepatitis B virus and used as a hepatitis B vaccine can be genetically engineered to carry foreign genes on their surfaces; thus they have the potential to be used in the production of vaccines for a range of other diseases. Delpeyroux et al. of the Institut Pasteur, France describe the insertion of a synthetic polio virus sequence into the gene for the major hepatitis surface antigen S. The polio antigen was expressed in biologically active form on the hepatitis envelopes: the engineered envelopes reacted with poliovirus-specific antibodies and also elicited poliovirus-neutralizing antibodies in mice and rabbits. Much of the immunogenicity of the hepatitis S antigen was lost, but the envelopes were assembled correctly and secreted from mammalian cells growing in culture. The secretion of engineered envelopes in large quantities should facilitate vaccine production; these are noninfectious envelopes that are of proven efficacy and safety. (Source: Science, Vol. 233, 25 July 1986)

Cloning and expression

Two companies announced that they have used rDNA to produce potentially important proteins. Integrated Genetics (Framingham, MA) reported the first cloning and expression of human Protein S, a co-factor to the anticoagulent Protein C, which could be used in the treatment of certain blood

clotting disorders. Biogen produced Mullerian inhibiting substance (MIS), which will be tried against several female reproductive tract cancers. MIS is made naturally in male embryos, where it causes the precursor tissue of female reproductive organs to shrink and disappear. (Extracted from Bio/Technology, Vol. 4, July 1986)

Advances reported on cystic fibrosis

A genetic marker for cystic fibrosis has been identified, opening new possibilities for research. The marker's presence in a sample allows easy detection of carriers and children with the disease, but is not specific enough to be used as a screen for the general population. The cystic fibrosis gene itself has not yet been found, but it is on chromosome 7 and very close to the marker gene. Researchers have also found a defect in cell function of people with cystic fibrosis.

Since Paul Quinton of the University of California at Riverside discovered in 1983 that sweat gland cells of cystic fibrosis victims are not very permeable to chloride ions, researchers have focused on the channels that carry chloride across cell membranes. Now they have shown the problem to be at the level of what controls the channel, not at that of the channels themselves. Researchers at the University of Alabama at Birmingham and at the University of Iowa in Iowa City and Case Western Reserve University in Cleveland made the discovery at the same time.

Normal chloride movement pulls water from the tissues to the lung lining; without this water, mucus in the lungs is too thick and sticky, and interferes with normal lung function. One in 2,000 US Caucasians is born with the disease, and half die by the age of 21. Current therapy consists of chest pounding to loosen the lung secretions, and antibiotics for the frequent lung infections.

The two groups independently found that the channels in cystic fibrosis patients' cells failed to respond to a chemical that usually stimulates chloride movement. The channels sit in the cell membranes, and when the cells were disrupted and just the membranes were tested, the channels responded properly, indicating that the problem lies in the cell's control over the channel. (Extracted from Medical World, 28 April 1986 and Science News, Vol. 130, No. 6, 9 August 1986)

Monoclonals block graft rejection

Bone marrow transplants can be kept from causing graft-versus-host disease, if monoclonal antibodies are used to remove the T lymphocytes from the donor marrow. Host-versus-graft rejection still remains a problem. Scientists at the University of Cambridge, UK, have discovered that the rejection is caused by two types of lymphocytes in the peripheral blood. They succeeded in blocking marrow graft rejection, again by using monoclonals to remove T cells, but this time killing them in the host. This may improve prospec' not only for marrow transplants, but for other tissue transplants as well. The Cambridge team had previously found that when all T cells were destroyed in mice, the mice accepted marrow grafts. Marrow transplants are done after the recipient has been irradiated to kill the marrow which produces T cells, so T cells in peripheral blood must cause the rejection observed in humans.

The Cambridge team used monoclonal antibodies that specifically attack certain subsets of peripheral T cells along with marrow grafts in mice to find out which ones are responsible for rejection. They irradiated mice to destroy their marrow, then transplanted marrow with the T cells removed. Some of the mice were also treated with monoclonal antibodies against two of the host's subsets of peripheral T cells, L3T4+ and Lyt-2+. (Extracted from New Scientist, 18 September 1986)

Cot deaths linked to faulty enzyme

An enzyme defect that prevents babies from metabolizing fat to provide the energy their brains require could be responsible for between 5 and 7 per cent of cot deaths, according to researchers at the Sheffield Children's Hospital.

Following studies of 700 consecutive cases of cot death the researchers identified defective activity of the enzyme known as medium chain acyl-coenzyme A dehydrogenase as responsible for up to 7 per cent of cot deaths in the Sheffield area. The defect is an autosomal recessive inherited defect. The abnormality means that babies cannot metabolize fat and are unable to make the sugars and ketone bodies that their brains need.

When researchers analysed liver samples from the 200 cot death babies, they found fatty changes in 14 of them identical to those in the livers of children with Reye's syndrome - the disease that has been linked, in some cases, with aspirin. In Reye's syndrome, the fatty changes are usually caused by a generalized malfunction of the mitochondria. But, by careful histochemical analysis, the Sheffield team pinned down the cause of the fatty change in the cot death babies to a single enzyme - medium chain acyl-coenzyme A dehydrogenase.

Fat is normally transported into the mitochondria where it is metabolized by the process of beta-oxidation into acetyl CoA, which enters the Krebs cycle, and ketone bodies. A vital part of beta-oxidation involves medium chain acyl-coenzyme A dehydrogenase; when this enzyme's activity is defective, fat accumulates within the cells and the production of energy is curtailed. Howat and his team found further evidence of a build-up of fat in the cells of the kidney tubules and in heart muscle and skeletal muscle of the babies with the defect.

Howat emphasized that his team's work on the enzyme defect is still at an early stage and would not be completed for another year. But he and his colleagues believe that their results are conclusive enough to begin to advise mothers in the area who have already lost one baby in this way on how to prevent the same thing happening again. The abnormality is rare, he stressed, affecting about one in 12,000 of the population. So far, screening for the defect is available only in the Sheffield area.

"Testing for the enzyme defect using amniocentesis techniques is probably not ethical", said Howat, because the effects of the abnormality can be counteracted and abortion would not be an option if the baby were found to have the defect. For now, the doctors in the Sheffield team use a snippet of skin or cultured lymphocytes from the baby to test for the defect.

The identification of one enzyme deficiency as a cause or contributory factor in some deaths suggests that perhaps other, similar defects might be responsible in other cases. (Extracted from New Scientist, 18 September 1986)

Research on animal genes

Pea genes help increase wool production in sheep

By inserting pea genes which code for a high-sulphur protein into alfalfa, Australian scientists anticipate increasing wool production in sheep by 10 to 100 per cent. The research by the

CSIRO Division of Plant Industry is fundamental to designing livestock diets with higher percentages of usable protein.

Because wool contains a high content of cysteine, a sulphur-containing amino acid, a sheep's diet must be rich in the element. For sheep, cysteine and methionine are essential amino acids.

Forage-plant proteins are typically high quality, but most of the sulphur amino acids are quickly degraded to hydrogen sulphide and urea in the rumen, the first stomach. When sulphur amino acids are introduced into the sheep's second stomach or intravenously, the rate of wool growth can be increased dramatically, up to 100 per cent.

The pea protein p-albumin-1 contains 11 per cent cysteine, 1 per cent methionine and resists rumen breakdown. Armed with this knowledge, Dr. Thomas Higgins and his team deduced that the protein would be an excellent dietary supplement for sheep. The problem was to get the pea's gene for p-albumin-1 into alfalfa.

They tried using tobacco tissue cultures, simply because of the experience and success many genetic engineers and breeders have had with that plant. E. coli and Agrobacterium tumefaciens were used to transfer the Pisum satigum gene. Using tissue culture methods, the scientists are trying to get expression in alfalfa, then perhaps clover or other pastoral species that sheep eat.

Alfalfa leaves should be ready for protein analysis before the end of the year. This depends on which hybrids regenerate from tissue culture. From tissue cultures, alfalfa may take four to six months to regenerate, whereas the tobacco cells take only 10 to 20 days. Seeds could be on the market within five years.

The plants still have to prove that they can provide sufficient quantities of the sulphur-bearing protein. If the protein comprises 3 to 4 per cent of the total leaf protein, wool production is likely to increase by 50 per cent. Unable to predict where the gene incorporates or the extent of gene expression, the team must rely on trial and error.

No side effects from sulphur supplements have been noticed. Assuming that basic nutritional needs are provided in forage or feed, quality of wool depends primarily on the breed. Although goats have not been tested yet, the high-sulphur protein could benefit their wool growth.

The researchers believe that the additional growth of wool will not nutritionally disadvantage a sheep or goat in any way. However, the extra weight could be a problem. For example, after heavy rain when the wool becomes sodden, an animal with the extra weight could become more easily bogged.

Another team at the Sydney laboratories has isolated two bacterial genes which control the two-step enzymatic conversion of hydrogen sulphide to cysteine. They intend to put the genes into sheep embryos, thus providing a plentiful cysteine source.

Australian scientists have also created the world's first "transgenic sheep" by inserting into an embryo a gene that codes for sheep growth hormone. The development is seen as a major step towards developing much larger, leaner and faster-growing animals. It will cut the time required for breeding improved livestock.

The transgenic sheep was created by inserting a gene for sheep growth hormone when the embryo comprised a single cell. The scientists then transferred the embryo into a surrogate mother. The sheep, a ewe, was born at the end of April this year.

It will be around six weeks before the scientific team know for sure if the extra genes are producing additional growth hormone, but CSIRO, Australia's largest research organization, is hopeful of success. Laboratory examination had shown that the genes had become incorporated into the cells of the transgenic sheep. In about five weeks, the extra growth hormone will be triggered into action by a dose of zinc, which will "switch on" the gene, by activating a regulatory sequence attached to the gene itself.

If successful, the technique could produce sheep up to 50 per cent larger than current animals. The transgenic sheep should also grow up to a third faster. (Extracted from Genetic Engineering News, July/August 1986 and New Scientist, 10 July 1986)

Luciferase gene cloned

Two scientists at the University of California in San Diego have cloned the gene that makes luciferase. UCSD researchers Marlene A. DeLuca and Donald R. Helinski are turning bacteria into biological factories for the enzyme. The light-generating substance is used to tag chemicals and genes so their movements and reactions can be tracked. Many companies hope to use luciferase for faster, cheaper tests to detect disease or bacterial contamination. San Diego's Analytical Luminescence Laboratory Inc. already sells such kits, using firefly luciferase, to screen urine samples for bacteria. (Extracted from Business Week, 23 June 1986)

Crabs may improve a biosensor

A crab has led to the development of a new type of biosensor that may be faster and less expensive than existing devices, according to Stuart Belli, a post-doctoral research fellow at the University of Delaware (Newark). Belli built the biosensor by attaching the antennules of blue crabs to electrodes. The device can selectively detect amino acids in solution down to three parts per million, he says, with a response time of seconds. Most other biosensors require minutes. Belli's device could theoretically have a response-recovery time of milliseconds - the limit of nerves. Sensitivity could also be increased because crabs can detect much lower levels of amino acids. Belli plans to experiment with such aquatic organisms as crayfish to detect other biological molecules. (Source: Chemical Week, 17 September 1986)

Simple animals lack body blueprint

Genetic analysis of mutant fruit flies with misplaced legs and antennae recently led to the discovery that a group of genes with a common short DNA sequence, the "homeobox", organizes the layout of the fly's body as it develops. Scientists later found homeobox genes in the DNA of a wide variety of animals, which suggests that a basic "blueprint" gene dictating body plan is widely conserved among animal groups.

Most of the species with the blueprint gene share one important characteristic: their bodies are segmented in the early stages of embryonic life. This suggests that the organizer gene somehow influences the head-to-tail subdivision of the body. But a few species with the gene are not segmented at any stage. This discovery led the scientists to consider a much broader base for the operation of the genes with homeoboxes.

Using molecular probes from homologous genes in fruit flies and mice, they searched for similar DNA sequences in 13 organisms, ranging from starfish down to slime moulds. As the researchers expected, the segmented invertebrate animals did have the blueprint DNA sequences. But so did some of the unsegmented animals, such as snails and sea slugs. Among even lower organisms, the signal gradually grew fainter until in nematodes, flukes, (trematodes), yeasts and slime moulds, the homologous genes were absent.

Clearly, the genes with the homeobox are important in guiding the development of all animals complex enough to have a body cavity (coelom) separate from the gut. In simpler, acoelomate, animals they are not required. It might soon be possible to use the characteristics of the body blueprint gene to build up new theories about the structure of the animal kingdom and the evolutionary family tree. (Source: New Scientist, 4 September 1986)

Extra genes reveal the route to resistance

Insects, with their short generation time and ability to mutate rapidly, always seem to be one step ahead of the measures taker against them. Strains of insects that are resistant to chemical pesticides appear almost as soon as a new agent is devised. A team of French toxicologists of the Institut National de la Recherche Agronomique, believe they may predict trends in pest resistance several generations before they appear.

Insect pests have a limited ability to inactivate lethal chemicals absorbed through their cuticle; this is accomplished by enzymes that convert the toxins to harmless derivatives that can be excreted. Evidence has been accumulating gradually that pests are developing an efficient system of defence by boosting their ability to neutralize poisons. In resistant strains, insects build up a large reserve of the enzyme in their blood so that it neutralizes any pesticides entering the body simply by overwhelming them by a process of gene amplification.

Taking their cue from Californian scientists who discovered a powerful detoxifying enzyme, called B1 esterase, in mosquitoes, the French researchers traced the gene that codes for the enzyme. When they compared the genome of their own pesticide-susceptible mosquitoes with that of a resistant strain isolated in California, they found hundreds of copies of the esterase B1 gene in the mutant.

Fortunately for those involved in pest control, an insect has to pass through several generations to ensure that a fully resistant mutant with sufficiently amplified genes is selected. This lag could give scientists the time they need to outwit their six-legged enemies. (Source: New Scientist, 25 September 1986)

Monoclonal antibodies developed to combat fish diseases

Oregon State University researchers are adapting monoclonal antibody (Mab) techniques to combat diseases afflicting salmon and trout, which are the most important commercial and sport fish in the Pacific Northwest.

The diseases, IHN virus (infectious hematopoietic necrosis) and BKD (bacterial kidney disease), have plagued hatchery production of salmon and trout throughout the Northwest. Regional losses attributed to the diseases amount to millions of fish per year, according to estimates obtained from state and federal fishery agencies.

Since the diseases can quickly reach epidemic proportions at an affected hatchery, rapid diagnosis is critical. Conventional diagnostic methods can take as long as two weeks to provide positive results, but the Mab techniques being adapted by the Oregon researchers will allow identification of pathogens in a matter of hours.

The researchers have sought to identify separate strains of bacterial disease, to improve their diagnostic procedures with both viral and bacterial diseases, and ultimately to build vaccines against both. Each goal involves the use of hybridomas. To determine whether different strains in fact existed, the researcher began by obtaining pure strains of isolates of the bacteria from three different locations. Then, following standard procedures for production of hybridomas, mice were injected with the bacterial strains, sacrificed when they showed antibody development, and their spleen cells fused with mouse myeloma cells. Screening of the hybridomas using ELISA showed that there were indeed three separate strains of BKD.

Neutralization assays of the 600 secreting hybridomas ultimately identified two of choice that were secreting neutralizing antibodies. From these the laboratory has produced Mabs against the two primary IHN strains. (Extracted from Genetic Engineering News, July/August 1986)

A DNA fingerprint for killer bees

Africanized bees, often called killer bees, have been on the increase ever since they were first released by accident from experimental hives in Brazil 28 years ago. Today most of South and Central America is occupied by Africanized bees ousting the more placid European variety.

Already a few isolated colonies are turning up in the United States, and fears are growing that these insect aliens will be swarming across its southern borders within the next five years. Africanized bees are very aggressive. They readily sting and will pursue their victims over considerable distances. Because they are difficult to handle and swarm frequently, Africanized bees are less suitable than European bees for honey production and the pollination industry. What is worse, even when the Africanized bees become established in an area and have had a chance to hybridize with local European bees, their ferocious characteristics are retained. The United States Department of Agriculture estimates that the beekeeping industry stands to lose up to $58 million a year when Africanized bees invade the US. Isolated introductions like one found in California last summer can be exterminated, and commercial apiaries in the area kept under quarantine, but as the numbers of Africanized bees increase, more rigid control methods will be required. Stocks of commercial breeders would have to be certified as either non-African or as acceptable hybrids. Breeders would regularly have to introduce new queens to commercial hives to prevent Africanized bees from taking over. In addition, breeding programmes could be instigated to find more docile hybrids.

Africanized bees are structurally very similar to European bees of Italian descent. In fact, Africanized bees and European bees are both classified as Apis mellifera, although grouped as separate subspecies. Hybrids between the two are even harder to tell apart, and at present identification is achieved through complex

morphometric analysis, including careful measurements of characters such as the veins in the wing.

Research at the Lawrence Berkeley Laboratory at the University of California has revealed a way to distinguish Africanized bees from European ones. Using genetic engineering techniques, the differences between the DNA of the two subspecies has been discovered.

The probes revealed fragments of DNA either present in the Africanized sample and absent in all the European samples or vice versa. These were the consequence of at least 12 differences in the DNA. It is intended to take more samples from a wider range of bee populations to verify this conclusion and to establish whether these fragment differences are unique to the African subspecies and can also be used to identify the hybrids. (Extracted from New Scientist, 31 July 1986)

Insect virus as super-vector

An insect virus that could become a second-generation recombinant vector is gaining a quiet following in biotechnology. The baculovirus is easily engineered and achieves both high synthesis rates and complex processing of recombinant products. A number of companies are investigating the system, but a Connecticut company called MicroGeneSys claims it has already foiled the competition.

The system is based on a cell line established in the late 1970s from the pupal ovarian cells of the moth Spodoptera frugiperda. When infected with baculovirus carrying a foreign gene, these cells can secrete recombinant products complete with post-translational modifications such as phosphorylation and glycosylation. The system may therefore dispense with costly downstream processing. Mammalian cell cultures offer the same processing advantages, but are not as prolific.

The productivity of the baculovirus derives from the efficiency of the viral promoter of the gene encoding the protein called polyhedron, the sole component of a crystalline matrix that acts as a protective shield for viral particles existing outside their insect host. Caterpillars eat the matrix and release the particles, which then temporarily suspend polyhedron synthesis. When the caterpillar is near death, the virus resumes matrix protein production until roughly 20 per cent of the larval host consists of polyhedron.

MicroGeneSys has already harnessed this productivity for a hepatitis-B vaccine which will enter clinical trials this year. The company is also developing vaccines against acquired immune deficiency syndrome and malaria infections. (Extracted from Nature, Vol. 321, 19 June 1986)

Research on plant genes

RNA plasmid discovered in maize mitochondria

Research on RNA continues to turn up surprises, the latest being the discovery of apparently independently replicating single- and double-stranded RNA species in maize mitochondria. Because these RNA molecules are unrelated to the DNA of the mitochondrial genome, their discoverers, Patrick Finnegan and Gregory Brown of McGill University, Montreal, have called them RNA plasmids. Their origin is currently obscure, but the McGill researchers are in the process of cloning and sequencing the four new RNA molecules they have found. The sequences may reveal some hint of their origin, if for instance they contain telltale remnants of viruses or transposable elements. The identification of any protein-coding regions would also be of considerable interest.

There are in fact four different mitochondrial DNA (mtDNA) variants in maize that are known as S, C, T, and M, the first three of which result in defective pollen production. So far the newly identified RNA plasmids have been recovered only from the S type. Restriction to the S strain implies that the plasmids are of fairly recent origin, having arisen since the divergence of the S, C, T, and M varieties. (Extracted from Science, Vol. 233, 8 August 1986)

Luminous gene tags

Among the most important questions worrying the public and federal regulators about using genetically engineered microbial pesticides in the field is if the bugs survive, where will they go? Now, ways to answer that question are coming from several laboratories where scientists are discovering fast and accurate methods for spotting gene-altered microbes in the environment.

One system under development at the Boyce Thompson Institute for Plant Research at Cornell University tags gene-altered microbes with a natural protein that glows in the dark. Scientists at Monsanto Co. in St. Louis are working on a method that turns genetically engineered bugs a vivid blue. Scientists also say that tracking methods will help prove that most gene-altered microbes will not spread out of control.

But because the tracking systems are based on additional genetic transplants, the US Environmental Protection Agency is likely to require extensive and expensive safety testing before allowing them to be used outdoors.

In the midst of research on a plan to make a common soil bacteria, Pseudomonas fluorescens, produce a natural pesticide, Monsanto scientists discovered that the bug was unable to break down lactose, a natural sugar. They also saw a way to put a tag on the bug.

Bacteria synthesize sugars to gain carbon, their principal source of energy. The researchers knew that another common bacteria, E. coli, which is in the intestines of many mammals, produces an enzyme called beta-galactosidase, which breaks down lactose. Two genes in the chromosomes of E. coli control the production of the enzyme.

By using genetic engineering techniques, Monsanto scientists took the two genes from E. coli and put them into Pseudomonas fluorescens. They then sprinkled the bacteria on a gel mixture containing lactose as the sole nutrient. The bacteria that accepted the genes thrived on the gel, formed colonies and were visibe as tiny white dots.

Monsanto scientists further refined the system by adding a chemical dye to the nutrient gel. Bacteria with the E. coli genes were able to synthesize the dye and turned blue.

Monsanto hoped to use the marking system with its other genetic engineering projects to convince regulators and critics of biotechnology that microbial pesticides are dangerous.

At the Boyce Thompson Institute, scientists have developed a marking system that makes gene-spliced organisms glow. The source of the luminescence is the enzyme luciferase that is found

in bacteria that live in the sea. Four years ago, Dr. Thomas O. Baldwin, a researcher at Texas A&M University, found that two genes in the bacteria produce luciferase.

Boyce Thompson researchers transplanted the genes into rhizobium. They also spliced into the chromosome of the rhizobium a series of genes that act as natural thermostats, which controlled the production of the luminescence genes.

The researchers then coated soybean seeds with the altered rhizobium, planted them in the laboratory and, weeks later, when the plants were nearly mature, pulled them out of their pots. Rhizobium form little nodules in the roots. When the scientists cut the nodules open, they emitted a blue-green glow bright enough to be seen in the dark. Scientists can also use X-ray film to detect the luminescent bacteria. The Boyce Thompson Institute, however, has not yet asked the Government for permission to test the system outside the laboratory. (Extracted from International Herald Tribune, 19 September 1986)

Gene inserted into sunflowers

Chesebrough-Pond's Stauffer Chemical Co. (Westport, CT) has introduced and expressed a foreign gene in sunflowers. The gene codes for a marker protein leading to antibiotic resistance; the achievement could lead to the development of disease- and insect-resistant sunflower plants. (Source: Bio/Technology, Vol. 4, June 1986)

Vanadium-containing nitrogenase isolated

The enzyme nitrogenase, which enables bacteria to fix nitrogen, is complex, but research over the last 25 years suggested that the enzyme and its genetic determinants were remarkably similar in all nitrogen-fixing bacteria. Now work at the AFRC Unit of Nitrogen Fixation at the University of Sussex, UK, suggests that this picture may be over-simplified. It is well known that molybdenum plays a crucial role in biological nitrogen reduction, being present in one of the component proteins of nitrogenase, but research carried out by Dr. P. E. Bishop shows that vanadium may also play a key role in some species.

Working with Azotobacter vinelandii, a common soil bacterium, Dr. Bishop and his colleagues, both in the USA and UK, showed that it possesses an "alternative system" for nitrogen fixation which, surprisingly, is antagonized rather than stimulated by molybdenum. This alternative system is genetically distinct from the conventional one. Using a genetically engineered strain of the closely related species Azotobacter chroococcum, scientists at the AFRC Unit have shown that it, too, has an "alternative nitrogenase", with many properties in common with conventional nitrogenase. But the enzyme contains vanadium, not molybdenum. This finding confirms disputed reports dating back 50 years that vanadium can replace molybdenum for nitrogen fixation. The research not only pinpoints the first biological role for vanadium, but also raises the possibility that nitrogenase based on other transition metals may be discovered. (Source: Biotechnology Bulletin, Vol. 5, No. 7, August 1986)

Gymnosperm tissue culture

Work being carried out by Pramod Gupta and Don Durzan (University of California, Davis) on somatic polyembryony in sugar pine has revealed one of the new successes in generating somatic embryos, and in large numbers, in gymnosperm tissue culture. Furthermore, the team's suspension cultures were derived from embryos excised from mature seeds that had been stored for nearly five years.

Most successes in gymnosperm culture have been in the promotion of shoot formation (organogenesis), usually on explanted cotyledons. Since these shoots typically form in bunches and without roots, each shoot must be individually separated and removed to a rooting medium. Many shoots do not root readily, and those that do must then be moved through a series of repottings and changes in environment until they can be put out in the field. It is a labour-intensive process and therefore expensive.

Somatic embryogenesis in conifers (as in all plants) offers the potential of large numbers of embryos, all separate from each other; roots already part of the structure because there is a natural division of labour as embryos differentiate; and dormancy induction in the embryos and/or encapsulation for efficient storage and delivery to the forest. The elucidation of proper procedures for initiation and growth of the proembryonic suspensions must go hand-in-hand with the development of the bioreactor and delivery technologies. (Source: Bio/Technology, Vol. 4, July 1986)

Direct gene transfer

Direct gene transfer between plants without the help of bacteria has been reported by Professor Virginia Walbot of Stanford University. Strong electrical fields have been used to transfer DNA fragments into corn cells. This method of electroporation is expected to prove a useful instrument for the transfer of characteristics between different plants when traditional methods of genetic engineering are useless. Electroporation could help to develop new types of corn in short time. (Source: Journal of Biotechnics '86, Hannover)

Research on yeast and fungus genes

Enzymes for pulping wood

For years researchers have been trying to find a better way to separate lignin from cellulose in wood. Traditional pulping methods use a lot of chemicals and energy, and they can be an environmental nuisance.

Repligen, Cambridge, Mass., claims to have isolated the active enzymes that break down lignin, cloned them, and produced them recombinantly. The company is now supplying the enzymes to its independent development partners - France's St. Gobain and Switzerland's Sandoz.

The developers would eventually like to replace existing know-how with enzymes. The key element is the white rot fungus Phanerochaete chrysosporium. The ability of the enzymes derived from the fungus to separate lignin from cellulose has long been known, but there has not been a way to gather enough together in one place to treat wood economically.

The Repligen technique promises to make enough enzymes available to transform pulp-making in all stages of the process. It could partly remove lignin to reduce energy requirements in mechanical pulping processes. As a catalyst in oxygen and peroxide bleaching, it could eliminate chlorine or chlorine dioxide. It could modify residual lignin to improve the brightness stability of mechanical pulps, and it could decolourize bleach plant effluents. In tests at North Carolina State University and the Forest Products Laboratory

(Madison, Wis.), investigators have destroyed 95 per cent of the phenolic compounds in the effluent and removed 90 per cent of the colour. (Extracted from Chemical Week, 3 September 1986)

Research on viral genes

Hepatitis virus binding site identified

Scientists at the New York Blood Centre and the California Institute of Technology used protein synthesizing machines to identify the binding site on the surface of the hepatitis B virus by which it plugs into liver cells when it infects them. They found that a 27 amino acid-long stretch of the hepatitis B protein coat, called the preS protein, attaches to liver cells. This protein segment, by itself, elicits an immune response and blocks the attachment of hepatitis B virus. Knowledge of the virus binding site could serve as the basis for tests for hepatitis B infection and the detection of antibodies to the virus. It could also lead to cheaper and more effective vaccines. (Source: Genetic Engineering News, September 1986)

Researchers discover new AIDS virus gene

Scientists have uncovered evidence for the presence of a seventh gene in the genome of the virus that causes AIDS. The discovery sheds light on the complex life cycle of the virus and its interaction with the human immune system and provides researchers with another potential target for drugs to combat the fatal infection.

The gene, designated art, was discovered by a team of Boston-based researchers at Dana-Farber Cancer Institute, Harvard Medical School, and Harvard School of Public Health led by William Haseltine of Dana-Farber. The same group in collaboration with researchers at the National Cancer Institute discovered a sixth AIDS virus gene, designated tat, last year.

With the discovery of the tat and art genes, the AIDS virus emerges as the most complicated virus of its class. The AIDS virus is a retrovirus. Such viruses contain RNA rather than DNA as their genetic material. In the process of infecting a cell, retroviruses produce an enzyme called reverse transcriptase, which allows production of DNA from the viral RNA. This DNA integrates into the infected cell's genome where it is known as a provirus and subsequently directs the production of new viral genetic material. (Source: Extracted with permission from Chemical and Engineering News, 2 June 1986. Copyright 1986 American Chemical Society)

Research instrumentation

DNA sequencing goes automatic

Leroy Hood and his colleagues at the California Institute of Technology have developed the first automated DNA sequencing machine. Their DNA sequenator can read off nucleotides at a rate that may soon approach 8,000 bases a day, which is at least tenfold higher than is currently achieved manually and at a small fraction of the current cost per base.

DNA sequencing remains a time-consuming and technically demanding exercise. By making the task largely automatic and by boosting the rate at least an order of magnitude, molecular biologists will be tempted to shift their thoughts to projects currently too ambitious to attempt.

The DNA sequenator joins three other instruments developed by the Caltech team - a protein sequenator, a DNA synthesizer, and a protein synthesizer - to form what Hood describes as a microchemical facility.

The Caltech team's DNA sequenator is based on the enzymic method, at least partly because it represented a more promising prospect in the face of the chemistry that would be involved. (Extracted from Science, Vol. 233, 4 July 1986)

New biosensor

A new biosensor using the antennules of blue crabs has been developed by S. Belli of the University of Delaware. The new device may be faster and more sensitive than existing biosensors. The unit can detect amino acids in solution down to 3 ppm, with a response time of only seconds. The response-recovery time could be limited to milliseconds, and sensitivity could also be improved. Organisms such as crayfish might be utilized for other biosensors. (Extracted from Chemical Week, 17 September 1986)

General

Spotlight on biocommunication

Scientists expect new findings in the field of biocommunication to have far-reaching consequences for both biotechnology and medicine. Physicists, biologists and medical researchers from eight European countries are currently preparing a research project which, on the basis of quantum biology, will investigate electromagnetic communications between biological systems.

It has been established that allergic patients are extremely sensitive to electromagnetic waves at individually varying frequencies. Experiments have also proved that unlike their healthy counterparts, tumour cells communicate with each other by means of photons. The application of the principles of biocommunication could well provide new insights into the causes of cancer and pave the way for the development of new drugs which "resocialize" the disturbed patterns of communication between tumour cells without causing adverse side effects.

Living organisms react to a broad spectrum of magnetic, electrical and electromagnetic influences, ranging from extremely long radio waves to UV radiation. Professor H. Fröhlich postulated the existence of long-range interaction in living cells. Recent findings have served to confirm this theory. There are now clear indications that coherent waves, especially those in the optical spectrum, play an important role in communication between cells.

The advent of extremely sensitive measuring techniques has effectively opened up the entire sphere of biocommunication to scientific investigation. It is expected that this will lead to the development of new methods of diagnosis and treatment for conditions which result from disturbances in biocommunication. The effect of environmental factors on the natural process of biocommunication will also be investigated - for example in relation to the healthy development of plant life. Homeopathic medicine is another field which will benefit from new scientific findings as well as the advances in measuring technology.

The scientists engaged in the research project all agree that biocommunication will provide scientific explanations for phenomena which previously belonged to the realm of speculative interpretation, such as the various effects of

acupuncture, weather conditions and underground water courses on the human organism. (Source: Journal of Biotechnica '86, Hannover)

Perfecting polymers to release drugs

In the future, drug release may be mediated by ultra-sound. This is one of the potential advantages of the bio-erodible polymer technology for drug delivery developed by Robert Langer and his associates at MIT (Cambridge, MA). The technology, recently licensed to Nova Pharmaceutical (Baltimore, MD), augments Nova's existing licence with MIT, which covers drug delivery to the brain to treat diseases such as brain cancer. Nova and Celanese (New York, NY) have formed a joint venture, NovaCel, to apply this technology to treating other cancers, infectious diseases, and cardiovascular and nervous system disorders.

Langer has developed bio-erodible polymers that degrade by surface erosion, in a non-homogeneous manner.

Langer's polymers are polyanhydrides, which were originally synthesized to be used in textile fibres but were deemed unsuitable because of their hydrolytic instability. It is just this instability that makes them good candidates for drug release matrices, according to Langer. A polymer that is hydrophobic but has hydrolytically unstable linkages will erode heterogeneously. As it is hydrolyzed, a polyanhydride will degrade into its non-toxic acid monomers. As water is taken up, it hydrates the incorporated drug and initiates its release. The drug diffuses through pores that form as the polymer degrades. The rate of drug release can be controlled by chemical modification of the polyanhydride backbone; simple changes can alter the rate by 1,000-fold.

Langer has devised several methods to formulate the drug and polymer. The mixture can be compression- or injection-moulded into small implantable cylinders or pellets; it can also be hot-melted into microspheres for injection.

The polyanhydrides are biocompatible, non-mutagenic, and non-teratogenic. In vivo studies in rabbits and rats have confirmed in vitro observations that the polymers do release incorporated substances in a steady, controlled manner. Diabetic rats that received implants of insulin-containing polymer, for instance, maintained normal blood glucose levels during the implantation period.

While steady drug delivery is appropriate in many clinical situations, some conditions require "demand delivery". These include "an extra shot" of insulin to maintain a diabetic's blood glucose levels at mealtimes. Demand delivery would also be useful to control ulcers with gastric acid inhibitors and to alleviate respiratory distress with epinephrine.

Langer and co-workers have found that externally applied ultrasound can trigger drug release from these polymer matrices. Apparently, ultrasound enhances the erosion rate by causing the polymer to dissolve faster; water can enter the matrix more easily, and speed release of the drug. It may be that small bubbles form, breaking up the polymer.

Langer says that studies on the in vivo applications of ultrasound-mediated release are very preliminary, and have no clinical significance yet. Perhaps the greatest obstacle will be to determine the ultrasonic wavelength that degrades the polymer but does not destroy surrounding cells. (Extracted from Bio/Technology, Vol. 4, September 1986)

Liposome research: new paths for drug delivery

For about the past five years, a handful of small, privately owned companies in the US have been trying to turn solutions of microscopic bubbles - liposomes - into a better means of delivering drugs to specific sites in the human body.

While a product among them is at least one year away, one company, Technology Unlimited (Wooster, Ohio) - formed by a group of inventors to develop liposome technology - says it has broadened the commercial potential of liposomes by developing and patenting one that extends the range of intravenous drug delivery by bypassing the human body's immune system.

In drug delivery, one of many emerging applications for liposomes, researchers can fill the microscopic man-made cells - formed from phospholipid material such as egg lecithin - with a concentrated drug or hormone and introduce them intravenously into the body. Once in the bloodstream, the liposomes are scavenged by macrophages. In the process, the liposomes are broken down and carried by the macrophages to the liver and spleen where the liposomes are disposed of by the reticuloendothelial system (RES), a branch of the immune system. Most companies that have developed liposomes for delivering drugs have worked in concert with this sytem.

However, Technology Unlimited says that its system bypasses the RES by masking liposomes from recognition and uptake by macrophages. To accomplish this, the company covers the liposomes' membranes with sialic acid, a naturally occurring amino sugar, giving them characteristics of red blood cells, which macrophages will not attack. The company holds a patent (US 4,501,718) for the process.

Because of their sialic acid outer layer, the company says, red blood cells evade the macrophages for a prolonged period of time. Then one of the body's enzymes - endogenous neuraminidase - sloughs off the acid layer and exposes galactose residues, which as spent cells are identified and removed.

Using the sialic acid technology, Technology Unlimited has developed two main types of liposomes. One, which has a permeable membrane, allows a drug to escape at a specified rate within a large area of the body. It is eventually removed from circulation by the endogenous enzyme action.

The other type has an impermeable sialic-acid-coated membrane, which incorporates a molecule that targets the liposome to the desired site of action. The sialic acid coating masks foreign membrane constituents and permits the liposomes to remain in circulation until the targeting molecule has directed the carrier to the appropriate site of action.

Technology Unlimited is expected to receive a patent (US 4,603,044) on a class of compounds that target liposomes to the metabolic cells in the liver. A drug maker is working with the company to develop a diabetes treatment based on the patent. A potential use of Technology Unlimited's targeted drug delivery system is a treatment for the lethal complications of acquired immune deficiency syndrome (AIDS). Antitumour treatment is another team effort. It is already being tested on animals and clinical trials are expected to start within the year.

Within the realm of non-targeted liposome technology, the other liposome companies have more potential applications than they currently have the time or resources to develop. TLC, which is in the process of going public, takes advantage of the body's natural processes to deliver liposomes. Many of the liposomes are intercepted at an infection site, where the immune system has summoned a large concentration of macrophages. The liposomes eventually break down at the site, releasing drugs. The result is a synergistic effect at an infection site between the natural fighting role of the macrophage, supplemented by the localized concentration of the antibiotic. To improve the efficacy of the technique, TLC has designed a multilayered liposome which resembles an onion in structure. The liposome traps more drug within more layers for extended timed release. The body ingests one layer, uses the drug, then ingests the next layer.

TLC is investigating the use of liposomes to treat cancer and to deliver anti-inflammatory, antifungal and antibody-enhancement drugs.

Before any of the liposome companies can wring profits from their research into intravenous delivery of liposomes, they will have to clear a number of developmental and regulatory hurdles.

Like TLC, the other liposome companies are looking into non-intravenous products. For example, working with Ohio State University, Technology Unlimited plans to commercialize a liposome containing a fluoride or antiplaque agent for teeth in less than two years.

Despite the many problems that stand between liposome technology and a commercial intravenous drug delivery product, liposome companies have five years of work and investment dollars in their favour. (Extracted from Chemical Week, 30 July 1986)

Biotechnology Conference on Biosensors sponsored by The Royal Society, London, UK

The Conference on Biosensors took place at the headquarters building of The Royal Society on 28 and 29 May 1986. The large attendance attested to the great interest of scientists in biosensors for biotechnology research and development. There were about 300 participants, of whom 114 represented industrial organizations. In addition, there were representatives from government policy departments and biotechnology journals. Although the UK accounted for most of the attendees, there were also scientists from France, the Netherlands, Sweden, Switzerland, Denmark, Italy, Germany, Federal Republic of, Norway, Canada, Israel and Japan.

There were 15 invited speakers presenting talks on various topics in the area of biosensors, including microelectronic chemical sensors, semiconductor biosensors, electron-transfer biosensors, enzyme electrodes, immunosensors, and optical biosensors.

It was evident from the presentations that biosensors will have a major effect on analytical science and will become important in agriculture, industry, medicine and defence. The subject offers exciting opportunities for the application of many scientific skills to a new technology and for commercialization. The current challenges include development of methods for microfabrication of stable devices and acquisition of biological elements with appropriate properties such as thermal and temporal stability. Success requires skills ranging from semiconductor technology to protein engineering.

A biosensor is a device, probe, or electrode which, when it makes contact with an appropriate sample, converts the presence of the desired analyte into an electrical signal. The biosensor is normally constructed by immobilizing a biologically sensitive material in intimate contact with a suitable transducing system to convert the concentration of the analyte into a quantifiable and processible electrical signal.

The use of biosensors can compete with costly capital-intensive machines such as mass spectrometers, gas chromatographs and nuclear magnetic resonance spectrometers (NMR). An important potential application in the health area is the use of biosensors for tests which can be carried out in physicians' offices, at patients' bedsides, in critical care units, etc. rather than in large central laboratories as is the situation at present. Some of the applications of biosensors are: replacement of existing bioassays; monitoring of water pollutants; remote sensing in adverse environments (e.g., for mine gases); monitoring fermentations and cell and plant cultures; and monitoring toxic and nerve gases (military application). Biosensors can be used to measure the concentration of ions such as Mg^{2+}, K^{+}, H^{+}, and Ca^{2+} and gases, including respiratory gases such as carbon dioxide and oxygen as well as ammonia, chlorine, hydrogen sulphide, methane, etc. Clinical use includes measurement of drugs, hormones and metabolites such as glucose and urea. One great advantage of biosensor systems is that they permit the measurement of biological substances present at very low concentrations, even in the femtomole range (10^{-15}M).

Some advantages of biosensors are: availability for a wide range of analyses, sensitive and selective, rapid response, continuous real-time assay, low cost, disposable, reagentless, operate in optically opaque and turbid solutions, computer compatible and operator insensitive.

Research on biosensors is interdisciplinary in that it involves microbiology, enzymology, electronics, immunology, physiology, recombinant DNA, and also protein engineering. Biosensors are already available commercially mostly as components of complex analytical devices. However, second-generation, simpler devices, based on more sophisticated science will soon be available for medical use. This has stimulated research and development aimed at biosensors for other applications, including fermentation and process control, food testing and environmental monitoring. A projected future world market for biosensors could be in the range of $20 billion. This very large market potential for sales of biosensors obviously accounted for the high proportion of attendees at the conference from industrial organizations. (Extracted from European Science News, September 1986)

D. APPLICATIONS

Pharmaceutical and medical applications

Tissue type matching

Matching of tissue types improves the chances of success for cornea transplants. Transplants are the only effective way of treating advanced cornea disease, the leading cause of blindness. Some 30,000 cornea transplants per year are performed in the USA alone. Matching of tissue types is usually not necessary in cornea transplants, although in 10 per cent of the cases, the probability of rejection is over 50 per cent. High-risk cases include patients who have previously rejected a

transplant or whose corneas are severely damaged. Researchers at the Duke University Medical School, the Durham Veterans Administration Medical Center and the Vanderbilt University School of Medicine found that a tissue-typing procedure that matches the human leucocyte antigens (HLAs) of the donor and receiver increases the probability that the cornea transplant will be accepted to 92 per cent. There are over 80 kinds of HLAs, which can form thousands of combinations. Each person has a combination that results in a particular tissue type. (Extracted from New York Times, 26 August 1986)

MABs used to prevent kidney rejection

Ortho Pharmaceutical Corporation has received US Food and Drug Administration approval to use monoclonal antibodies to reverse the rejection of newly transplanted kidneys.

Ortho received the approval about two years after it filed an application with FDA and thus became the first to receive approval to use monoclonal antibodies as a treatment. Called "Orthoclone OKT3", Ortho's drug successfully reversed the rejection of newly transplanted kidneys in 94 per cent of cases in a comparative clinical trial. Other conventional therapies, such as high dose steroids and polyclonal antibodies were successful about 75 per cent of the time. The study involved 123 patients in 11 centres.

Saving transplanted kidneys is said to be critical both for the patients' well-being and because demand for transplanted kidneys far exceeds supply.

Dr. Douglas J. Norman, associate professor of medicine at Oregon Health Sciences University, Portland, and a clinical investigator at Ortho, says that despite advances over the years, most treatments either fail to control rejection completely, or fail to achieve success without total suppression of the immune system, leaving the patient vulnerable to infection. (Extracted from Chemical Marketing Reporter, 23 June 1986)

Monoclonal antibody test developed for diagnosing Alzheimer's disease

Scientists at the Institute for Basic Research (IBR), New York, have developed a laboratory diagnostic test for Alzheimer's disease. The research was done in conjunction with Senetek PLC, based in Mountain View, Calif. A US patent application has been filed for the monoclonal antibody (Mab) based test kit which is based on the quantification of a specific antigen in cerebrospinal fluid.

Senile dementia affects between 10 and 15 per cent of senior citizens worldwide, the most devastating form of which is Alzheimer's disease.

The causes of the disease are unknown. Twenty per cent of patients labelled as having Alzheimer's are misdiagnosed and may actually have other, treatable illnesses. Currently, the only sure way to diagnose the disease is by examining the brain after death for the presence of abnormal fibrils called paired helical filaments (PHF) in the cytoplasm of neurons. PHF, also known as Alzheimer neurofibrillary tangles, appear in the main body and terminals of the nerve cells. The affected nerve cell terminals form the second leading histopathological lesion, plaques. Both plaques and tangles are also found in the brains of non-demented, normal people age 70 and older, but only in small numbers. Only about 25 per cent of people with lesions develop dementia. If only small numbers of lesions occur, the rest of the brain compensates and the person functions normally. Alzheimer's is a condition where the lesions pervade all parts of the brain. The latest data show the Mab test for spinal fluid is 90 per cent accurate.

Scientists have probed sections of Alzheimer-diseased brain tissue with antibodies to various normal brain proteins using immunocytochemistry. This technology led to the discovery of the reactivity of PHF with antibodies to normal brain fibrils called microtubules in 1979. Antibodies to a number of normal brain proteins were also shown to react immunocytochemically with PHF, but the origin of the structures labelled with the antibodies was not revealed because the technique does not discriminate between homologous proteins and proteins with only superficial similarities.

Dr. John P. Bennett of Senetek expects the diagnostic kit to be tested in Europe in six to nine months. Tests will probably not begin in the US for two years. The test kit is being developed for Senetek by Immuno Products Industries (IPI) of Middlesex, N.J. It is being developed in four phases. The first phase was completed in August when the project team was assembled, literature searches were conducted and background material was obtained. Phase two is the longest and is expected to take about four months. The third phase is in-house clinical trials which include age matches, samples of cerebrospinal fluid and double blind studies. At this stage modifications of the product may be made. The fourth phase is European testing which will take one to two months and will be done in university laboratories. (Extracted from Genetic Engineering News, September 1986)

Potential uses of monoclonal antibodies

Monoclonal antibodies, already used for diagnostics, are about to become a significant force in therapeutics. Since their introduction in 1975, monoclonals have been harnessed for many in-office tests for pathogens, drug serum and hormone levels. Research laboratories use monoclonals to type many kinds of cancers. The US Food and Drug Administration now has about 150 monoclonals designated as investigational new drugs for use in organ transplants, auto-immune diseases, bacterial and viral infections, assessment of myocardial damage and cancer diagnosis and therapy.

Antibodies primarily function as immunomodulators. OKT3, produced by Ortho Pharmaceuticals, is almost ready for approval to treat acute rejection of renal transplants. Monoclonals are also used in research into auto-immune diseases. Monoclonals could soon be available to treat infectious diseases, starting with the common cold. The antibodies are being used in four ways in cancer therapy: to stimulte the immune system, to bind agents needed for tumour growth, to link the antibodies to drugs or toxins for delivery to tumours, and binding to radioisotopes. Other researchers are investigating the use of monoclonals to treat Alzheimer's disease or blood clots, while other possibilities include diagnosis of congenital rubella or analysis of lipoproteins. Applications of monoclonals seem to be limited only by researchers' imaginations. (Extracted from Medical World, 9 June 1986)

Human trials under way to test effectiveness of recombinant malaria vaccines

An arsenal of vaccines to fight two key stages of malaria is on the horizon, thanks in large part to recent developments in biotechnology.

Researchers have begun clinical trials of vaccines that would protect humans at the time they are bitten by a malaria-carrying mosquito. They have also developed several candidate vaccines for people already stricken with malaria.

The vaccines undergoing clinical trials could be available to travellers and military personnel within three years, according to malaria researchers. A vaccine for the red blood cell stage of the disease could be available for use by malaria victims worldwide in five or six years, they predict.

Malaria infects more than 200 million people a year, killing from one to three million. Most of the deaths occur in African children. The need for malaria vaccines is especially urgent because of the increasing insecticide resistance among the Anopheles mosquito species that carries the disease and the increasing resistance of the causative protozoa to prophylactic drugs.

The ultimate goal is a cheap, safe and effective multiphase vaccine. Four protozoan species commonly cause malaria, but the infections caused by one, Plasmodium falciparum, are the most severe. Thus, scientists have concentrated on a vaccine for this parasite.

The strategies malaria researchers have followed in developing vaccines take into account the life cycle of the parasite. Anti-mosquito stage vaccines are designed to neutralize the sporozoites before they reach the liver and anti-red cell vaccines to alleviate or eliminate existing infection; anti-gametocyte vaccines would prevent transmission of the disease. Most progress to date has been made with the first two types of vaccines, and it is the anti-sporozoite ones that are in clinical trials. The anti-sporozoite vaccine would provide protection for visitors and uninfected inhabitants of endemic areas, but it would not help those already infected.

Human trials began in March at the Walter Reed Army Institute of Research on an anti-sporozoite vaccine developed by the Dept. of Defense and SmithKline & French Laboratories. This vaccine was produced in E. coli using recombinant DNA techniques.

Human trials were scheduled to begin in July on an anti-sporozoite vaccine prepared by Drs. Ruth and Victor Nussenzveig and colleagues at the New York University School of Medicine and Hoffmann-La Roche Inc. of Nutley, N.J. This vaccine, based on a synthetic peptide, will undergo trials at the University of Maryland School of Medicine.

Both vaccines are designed to stimulate immunity against repeating subunits of the P. falciparum circumsporozoite protein, a key antigenic determinant.

Several developments in the search for red cell vaccines have been revealed at the meeting. Dr. Wasim Siddiqui of the University of Hawaii reported that his group had developed a peptide vaccine for the red blood cell stage that protected monkeys challenged with malaria. His work also demonstrated a successful in vitro assay that correlates with in vivo protection.

The NYU researchers have reported completion of a genetically engineered anti-sporozoite vaccine for a different species of malaria-causing protozoan, P. vivax. Monkey tests of this yeast-generated vaccine, developed in collaboration with Chiron Corp. (Emeryville, Calif.), were under way.

Many of these newer vaccines could begin human trials by the end of the year, but the two P. falciparum anti-sporozoite vaccines would be the first available.

As part of the EUREKA programme, Hoechst's Behringwerke subsidiary and the Institut Pasteur are to launch a $13 million, three-year research programme to develop a malaria vaccine. (Extracted from Genetic Engineering News, July/August 1986 and European Chemical News, 14 July 1986)

Recombinant vaccine against cholera and typhoid soon to be tested

A live oral vaccine against cholera and typhoid fever, consisting of genetically engineered Salmonella typhi bacteria, will soon be tested on volunteers at the University of Adelaide in Australia. The administration of such genetically manipulated bacteria represents a new approach in human vaccination.

Genes from Vibrio cholera were cloned in a nonvirulent strain of S. typhi. Prof. Derrick Rowley and his department of microbiology team then developed the oral vaccine which is expected to overcome the problems of incomplete and short-lived immunity that hamper the efficacy of the established parenteral vaccines. Parenteral vaccines also have been costly and difficult to administer widely in vaccination programmes.

Because typhoid and cholera are endemic and epidemic in most developing countries, they are serious threats to indigenous peoples and travellers. If produced cheaply enough, the vaccine could provide interim protection for a third world community while clean water supplies and public health facilities are improved.

Starting with "several dozen" cholera antigens, the researchers have narrowed the number of immunogenic candidates to about six. For cholera, at least two immunogenic lipopolysaccharides have been isolated.

After the V. cholera genes are inserted in the nonpathogenic Ty21A salmonellae, the bacteria are taken orally in an enteric-coated pill. They become active in the intestine and produce the immunogenic antigens over several days. Enteric administration is preferable because cholera antigens produced in the gut provoke a more protective immune response, resulting in IgA antibodies.

After the Adelaide trials on about 100 volunteers have quantitated the immunological response in the human gut, the Australians will take their vaccines to Baltimore in 1987 for human testing at the Center for Vaccine Development, which is the only facility accredited by WHO for a full-fledged challenge in human volunteers with cholera bacteria. While proper medical care can prevent the majority of cholera cases from becoming fatal, typhoid testing is not allowed because of the logistics of administering the tests (people would have to be confined in one area for a long period of time), and because some people become permanent carriers.

Provoking cholera in humans appears to be a severe testing procedure, but no animal models are satisfactory, although infant mice can be infected. General toxicity and pharmacological tests have used adult mice and rabbits.

When the Baltimore testing is completed, field trials will begin in China, India and Bangladesh, involving several hundred thousand people.

To develop and market the vaccine, the University of Adelaide and F. H. Faulding, a South Australian pharmaceutical firm, have formed (as equal partners) the company Enterovax Research Pty. Ltd. (Extracted from Genetic Engineering News, September 1986)

New hepatitis B vaccine

Chiron has developed a new gene-spliced vaccine for hepatitis B, making it the third company to win FDA approval for a gene-spliced human pharmaceutical. The problem of infection from contaminated blood is eliminated with the new vaccine, since it is produced in genetically modified yeast, not blood. Analysts are predicting that it will command a broad market, including third world countries where 10-20 per cent of the population may become infected with the disease. Estimates are that first-year revenues could be around $200 million, but many medical experts fear the vaccine will not be widely used until the price comes down.

Merck Sharp & Dohme's genetically engineered vaccine for hepatitis B has FDA approval, marking the beginning of the application of genetic engineering to disease prevention. Produced in Saccharomyces cerevisiae yeast cells, which have the genetic materials to code the hepatitis B virus protein coat inserted in their DNA, the vaccine has been administered to 3,800 people and proved over 90 per cent effective in preventing hepatitis B. The disease is considered serious, with over 200 million cases per year worldwide and 200,000 cases per year in the US alone. The FDA and Merck recommend that high-risk individuals, but not the general public, be inoculated against hepatitis B. High-risk groups include dental and medical workers, drug users, pregnant women who are immigrants from hepatitis-endemic areas, and persons travelling to such areas.

The new vaccine will be no cheaper than the plasma-derived one, which costs £70 a dose in Britain. The cost is prohibitive for many countries in Africa and the Far East where hepatitis B is particularly common.

Other approaches may yet produce a cheaper vaccine. Several biotechnology companies are engineering mammalian cells to produce viral proteins for a vaccine. These cells yield greater amounts of antigen, which they secrete, perhaps making purification easier. But these "transformed" cell lines - which resemble cancerous cells - are not now licensed for human vaccines.

A cheap vaccine would be a boon to public health programmes now under way in many countries, including China, Japan, Malaysia and parts of Africa. The World Health Organization has set a high priority on immunization against hepatitis B. (Extracted from Business Week, 4 August 1986 and New Scientist, 4 September 1986)

Further progress with prototype AIDS vaccine

Scientists at Genentech, Laurence Lasky and Phillip Berman, together with Jerome Groopman of the New England Deaconess Hospital have developed a prototype vaccine against AIDS using cells of a Chinese hamster to produce gp120, the coat protein found on the AIDS virus. Earlier in the year Genentech announced that it had developed a method for synthesizing the protein.

Now that the prototype vaccine has been shown to kill the AIDS virus in the test-tube, the next step will be to carry out animal trials, ultimately including tests on chimpanzees. One likely problem is that AIDS virus strains do vary considerably, which suggests that a vaccine made from a single strain may not be effective. The virus may change its coat proteins, enabling it to slip past the immune defences of those who have been vaccinated. Dr. Lasky reports that Genentech plans to try mixing coat proteins from several strains, in an attempt to produce a 'polyvalent' vaccine - like those used to combat polio. However the AIDS virus is lethal even when stripped of its genetic material. A lethal virus could be made with just the coat protein and the proposed vaccine could prove to be as deadly as the virus itself.

Perhaps the most exciting work on an AIDS vaccine will take place later this year when a prototype vaccine is tested on chimpanzees, the only animal other than humans that can be infected with the AIDS virus. Shiu-Lok Hu, from Oncogen in Seattle, has shown that it is possible to insert the entire env gene from the AIDS virus into the genetic material of a type of cowpox virus, vaccinia, which formed the basis of the smallpox vaccine. The vaccinia then makes envelope protein. When vaccinia is injected into mice, the animals make antibodies to these proteins, and, importantly, to one particular protein, called gp41. This protein is important because, unlike many other envelope proteins, it changes very little. Its "conserved" nature makes it a good protein on which to base a vaccine.

Hu has also tested his vaccine on macaque monkeys and found that the animals can make T cells that can recognize, but not necessarily kill, the foreign proteins. This cell-mediated immune response is an important requirement if the vaccine is to work properly in humans.

If the vaccine works on chimps, the next stage is to test it on humans. Many people are concerned, however, about using a derivative of cowpox virus, not least because vaccinia causes encephalitis in some people who are inoculated with it.

AIDS DNA mutates up to a million times faster than the standard DNA mutation rate, according to B. H. Hahn of the University of Alabama. Samples of AIDS virus taken from three people at intervals over one-two years indicated the high mutation rate. Exclusivity of infection implies, however, that infection by one AIDS virus may protect against infection by another. (Extracted from Biotechnology Bulletin, Vol. 5, No. 6, July 1986, New Scientist, 3 July 1986 and Science News, 28 June 1986)

Vaccine for simian AIDS developed

Researchers at the University of California, Davis, have developed a vaccine that protects rhesus monkeys against a virus that causes a disease very similar to AIDS. Development of a vaccine against the simian acquired immune deficiency syndrome (SAIDS) virus provides hope that a vaccine also can be developed that will protect humans against AIDS.

Both the SAIDS virus and AIDS virus are retroviruses. Both attack the immune system of the infected organism, effectively destroying its ability to fight off disease. This leads to so-called opportunistic infections by other pathogens. However, despite their similarities,

AIDS and SAIDS are caused by different viruses, which attack different immune system cells. The SAIDS vaccine cannot protect humans against the AIDS virus. Also the way the vaccine was produced - by killing live virus particles - is unlikely to be acceptable for producing a vaccine against AIDS for use in humans.

Researchers produced the vaccine by a technique similar to that used by Jonas Salk to develop the first polio vaccine. SAIDS virus was isolated from infected monkeys, raised in cell culture, and killed by treatment with the chemical formalin. In February 1985, six monkeys at the California Primate Research Center, which is operated by the university, were injected with the resulting vaccine. The treatment was followed by two booster injections. In July, the monkeys were injected with what are normally fatal doses of the SAIDS virus. Six control monkeys also were exposed to the SAIDS virus at that time.

The vaccinated monkeys all are thriving and show no signs of SAIDS, according to Marx. Three of the control monkeys have died of SAIDS and the others show signs of the disease.

Although in theory the same technique could be used to produce an AIDS vaccine, a number of factors make such a development unlikely. The most important is that previous research with polio virus shows that formalin treatment does not always result in complete destruction of all virus particles. Companies pursuing an AIDS virus generally are focusing on recombinant DNA techniques to develop an AIDS vaccine protein that will cause production of neutralizing antibodies. (Extracted with permission from Chemical & Engineering News, 8 September 1986. Copyright 1986 American Chemical Society)

Vaccines without side-effects

An important role in the new vaccine technology is played by the tree Quillaja saponaria molina of South America. A glycocide, Quil. A., is extracted from the bark of the tree because it has the capacity to stimulate the immune defence of the body to react more strongly to vaccination. Professor Morein of the Agricultural University, Uppsala, Sweden uses Quil A. as a kind of skeleton when a vaccine is built up. With the presence of Quil A. the vaccine's effect is up to ten times stronger and without negative side-effects. (Source: Journal of Biotechnica '86, Hannover)

Drug sensitivity testing with potential for cancer chemotherapy on patient tumour cells may soon be available through Chemoscreen

A predictive chemo-sensitivity research kit for breast cancer is now available from IBT International Biotechnologies Ltd. of Jerusalem, Israel. The kit is intended for research into the development of improved in vitro methods for evaluating the efficiency of anti-tumour agents. Based on the ECM technology, Chemoscreen provides optimal conditions for the culture of primary malignant epithelial cells, yielding results which closely resemble the in vivo situation. The kit represents a breakthrough in the in vitro assessment of drug therapy, without subjecting the patient to the often debilitating effects of drug sensitivity tests in the search for the most suitable treatment. ECM - extracellular matrix - is a naturally secreted substratum which closely resembles basement membranes of the body in composition and supramolecular structure. ECM contains interstitial collagen type III, basement membrane collagen types IV and V, fibronectin, laminin, heparin sulphate and dermaten sulphate proteoglycans. In contrast with cells plated on regular plastic surfaces or isolated components of the matrix, ECM-plated cells better resemble their in vivo counterparts: they maintain their differentiated properties; show improved attachment and flattening, and rapid migration; they show faster proliferation and exhibit longer life span.

Malignant epithelial cells of human origin are normally difficult to culture due to poor plating efficiency, clonal density and overgrowth by stromal fibroblasts. ECM, due to the above properties, improves the success rate and yield of cultured cells. Chemoscreen thus increases plating efficiency and growth of epithelial cells from mammary biopsy specimens while suppressing the proliferation of stromal fibroblasts. This improved cell culture from the individual patient's tumour facilitates in vitro anti-cancer drug screening.

The minced tissue, after undergoing an initial digestion period, is transferred to ECM-coated culture plates for several days, after which radiation effects can be studied. Following trypsinization, the cells are seeded into ECM-coated microtiter plates where, after a further culture period, they can be exploited for chemosensitivity studies. (Source: Company News Release, September 1986)

Biodegradable polymer to treat brain cancer

A new joint venture company, NovaCel, is to develop controlled release drug systems. Initially the new venture will concentrate on a system to treat brain cancer using a biodegradable polymer. Developed at the Massachusetts Institute of Technology, the polymer will be under a worldwide exclusive licence to NovaCel. The new firm plans to begin clinical trials with the system later this year. Nova is also developing drugs for heart disease, asthma, epilepsy, pain relief and Alzheimer's disease. (Source: European Chemical News, 14 July 1986)

New approach to combat tumours

Cetus may be able to launch its interleukin-2 analogue following a mid-1987 filing by mid-1988. Furthermore, a new approach to the adoptive immunotherapy of cancer using tumour-infiltrating lymphocytes (TILS) developed by Steven Rosenberg and his colleagues at the US National Cancer Institute is likely to boost the company's confidence.

Rosenberg and his colleagues have recently reported that the adoptive transfer of TILS expanded in interleukin-2, in combination with cyclo-phosphamide, to mice with large heart and kidney tumours helped eliminate the cancers. Rosenberg has now developed a method to isolate TILS from human tumours and plans to use them in the treatment of humans with advanced cancers. (Extracted from European Chemical News, 29 September 1986)

Alpha-2b interferon used against basal cell carcinoma

Recombinant alpha-2b interferon can destroy basal cell carcinoma tumours, according to researchers at Schering-Plough and Scripps Clinic and Research Foundation. Cancerous cells were completely eliminated in eight patients. The interferon may prevent the cancerous cells from proliferating, it may enhance the body's immune

system, or it may do both. A 20-patie ·· ·al is now under way. Basal cell carcinoma is ··ted to the amount of pigment in the skin, and is most common in sunny regions.

Alpha-2b interferon is already approved for treatment of hairy cell leukaemia. (Extracted from Chemical Week, 17 September 1986)

Biotherapeutics Inc. and Scripps Clinic and Research Foundation establish cancer research programme

Biotherapeutics Incorporated, a patient-centered cancer research company, announced the establishment of a new cancer research laboratory in La Jolla, California and the appointment of Robert O. Dillman, M.D. to head that facility. The new cancer research programme will develop and apply individually-tailored biotherapies for cancer treatment using biologicals such as monoclonal antibodies, interleukins, interferons and tumour necrosis factor. The programme will enable medically suitable cancer patients to access promising new technologies which are generally not available.

The research programme is based on the concept that cancers among people are more different than alike and that each tumour in each patient is different. This approach to cancer research and treatment is based on the belief that effective cancer management strategies require collaboration between laboratory scientists and clinicians to better understand the individual characteristics of each patient's tumour.

International Genetic Engineering, Inc. (INGENE) also recently announced it has agreed to supply its proprietary human tumour antigen associated with tumour regression to Biotherapeutics Inc. for laboratory research and development purposes. Upon successful completion of required pre-clinical testing and development activities and subject to authorization by regulatory authorities, Biotherapeutics and the Biological Therapy Institute will conduct studies to evaluate the safety and clinical efficacy of this novel active immunotherapeutic approach to cancer treatment.

INGENE's human tumour antigen may offer a new approach, one that differs from, yet may complement, the use of other biological approaches for cancer treatment including monoclonal antibodies, interleukin-2 (IL-2), and interferons. These antigens may stimulate the patient's ability to produce antibodies against cancer cells much as the surface antigen of hepatitis B virus stimulates in humans the production of antibodies against the virus and protects the body from an active infection by this virus. (Source: Company News Release, 2 and 3 October 1986)

Cancer markers

Cancer markers - antigens aberrantly expressed by oncogenically transformed cells - are useful in cancer diagnosis and management. Unipath's subsidiary Oxoid markets one of the widest ranges of monoclonal antibodiess to cancer markers for immunohistology and diagnosis. Included in the range are: Alpha foeto protein (AFP), carcinoembryonic antigen (CEA) and Placental alkaline phosphatase (PIAL), useful in the identification of testicular seminoma and ovarian carcinoma. Unique to Oxoid are the monoclonals HMFG 1 and 2, which are specific for lobular and ductal carcinomas of the breast. Also available are epithelial keratins; prostatic acid phosphatase (PAP); prostate specific antigen (PSA); and Kappa and Lambda chain immunoglobulins. (Source: Biotechnology Bulletin, Vol. 5, No. 8, September 1986)

Alpha interferon product has UK marketing approval

Roche Products has received UK clearance to market its alpha interferon to treat Kaposi's sarcoma. This is the first UK approval for Roche's gene-spliced product marketed as Roferon A.

Clinical studies indicate that Roferon A can double the life expectancy of Kaposi's sarcoma sufferers. Patients treated with the product responded with a four- to 20-month respite from the disease. The median life expectancy of these patients is 28 months compared with 14 months for those not treated.

To be manufactured in Switzerland, where approval for treating hairy cell leukaemia and Kaposi's sarcoma was granted last month, Roferon A is now available for use. Roche has received approval to treat hairy cell leukaemia in the US. Approval for this indication in the UK has been granted to Wellcome and Schering, which also has marketing permission in the US and Canada. In addition, Schering, Roche's biggest rival, has won approvals for treating Kaposi's sarcoma in a number of other countries.

Estimates of market potential for Kaposi's sarcoma are tied to the numbers of AIDS sufferers. Worldwide, AIDS has struck about 80,000 people to date, with one-third suffering from the skin cancer, and this number looks set to increase rapidly in the next few years as the symptoms appear in dormant carriers of the disease. (Extracted from European Chemical News, 21 July 1986)

Test to detect genetic susceptibility to diseases

Focus Technologies (Washington, DC) have developed a blood test which may predict genetic susceptibility to certain diseases. Such a test could, for example, determine if smokers are likely to eventually develop emphysema unless they quit the habit while still healthy. Other detectable disorders include asthma, heart-disease, diabetes, ulcerative colitis, female hormonal dysfunctions and cancers of the skin, breast, cervix and lung.

The mechanics of the test are quite simple. Those destined to have emphysema produce low levels of alpha-1 antitrypsin (AAT), an enzyme that detoxifies tar, such as that found in cigarette smoke. An individual's protection of AAT is determined by his genes. As advances in decoding all the 50,000 or so genes that reside in the nucleus of every human cell are made, predictions of the potential ills of a person could be made at relatively low cost. An early knowledge of susceptibility could then be used to prevent the disease. Since everyone has some genetic susceptibility, critics of such tests worry that discrimination by employers or insurance companies against people with a given biological makeup will occur. (Extracted from The Economist, 27 July 1986)

A DNA probe that detects tuberculosis

A nonradioactive DNA probe for the early detection of Mycobacterium tuberculosis - the bacterium that causes tuberculosis - has been

developed by Enzo Biochem (New York City). The probe is said to provide identification of the organism within 24 hours, compared with the 4-8 weeks required by the current culture-based method. Enzo has also isolated specific DNA probes for another strain of tuberculosis, Mycobacterium avium intracellulare, currently a major secondary infection in AIDS patients. (Source: Chemical Week, 30 July 1986)

Monoclonal antibodies are used in a gonorrhea test

A new diagnostic test for gonorrhea, based on monoclonal antibodies, has been introduced by Syntex (Palo Alto, Calif.). The test has been approved for sale by the US Food and Drug Administration. It employs labelled monoclonal antibodies to detect the bacterium that causes gonorrhea. Syntex says that the test gives results within 30 minutes and has demonstrated 100 per cent sensitivity (no false negatives) and 100 per cent specificity (no false positives). It was jointly developed by Syntex and Genetic Systems (Seattle). (Source: Chemical Week, 10 September 1986)

DNA probes

The US Food and Drug Administration's recent approval of two DNA probes made by Gen-Probe (San Diego, Calif.) signalled a milestone in the development of probe technology. The event marked the first time that the FDA had cleared DNA probes for clinical use directly on patient specimens. Both probes are for diagnosing atypical pneumonia. One is specific for Mycoplasma pneumoniae, the cause of "walking pneumonia"; the other, for Legionella, the micro-organism responsible for Legionnaires' disease.

DNA probes are single-stranded DNA segments synthesized by so-called gene machines. The probes are constructed so that the gene segments match gene sequences directly associated with genetic disorders, cancer, and disease-causing bacteria and viruses. They can also identify those people who may be predisposed to heart disease. Probes permit quicker laboratory analyses and swifter and more accurate treatment.

For instance, DNA probes could detect a specific organism which may occur in a number of different types (e.g. papilloma virus). This would be a difficult task for Mabs. They could also help identify viruses (AIDS, influenza, common cold) that change their surface antigens so quickly as to preclude the use of monoclonals.

Not surprisingly, pharmaceutical and medical instrument companies are becoming increasingly interested in the small R&D outfits who pioneered probe technology.

DNA probes are particularly suited to the diagnosis of genetic disease simply because of the role played by human DNA in genetic disorders. Changes, deletions and other variations in gene sequences are directly responsible for many genetic diseases.

From the perspective of the current DNA probe market, genetic disease presents a major paradox: although the frequency of genetic disease in individuals is usually quite low, the total number of such disorders is huge. Currently, DNA probes are available for about half a dozen disorders. Research, however, goes on with the dual aim of extending the scope of the testing to include more diseases and of improving probes so that kits can be made available to hospitals, physicians and testing laboratories.

Integrated Genetics (Framingham, Mass.) is perhaps the most solidly organized to provide a testing service. The company recently established a licensed genetic disease reference laboratory - the first of its kind - that uses DNA probe technology for carrier and prenatal identification.

A technique that screens for an indicator strip of DNA, not for the gene itself, has fueled the rapid expansion of tests for genetic diseases, thus permitting the establishment of a facility such as Integrate Genetics' laboratory. (Direct screening for the genes that cause most inherited diseases are years away, as more than one gene could be involved in some cases.) Known as restriction fragment length polymorphism (RFLP), the technique is based on the finding that individuals show considerable variation in the length of DNA fragments after DNA is digested by different restriction enzymes.

These fragments often are identical in people with the same genetic disease. Detection of these characteristic fragments (or polymorphisms) can be used as a test for genetic disorders. In some cases they can provide information on the approximate location of the genetic change responsible for the genetic disease.

Obviously, this comprehensive service falls outside the reach of the normal population but is valuable to families who have a history of genetic disease and are considered high risk.

Integrated Genetics recently entered into a joint venture with Amoco Corp. to develop and market new DNA probe-based tests for the food microbiology and clinical diagnostic markets. The Small Business Innovative Research Program (SBIR) gave Integrated Genetics a grant covering continuing work in the diagnosis of Huntington's disease, a fatal neurological disorder.

In therapeutics, Integrated Genetics is working in several areas, all with the help of corporate partners in the pharmaceutical industry. Its cardiovascular drug, the blood-clot dissolver known as tissue plasminogen activator (TPA), is currently undergoing clinical trials in the Far East conducted in conjunction with Toyobo and Daiichi Seiyaku Pharmaceutical of Japan. Its hepatitis B vaccine will soon be starting clinical trials conducted by Connaught Laboratories (Canada). Integrated Genetics is also making fertility hormones for humans (with trials set to begin next year) and animals and is developing substances known as blood cell growth factors designed to help patients regenerate new cells after suffering blood loss. All of the company's therapeutic products share an unconventional twist in manufacturing technology: cloned genes are grown in mammalian-tissue culture cells, rather than in more commonly used bacteria. Company scientists believe this may provide a biochemical milieu closer to that of humans and animals, thus aiding in the substance's effectiveness.

Collaborative Research currently has a number of DNA diagnostic tests under development including those for adult polycystic kidney disease, Alzheimer's disease, Duchenne's Muscular Dystrophy and diabetes. Diagnostic services in the company's licensed DNA reference laboratory are already available for cystic fibrosis, determining paternity, and monitoring bone marrow transplants.

Collaborative has filed for patents on those RFLPs with possible applications in these areas.

Californian Biotechnology (Mountain View, Calif.) has embarked on a heady adventure in probe technology. Company scientists have reported finding three markers correlated with cardiovascular disease, and the company has filed patent applications for them.

Efforts are also focused on oncogene probes for cancer markers. Here, everyone would be included in the target test population. However, long-term realization of this potential will be tied to the ability to localize the site of the cancer.

Gen-Probe is interested in this area, too. The company signed a five-year agreement with the Wistar Institute of Philadelphia in July for work in the detection of oncogenes and oncogene-related products.

Cetus (Emeryville, Calif.) recently announced the development of an AIDS virus probe which illustrates how an ingenious innovation can endow DNA probe technology with an edge in infectious disease diagnosis - a field dominated by immunology-based tests. There is simply not enough infectious DNA (viral or bacterial) early in the course of an infection to allow probe diagnostics to compete with immunological methods. Cetus, however, found a way around this problem.

The innovation leading to a commercially viable probe for the AIDS virus was a method developed by Cetus scientists for amplifying DNA.

The DNA amplification method has wide application, and the company has already utilized it in the development of DNA probes for sickle-cell anaemia and white blood cell identity.

Amplification involves the addition of the 20 base pair sequences flanking the target sequence to a denatured sample. This is followed by addition of DNA polymerase and excess nucleotides in the form of triphosphates. Newly created strands serve, in turn, as primers through several cycles of amplification.

The DNA scarcity problem was also circumvented by Gen-Probe.

The DNA-to-ribosomal RNA probe gives the test a several thousand-fold increase in sensitivity due to the greater abundance of ribosomal RNA produced by microbes, as compared to their DNA output. Another advantage is that the rate of hybridization is from four- to 10-times faster using the ribosomal target than is the case with the conventional DNA-to-DNA probe.

Critics say this approach is not without its limitations. For one thing, it cannot be employed for viral diagnostic work because viruses do not have ribosomes.

Several companies, looking to carve a niche in the infectious disease diagnostics market, have branched into other areas using probe technology. Integrated Genetics has entered the food processing diagnostics arena with its Salmonella probe and Enzo Biochem (New York, N.Y.) is utilizing probe technology for plant diagnostics.

As the US population continues to age, gum disease is becoming increasingly common. Approximately 10 per cent of Americans - 23 million people - show evidence of periodontal disease, the leading cause of tooth loss for those over 35. About $4 billion is spent every year to detect and treat these diseases.

Biotechnica International (Cambridge, Mass.) formed a subsidiary last year, Biotechnica Diagnostics, to develop a DNA probe test to detect bacteria that cause periodontal disease. The company has identified three types of bacteria responsible for gum disorders. Working in collaboration with the Forsyth Dental Center of Boston, Biotechnica expects to have a laboratory-based test available, using the firm's clinical lab in Cambridge, in early 1987.

Biotechnica Diagnostics is also developing a test kit that will allow dental professionals to perform the test in their offices, thus permitting them to monitor the success of their treatments and to evaluate less costly and less painful non-surgical therapies (i.e. antibiotics) for periodontal disorders.

Lifecodes Corp. has spotted and claimed a vacant role in the theatre of DNA probe technology. The unoccupied slot is the crime laboratory, and scientists at the Elmsford, N.Y.-based company expect criminologists to avidly latch onto what could cause a revolution in crime-detection - the DNA-Print.

The DNA-Print test can be utilized in almost any crime case demanding identification of an individual from body specimens or remains.

The test, which depends on RFLPs, was first developed in 1985. But the main advantage on the practical level came just this spring when Lifecodes' scientists demonstrated that the probe could finger individual DNA in a line-up of samples of blood and semen. The company says the DNA-Print is 100 times more accurate than current tests which rely on blood protein antigens.

Right now, Lifecodes offers the DNA-Print as a service on a selective basis, with 1987 eyed for a commercial debut.

Researchers are uncovering new opportunities for DNA probes at a rate that will keep commercial entrepreneurs busy for a long time to come. Recently a team of investigators at Georgetown University reported they had worked out what may prove to be an important DNA probe for the elusive delta virus implicated in carrier states of hepatitis.

DNA probes seem destined to serve as diagnostic tools for a number of disorders, the origins of which are only now beginning to be revealed in human genes. For example, one type of skin cancer appears to stem from a genetic origin. It is even possible that manic depression may join the list of inherited diseases determined by single genes, thereby making it a perfect candidate for DNA probe diagnosis. (Extracted from Genetic Engineering News and High Technology, September 1986)

Table 1. Commercialization of DNA Probes for Medical Diagnosis

Probe	*Target Population/U.S. Market ($)*	*Companies*	*Status*
Genetic Disease			
Cystic Fibrosis	33,000 afflicted; another 132,000 at risk; 8 million projected tests yearly	Collaborative Research Bedford, Mass.	Test is available
		Integrated Genetics Framingham, Mass.	Part of genetic disease reference laboratory service (Gene-trak™)
Duchenne's Muscular Dystrophy	10,000 afflicted; 50,000 at risk	Collaborative Research	In development
Susceptibility to heart disease (atherosclerosis and hypertension)	62 million people; $1 billion market	California Biotechnology Mountain View, Calif.	Investigative program with American Home Products
Huntington's Disease	25,000 afflicted; 50,000 at risk	Integrated Genetics	Field trials
Polycystic Kidney	11,000 new cases each year; over 200,000 have the disease	Collaborative Research Integrated Genetics	In development Available as service
Sickle-Cell Anemia	2 million Afro-Americans carry the gene; 50,000 have the disease	Cetus Emeryville, Calif.	In development
		Integrated Genetics	Service available
		Lifecodes Elmsford, N.Y.	Selective service available at university medical schools
		Miles Elkhart, Ind.	In clinical trials
Cancer			
Leukemia/lymphoma	25,000 new cases in 1985; $4 million market	Collaborative Research	In development
		Lifecodes	In development
		Oncogene Science Mineola, N.Y.	In trials
		Oncor Gaithersburg, Md.	Kits for research
Oncogenes	Undetermined; potentially everyone could be tested	Amersham Arlington Hts., Ill.	Marketed for research
		Amgen Thousand Oaks, Calif.	In development with Abbott
		Oncogen Seattle, Wash.	In development with Bristol-Myers
		Oncogene Science	Wide range available; collaboration with Becton-Dickinson
		Oncor	Some nonisotopic probes are available for research
Infectious Diseases—Sexually Transmitted			
AIDS	70-80 million tests per year; $100 million market estimated worldwide	Cetus/Eastman Kodak	Projected for marketing by end of 1987
Chlamydia	3 million women per year	Enzo Biochem New York, N.Y.	Marketed for research
		Amgen	In development with Abbott
Herpes I & II	2 to 4 million cases per year	Enzo Biochem	Marketed for research
		Molecular Biosystems San Diego, Calif.	Marketed for research by Du Pont
Other Infectious Diseases			
Periodontal bacteria	23 million people	Biotechnica Int'l. Cambridge, Mass.	In development with Forsyth Dental Center
Campylobacter	5.5 million cases per year; $25 million market	Integrated Genetics	Field trials
		Molecular Biosystems	Marketed for research by Du Pont
Cytomegalovirus	.5 million cases per year; $5 million market	Integrated Genetics	Field trials
Salmonella	5 million tests per year; $50 million market	Integrated Genetics	Being sold to food companies
Hepatitis B virus	300,000 new cases per year	Integrated Genetics	Licensed by Fujirebio; awaiting approval for Japanese market
		Molecular Biosystems	Marketed for research by Du Pont
Legionnaire's bacteria	1.2 million tests per year; $12 million market	Gen-Probe	First FDA approved probe
Walking pneumonia (*Mycoplasma pneumoniae*)	1.2 million tests per year; $12 million market	Gen-Probe	FDA approved
Rubella virus	Potential threat in pregnancy	Amgen	In development with Abbott

A DNA probe for the detection of Campylobacter

A rapid diagnostic test for detecting Campylobacter bacteria in stools has been introduced by Integrated Genetics (Framingham, Mass.). The new Gene-Trak assay - a nonisotopic, DNA-probe-based test - will be marketed to clinical laboratories. It is said to detect the presence of Campylobacter - a major cause of severe gastrointestinal infections - in stool samples in less than 16 hours, compared with 72-96 hours by culturing, the present test. (Source: Chemical Week, 23 July 1986)

AIDS infection detection kit

Fuji Chemical will commercialize a kit to detect infection by the AIDS virus that was developed by A. Karpas of Cambridge University (UK). The new test provides a positive result within a few hours, and the only equipment needed is a microscope. The test is based on the fact that a cell line taken from a leukemia patient is extremely susceptible to the AIDS virus. The cells harbour hundreds of thousands of viruses, making them highly antigenic and good at detecting the presence of AIDS antibodies. Ordinary microscope slides coated in Teflon have 30 wells coated with the virus-infected cells fixed in acetone to expose the viruses. A drop of blood is placed in a well. The blood is washed away after one hour. Any antibody present in the blood will bind to the antigen attached to the slide. A protein is added that will bind to the antibody-antigen complex, and peroxidase attached to the protein can then be detected when aminoethlycarbazole is added. This compound changes colour in the presence of the peroxidase. (Extracted from New Scientist, 28 August 1986)

Another possible target for interferon

Preliminary experiments with gamma interferon indicate it may be useful in treating lepromatous leprosy, a form of Hansen's disease. While drugs that kill the leprosy bacterium are already available, drug-resistant strains have recently appeared.

There are two major forms of the disease, lepromatous leprosy and tuberculoid leprosy. In tuberculoid leprosy, the bacteria infect the body and the body mounts an immune response. In lepromatous leprosy, the same bacteria are present but the body fails to recognize them and mount a response. The tuberculoid form is generally milder and only a couple of years of treatment are needed. Treatment for lepromatous leprosy can last a decade or more, or for life.

Carl F. Nathan of Rockefeller University in New York City and researchers from several other institutions injected gamma interferon into leprosy skin sores of six patients. The interferon resulted in a local immune response against the bacteria where there had been none. Because tuberculoid leprosy is easier to treat, the researchers suggest that gamma interferon could be useful therapeutically. (Extracted from Science News, Vol. 130, 2 August 1986)

Gamma interferon reported active in treating rheumatoid arthritis

In preliminary clinical studies in the United States, 23 of 30 arthritic patients receiving gamma interferon injections experienced a reduction in the common symptoms of arthritis, such as swollen joints and joint tenderness. No patients discontinued treatment due to discomfort from side effects. In a similar trial in the Federal Republic of Germany, 24 of 40 patients improved, reporting a decrease in pain and/or an increase in mobility. Biogen and its FRG affiliate Bioferon have been studying gamma interferon in the treatment of rheumatoid arthritis for over two years, following the incidental observation of improvements in the relevant symptoms in cancer patients treated with interferon. To date, over 250 people have participated in the trials. (Source: Biotechnology Bulletin, Vol. 5, No. 7, August 1986)

Beta-interferon effective against hepatitis B

According to the Japanese Ministry of Health and Welfare's Central Pharmaceutical Council Toray Industries' (Japan) beta interferon is effective against two types of chronic hepatitis B. The Ministry is expected to give its formal approval for this application before the end of the year. Toray's Feron brand interferon has been available since late 1985 to treat melanoma and a type of brain tumour. The product was also found to be effective against HBe antigen positive chronic active hepatitis and DNA polymerase chronic active hepatitis. (Extracted from Japan Economic Journal, 13 September 1986)

Cetus plans European subsidiary

Cetus, the California-based biotechnology company, is to establish a wholly-owned subsidiary in Europe. The new venture, EuroCetus, will develop, manufacture and market cancer therapeutics in European markets. Products which will be the initial focus of the subsidiary are interleukin-2, tumour necrosis factor, colony stimulating factor-1, human monoclonal antibodies and immunotoxins for breast and ovarian cancer. All these products are either in human clinical trials or late-stage preclinical testing in the USA. Human trials of interleukin-2 are expected to start in Europe early in 1987. Cetus has evaluated several locations for a development and production facility and expects to announce a site for the unit later this year. In the long term, Cetus expects therapeutic products will flow both from and to the new firm. (Extracted from European Chemical News, 25 August 1986)

Promising drugs for treatment of AIDS

Antiviral agents known as nucleoside analogues may be promising drugs for the treatment of AIDS. Nucleoside analogues have been shown to inhibit reverse transcriptase, an enzyme involved in the replication of the AIDS virus. They are structurally similar to the cell's natural genetic material and block viral replication by interfering with DNA synthesis. The National Cancer Institute recently completed a phase I trial on the nucleoside analogue azidothymidine (AZT) and began phase I trials on dideoxycitidine in late 1986. Some 15 of 19 AIDS patients treated with AZT showed measurable improvement, including short-term increases in the number and function of helper T cells, which help protect the body against infections. The clinical efficacy and safety of AZT are now being tested in AIDS patients at 12 medical centres using a randomized placebo-controlled procedure.

Burroughs-Wellcome, the US pharmaceuticals unit of Wellcome, plans to file a new drug application with the US Food and Drug Administration for AZT by the end of October. With fast-tracking through the regulatory procedures, AZT could be on the market by January 1987.

Nevertheless, US health officials admit that AZT is not a cure for AIDS but merely a palliative that eases symptoms and extends patient life. During the six-month study, patients receiving AZT suffered fewer infections and saw improvements in

immune responses. Anaemia, a serious side effect of the drug, may limit its usage.

The company says it will supply the drug to AIDS victims suffering from pneumonia linked to the disease free of charge, but will not be doing the same for ARC patients.

How AZT works is still unclear. The compound is 3'-azido-3'-deoxythymidine. It was first isolated by cancer researchers in the mid-1960s. Although AZT failed to help cancer patients, it was shown to hinder a virus's reproductive process.

An invading AIDS virus injects its own genetic identity, in the form of RNA, into a certain type of T-cell - one of the cells in the human immune system. Using an enzyme, reverse transcriptase, the virus directs the RNA to replicate itself into two strands of DNA that become the new blueprints for the infected cell. The cell now makes and expels more virus, then dies.

AZT is an analogue of thymidine, one of the nucleosides that is a buidling block of DNA. It may work by substituting in form but not in function for the real thing, so blocking reverse transcriptase, and foiling the virus' building plan. Scientists note that AZT also crosses the barrier between the circulating blood system and the brain, which means that it might be effective in combating infection there.

British researchers are working on what they claim to be the most potent anti-viral agent in the world. Studies in the laboratory show that the chemical is ten times better at de troying the reproductive capacity of the AIDS virus than AZT. The researchers have begun to test the compound on animals to see how toxic it is. Clinical trials on humans should follow next year.

The identity of the chemical, a natural compound that was discovered by scientists in California, remains secret. Patents on it have only recently been filed by the owners of the licensing rights, the biotechnology firm Porton International. This week, the company revealed that the Government's Centre for Applied Microbiology and Research, part of the Public Health Laboratory Service at Porton Down, is testing the compound on strains of the AIDS virus taken from people living in central Africa. The centre is looking for clues as to how the compound affects the AIDS virus. It seems to work by blocking the virus's reverse transcriptase, an enzyme that is essential for the manufacture of DNA from viral RNA. Researchers only began to discover the effect the compound had on the AIDS virus five months ago. The molecule is not a protein, and its detailed structure was a mystery until a short time ago. (Extracted from Chemical and Engineering News, 11 August 1986, New Scientist, 25 September 1986 and European Chemical News, 29 September 1986)

Growth hormone trials to begin

Dr. Kowarski and colleagues at the University of Maryland School of Medicine are co-ordinating national trials to treat unusually small children with the first synthetic growth hormone to be chemically identical to the natural substance produced by the pituitary gland. The synthetic hormone was developed in Israel in the laboratories of New York-based Bio-Technology General Corp. The Maryland researchers have also devised a more sensitive test method for detecting growth hormone deficient children, in which the patient wears a portable pump that continuously removes blood over a 24-hour period. Test tubes are changed every half hour, and the hormone levels are averaged. (Source: Genetic Engineering News, September 1986)

Müllerian inhibiting substance to be tested

Biogen's Müllerian inhibiting substance (MIS) will be tested against several types of female reproductive tract cancers at Massachusetts General Hospital. MIS, produced via genetic engineering techniques, is produced naturally in male embryos and causes the formation of precursor tissue to female reproductive organs. In female embryos, Müllerian duct cells grow to form the female reproductive system. Because MIS suppresses the growth of embryonic, female reproductive system cells, it may also inhibit tumour growth in mature cells of Müllerian duct origin. It may be a suitable treatment for endometrial, fallopian tube, cervical, ovarian and vaginal cancers. Laboratory studies using natural MIS indicate that the protein inhibits the growth of human cancer cell lines, principally from patients with ovarian cancer. Biogen isolated the human gene that governs production of the protein and inserted it into animal cells. The inserted gene then directed the animal cells to produce MIS.

Until now researchers have been able to carry out only limited studies into the effects of MIS on tumours because the protein is produced in trace quantities and disappears shortly after birth. They did find, however, that in vitro, MIS reduced 25 of 28 ovarian tumours.

Cancer of the reproductive organs are third only to breast and lung cancers as a cause of death from malignant disease in women. Armed with a means of producing unlimited supplies of the fetal hormone by genetic engineering, scientists can now begin larger trials with the substance. (Extracted from Chemical Marketing Reporter, 16 June 1986 and New Scientist, 10 July 1986)

Clinical trials to begin for GM-CSF

Sandoz, the Swiss-based drugs company, has been given permission to conduct human clinical trials for granulocyte-monocyte colony stimulating factor (GM-CSF) in the US. The US Food and Drug Administration has now completed its review of the investigational new drug filing for the gene-spliced human protein.

Under licence from Genetics Institute, Sandoz will test GM-CSF in the treatment of blood cell deficiencies such as those caused by cancer chemotherapy, radiotherapy, AIDS and aplastic anaemia. Genetics Institute provide GM-CSF for the pre-clinical studies and will supply material for the human trials. (Source: European Chemical News, 1 September 1986)

Biotechnology to find cosmetic applications

Already used commercially as an aid to eye surgery, the natural polymer hyaluronic acid (HLA) could find wide application in cosmetic formulations as a moisturizing agent providing a low-cost production route can be found.

A complex mucopolysaccharide, HLA is conventionally obtained from cockscombs and umbilical cords. Bacterial fermentation routes have also been looked at lately. The polymer occurs in the skin, where it binds water. As the skin ages and wrinkles the HLA content decreases. Inclusion of HLA in skin creams is thus projected to have a beneficial effect.

Although the polymer in its sodium salt form has been tried in cosmetics, application is limited by the product's very high cost - as much as $2,000-4,000/kilogram. Jean-Paul Sachetto of Battelle-Geneva research centre has been developing a cheaper substitute with similar water-retention properties.

The starting point of the Battelle work, which is still at an early stage, is the chemical similarity between HLA and chitin, a natural polysaccharide which occurs in the shells of crabs and other crustaceans. Chitin is already produced commercially from shellfish in Japan and is available at a cost of $5-10/kilogram. Several commercial applications are under investigation.

The most significant difference between HLA and chitin, in Sachetto's view, is the absence of a glucuronic acid structure in chitin. The Battelle scientists converted chitin into an HLA substitute using a selective oxidation process.

Carried out in one stage under mild conditions with high selectivity, the selective oxidation process converted a primary alcohol group on the chitin molecule into a glucuronic acid moiety. Different grades of products were produced by varying the reaction conditions.

Comparison of oxidized chitin with sodium hyaluronate and commercially-used moisturizing agents showed that the two polysaccharides both acted as moisture buffers with very similar water-retention capacities. Initial investigations of oxidized chitin in skin cream gave a smooth, homogeneous result, Sachetto reported. Safety tests need to be carried out before the product is commercialized as a cosmetic ingredient. (Extracted from European Chemical News, 29 September 1986)

Livestock applications

DNA coding for vaccine virus

Novagene (Houston, TX) has devised a way to brand DNA so that later generations of a virus can be easily detected with a DNA probe. The coding is inserted into the viral DNA where it will not interfere with the organism or code for any protein, but is still passed on to succeeding generations of the virus. The company will use the codes on a genetically-engineered virus that is the base for a cattle and hog vaccine. That way, if a farmer claims his herd became sick after being vaccinated, the company can easily detect whether its product was at fault. In addition, government inspectors can use a probe to determine whether animals have antibodies to a disease because they were vaccinated or were exposed to the disease. (Extracted from Business Week, 9 June 1986)

Vaccine against foot-and-mouth disease

Eli Lilly has developed a synthetic peptide containing two parts of the foot-and-mouth disease virus coat protein for use as a vaccine. The peptide matches amino acid residues 141-158 and 200-213 of the foot-and-mouth disease viral coat protein. Preliminary tests show the vaccine to be 100 per cent effective. Conventional vaccine is made from killed virus, and there is some risk of contamination. (Extracted from Chemical Week, 25 June 1986)

Transgenic sheep and foot rot vaccine

Australian scientists at CSIRO, the Australian Government's research organization, have produced what they describe as the world's first 'transgenic sheep', which they expect to be up to 50 per cent larger than normal sheep. The transgenic animals were created by inserting a gene for sheep growth hormone into a female embryo which was then implanted in a surrogate mother. CSIRO hopes to be able to extend its achievement by eventually transferring genes promoting, for example, wool growth and disease resistance.

CSIRO scientists have also developed a recombinant vaccine against foot rot in sheep, which has already been tested. Two biotechnology companies, Biotechnology Australia and Arthur Webster plan to put the vaccine into commercial production within two years.

The technique involves transplanting a bacterial gene, which codes for the filaments on the foot rot bacterium's surface. These filaments are extremely important in the transmission and development of foot rot. The bacterium Bacteroides nodosus, lives in the hoof of the sheep and strikes commonly in wet conditions. The bacterium then attaches itself to the sheep's hoof through hairs or filaments and causes the animal to create antibodies to defend itself. The antibodies will not work if they have never previously come into contact with the bacterium. Conventional vaccines contain these filaments to allow the animal to develop resistance to the bacteria.

However, in the laboratory, the bacteria grow slowly, making it difficult to produce sufficient quantities, and also making the vaccine extremely expensive. Using the new technique, the filament gene was transferred into a fast-growing bacterium, Pseudomonas aeruginosa, where it was engineered to produce the filaments which form the basis of the vaccine.

The scientists now believe that the technique can produce vaccines against other bacteria which have similar filaments, such as the gonorrhea bacterium, and against Pseudomonas aeruginosa, which itself attacks people. (Extracted from Biotechnology Bulletin, Vol. 5, No. 6, July 1986 and New Scientist, 3 July 1986)

New biotechnology facility for livestock

International Minerals and Chemicals Corp. is to build a $100 million biotechnology facility. By 1988 the production centre will make animal growth products including the porcine growth hormone, somatotropin, using technology licensed from Biogen. IMC is focusing its research efforts to find new compounds to enhance the utilization of nutrients consumed by animal livestock. (Extracted from European Chemical News, 7 July 1986)

Vaccine for poultry

Vineland Laboratories has developed a combination killed-virus vaccine for bursal and Newcastle diseases of poultry. The US Department of Administration has issued a conditional licence for the vaccine. Bursal attacks a chicken's immune system, and a strain of the disease has developed that is resistant to existing vaccines. Newcastle is a viral upper respiratory infection of chickens. (Extracted from Chemical Week, 25 June 1986)

French develop rabies vaccine

French researchers have developed a genetically engineered vaccine that can be administered in the wild to combat rabies, a disease that kills thousands of domestic animals and several people each year.

The scientists expressed hope that the new vaccine would confer immunity on enough wild animals to control the spread of the disease. Wild animals serve as the major reservoir of the rabies virus. The new vaccine, which can be administered in bait, consists of a genetically altered vaccinia virus bearing a protein found on the rabies virus. The virus in the vaccine triggers the animal's immune system to produce antibodies against rabies, thereby protecting the animal from infection. The vaccine virus does not harm the animal.

Developed by the French genetic engineering company Transgène in Strasbourg, the vaccine will be commercialized by Mérieux of Lyons. French regulations require approval of field trials by the ministries of health and agriculture, but Mérieux has not so far applied for permission. The company has supplied vaccine for tests by the Wistar Institute in Philadelphia, but use of the vaccine in the wild is likely to take place in Europe first.

The scientists said they had successfully tested the vaccine in foxes, the predominant carriers of the disease in Europe. Skunks and racoons are the predominant carriers in the United States. (Extracted from Nature, Vol. 322, 24 July 1986 and International Herald Tribune, 7 August 1986)

Monoclonals for early detection of canine heartworm

Canine heartworm is a disease which affects 70 per cent of dogs in the southern US and is spreading to other parts of the country and to Canada. The Canadian company Allelix has developed monoclonal antibodies against the causative organism, Dirofilaria immitis, which it hopes will win a significant share of a market estimated to be worth over $60 million. The disease, which can be fatal, develops slowly and extensively damages the affected animal's internal organs before any external symptoms show. Current tests look for microfilariae in the blood of infected dogs. The problem is that 35 per cent of infected dogs may harbour the adult worms without having microfilariae circulating in their blood. Allelix claims that rapid enzyme immunoassay tests based on its monoclonals will significantly improve the situation. (Source: Biotechnology Bulletin, Vol. 5, No. 5, June 1986)

Kits to diagnose fish disease

Furunculosis, bacterial kidney disease, and enteric redmouth are three of the infections that fish farmers will be able to detect more quickly than before by using dipstick tests to be marketed shortly by Aquabio Ltd. Based on highly specific monoclonal antibodies married to an enzyme-linked immunosorbent assay (ELISA) system, the kits were developed by Brian Austin of Heriot-Watt University, together with scientists at other institutions in Edinburgh, including Bioscot Ltd., which was established by Heriot-Watt and Edinburgh universities in 1983 with financial support from the Scottish Development Agency. Bioscot has now launched Aquabio in collaboration with Aquaculture Vaccines Ltd. of Bishop's Stortford in England and is the first British company to make and market fish vaccines commercially.

The Aquabio method does not require sophisticated equipment such as a spectrophotometer. It takes just 25 minutes, uses ambient temperatures for incubation, and needs only tap water for the washing steps. (Extracted from Bio/Technology, Vol. 4, June 1986)

Agricultural applications

New developments in biotechnology will have major effect on future of biopesticides

Interest in biopesticides is growing while agrochemicals decrease in public favour. Recent innovations in biotechnology are expected to substantially increase this interest and to have a major impact on the commercialization of biopesticides. UK consultants, Biotechnology Affiliates, is examining the current trends in this field.

The agrochemical industry, worth $15 billion in worldwide sales, is coming up against increasing pressure from environmental groups and a public concerned about the potential hazards that chemicals pose to non-target organisms and the environment.

Useful new chemicals for pest control are becoming harder to find and the development of biological resistance in the target organisms is shortening the marketable life of those currently in use.

The agrochemical industry is being forced to consolidate into larger units due to rising R&D costs and the increasing expense of extensive toxicological testing. Biological products based on micro-organisms are therefore receiving much attention, as they present a safe and specific alternative to synthetic chemical pesticides.

Although there has been a high volume of research in the public sector for many years now, the output of biopesticide products is still relatively small: the estimate for annual sales is only $20-40 million, 95 per cent of which is Bacillus thuringiensis (Bt). Strains of this sporulating bacterium produce a crystalline protein which is toxic to various species of Lepidoptera and Diptera. As yet no microbial pesticide has had any real commercial impact; their limitations are a variety of interacting factors ranging from process development and formulation problems to slow kill, dependence on environmental conditions and narrow host-range.

Even so, the demand for alternatives to chemicals has never been greater; but are there adequate market opportunities to ensure the commercial viability of biopesticides? One of the biggest markets for biopesticides in agriculture was control of insect pests on Brassicae. However, synthetic pyrethroids have taken virtually all this market due to substantially lower costs to the user. Nevertheless there are serveral potential niches which could be exploited by biopesticides: disease control (especially on grapes and peanuts) and weed control for example. With reference to the latter, there are currently two mycoherbicides on the market: Collego (Norsm, US) based on Colletotrichum gloeosporoides against Northern Joint Vetch and Devine (Abbott Laboratories, Chicago, US) against Milkvine weed of citrus in Florida.

Other potential markets that could be successfully exploited by biopesticides are those which are less sensitive to cost, for example amenity areas and parks and the public health sector. Here, use of the cheapest pesticide available will not be a critical requirement if public safety and health are at risk. Another very promising outlet for biopesticides is in enclosed environments, where the crop to be protected is of high value and resistance to chemicals is an increasing problem. Such environments can be manipulated (in terms of temperature and humidity)

to provide the ideal conditions for optimal use of microbials.

Many of the limitations will or can be alleviated by novel techniques in biotechnology, such as genetic engineering. Due to the rise in microbial genetic research, there has been much success in elucidating details of gene structure and gene expression.

Such extensive molecular studies of Bt have led to strain improvement via recombination and conjugation (as well as the more traditional screening methods). Recombinant DNA techniques are being used to insert a Bt toxin gene into a different microbial host, as a means of improving toxicity in the field or to direct activity in a particular ecological area. Monsanto has genetically engineered soil-inhabiting Pseudomonads to produce Bt endotoxin, in order to direct the insecticidal activity to the feeding sites of the target insects (cutworms).

Monsanto is, however, facing delays to field testing, as the Environmental Protection Agency (EPA) has requested that the firm submits more data on the pesticide's potential effects on non-target organisms such as honey bees. Nevertheless, Monsanto is still pursuing other microbial research programmes including a search for nematocidal genes to transfer to strains of Pseudomonas florescens that live on the roots of soya bean.

Mycogen Corporation and others have discovered new strains of Bt with direct activity against coleopterans (previous strains have only been effective against species of Lepidoptera and Diptera). This immediately widens the Bt market to other economically important species such as the boll weevil (Anthonomus grandis) and the Colorado potato beetle (Leptinotarsa decemlineata). Mycogen has also successfully cloned a Bt toxin gene into a Pseudomonad and received permission over a year ago to test the resultant recombinant (though dead) pesticide.

Non-recombinant techniques are also showing promise as ways of promoting new more potent Bt strains. Ecogen is employing conjugal transfer techniques to replace less active toxin genes of Bt var kurstaki with more active ones. The company was given permission to test the pesticide in eight US states against bollworms and budworms. The advantage of using such non-recombinant techniques is that they do not raise the same regulatory issues as does the release of recombinant strains. Bruce Carlton, vice-president of Ecogen, sees bacterial conjugation "as an exact parallel to traditional plant breeding".

Plant Genetic Systems has genetically engineered a gene from Bt into tobacco plants to make them insect-resistant. Expression of the gene shows that the technique has potential for use with important crop plants (especially as the gene coding for the insecticidal protein is stably inherited). Another approach is being taken by Boulter and co-workers at Durham University who are isolating and cloning the genes encoding insect antimetabolic proteins (lectins) from garden pea Pisum sativum and French bean Phaseolus vulgaris. They hope to use modified Ti (tumour inducing) plasmids of Agrobacterium tumefaciens (the causative organism of Crown gall disease in many higher plants) to transfer the lectin genes to susceptible crop plants.

A similar DNA transfer system using A. tumefaciens has recently been developed in loblolly pine (Pinus taeda), a commercially-important species native to the southeast USA. Such genetic engineering is especially useful in forestry because specific genetic changes could be made in a short period of time compared to conventional plant breeding, thus ensuring early financial rewards.

Another example of the potential for genetic engineering of biopesticides concerns the control of crown gall disease on grapevines. The disease, caused by A. tumefaciens, decreases yield and causes unsightly tumours and often the only solution is destruction of the infected crop. A bacterial strain (J73) has been isolated which inhibits grapevine pathogens via production of a toxic compound (agrocin). Genetic engineering will be needed to cure the strain of its Ti plasmid prior to extensive field trials in case it proves to be pathogenic to other plants, although it does not cause gall formation on vines. The gene coding for agrocin production in J73 may then be engineered into a different strain possessing more effective colonization abilities.

Such novel biotechnologies have caused an increasing number of large companies to take an active interest in biopesticides. ICI has been recruiting Bt scientists while Abbott Laboratories is investing over $20 million in a new recovery pilot plant for its chemical and agricultural products division. The new facilities will be used for the production of biorational and genetically engineered products including microbial insecticides and biological herbicides.

However, it has been said that finding a biopesticide is liable to be far easier than the subsequent processes of scale-up and selling the product. This has been especially evident with regard to the commercialization of entomopathogenic fungi. Despite intense research interest, only four fungal products are on the market: Vertalec and Mycotal (Microbial Resources), Collego and Devine. This is because chemical pesticides still remain a cheaper and more reliable control measure. Constraints on production are cost, process difficulties, short shelf-life (cold storage is often necessary) and specificity (limited market). Environmental restraints such as temperature and humidity requirements are also a problem both during production and application; and finally fungi are often slow to kill.

Current research in biotechnology is working towards overcoming these constraints using techniques of strain improvement. For instance, a new strain of Verticillium lecanii has been developed by Jane Drummond and workers at King's College, London, which is reported to be 10 times more infective than previous isolates. Genetic mutation and selection can improve the toxin yield of many fungal pathogens and the use of submerged fermentation and changes in down-stream processing will further improve the production of fungal pesticides.

However, the very fact that the successful development of microbials may depend on the use of recombinant DNA technology may itself become a constraint. R&D costs rise substantially and securing approval and registration will certainly be more difficult. The financial requirements can only be met by large companies; so collaboration is the answer if the smaller companies and their scientific expertise are to survive.

Registration of biopesticides is both expensive and time consuming. As the registration process accounts for part of the patent life there is an economic necessity for increased profits per year and high profits in the early years. The number and

variety of markets which can supply these requirements are therefore reduced. The senior vice-president of R&D at Monsanto has been quoted as saying: "If it gets delayed much longer (i.e. regulatory approval), we're just going to quit developing microbial pesticides".

The uncertainty about registration of naturally occurring microbes is finally being resolved, as the guidelines for UK and US regulations are now working and evolving. Guidelines for the release of recombinant organisms are in preparation and in fact the Institute of Virology in Oxford has received permission to release a genetically-tagged virus which kills caterpillars of pine moth (Panolis flammea), a pest of lodgepole pine.

Public goodwill is vital to the future of genetically engineered pesticides. The recent, widely publicized, controversy over field tests of engineered frost protective agents (Pseudomonas fluorescens and P. syringae) was aggravated by the company involved, Advanced Genetic Sciences, refusing to disclose the location of the planned trials. When residents living close to the proposed site found out, the subsequent uproar led to a ban.

A study on this subject is being compiled. Details from Biotechnology Affiliates, PO Box 8, Checkendon, Reading, UK. (Source: European Chemical News, 22 September 1986)

Disease resistant peach plants cultured

Dr. Freddie Hammerschlag, a plant physiologist with the US Dept. of Agriculture's Agricultural Research Service, has produced a peach tree cultivar that resists infection by Xanthomonas campestris p. v. pruni, a bacterium that causes black spots on the fruit and eventually kills the trees.

After repeatedly exposing 400 calli to the bacterial toxin, Dr. Hammerschlag isolated two survivors. From these calli, she produced clones whose plantlets yielded resistant saplings. Dr. Hammerschlag employed the tissue culture technique rather than genetic manipulation because it is much easier to regenerate a plant from a callus than from a single cell. She is hopeful that the technique can be applied to citrus trees to induce resistance to a bacterium which causes citrus canker which causes the fruit to fall prematurely and is, at present, incurable. The disease is so contagious that exposed as well as infected trees must be destroyed.

Cloned specimens of the disease-resistant peach trees are currently thriving in hothouses in North Carolina. Over the next two years, the trees will be planted outdoors and should bear the first black spot resistant peach crop in 1988. (Extracted from Genetic Engineering News, September 1986)

Improved tomato

DNA Plant Technology has been given a Plant Variety Protection certificate for a biotechnologically-produced tomato which has 20 per cent higher solids content than any other commercially grown tomato. The certificate gives DNA Plant Technology the exclusive right to exclude others from selling, reproducing, importing, exporting or cross-breeding the variety for 18 years. DNA Plant Technology will get a percentage of the raw material and processing savings accumulated by Campbell Soup, which funded the research. The new tomato was produced via somaclonal variation.

NPI (Salt Lake, UT) will begin marketing seed for a new tomato that has a built-in insect defence produced genetically, from genes borrowed from a wild tomato plant. The company said it used genetic probe technology that allows breeders to identify plant genes in the laboratory rather than having to wait until a plant is full grown to see what kind of genetic traits it displays. This reduces the number of growing seasons needed to develop a new genetic variety. The new tomato is one of the first commercial fruits of the new DNA probe technology and illustrates how it can speed development of new varieties. NPI's new commercial, pest-resistant tomato was produced in four generations of cross-breeding in the greenhouse, compared with the 8-12 generations of cross-breeding in the field that conventional methods would have required. Probe libraries for melons, cucumbers, cabbage, broccoli and peppers are also in development. (Extracted with permission from Chemical and Engineering News, 1 September 1986. Copyright 1986 American Chemical Society and Wall Street Journal, 16 June 1986)

Permission granted to field test pesticide and herbicide resistant tobacco

Rohm & Haas has received US Department of Agriculture approval for a field test of tobacco genetically engineered to be resistant to caterpillars. The plants now contain a single gene from the Bacilius thuringiensis bacterium, which is a commonly used insecticide to control moth caterpillars. If the technique is useful, it could be adapted for use in tomatoes, citrus, cotton, soybeans, corn, etc. Moth caterpillars are the most destructive insects to world agriculture and forestry, and include the gypsy moth, cotton budworm, cotton bollworm, cutworm, armyworm, corn ear worm, cabbage looper, spruce budworm and pine borer.

Ecogen Inc. also has started small-scale field trials with its genetically altered strains of Bacillus thuringiensis to test their effectiveness as microbial pesticides against budworm and bollworm. The commencement of the trials follows the announcement on 12 June that the US Environmental Protection Agency had approved the trials. These tests are the first to be sanctioned under the EPA's interim policy on small-scale field testing of novel microbial pesticides without the requirement for an experimental use permit.

Meanwhile Ciba-Geigy has received US Department of Agriculture permission to field test tobacco plants genetically engineered to resist the company's atrazine herbicide. A synthetic gene similar to one found in corn has been inserted into the plants. Tobacco, soybeans and some other crops cannot be planted in fields treated with the widely used herbicide, but corn, sorghum and some others contain natural resistance. The gene inserted by Ciba-Geigy's researchers into tobacco plants allows them to produce the same chemical produced by corn to detoxify the herbicide. (Extracted with permission from Chemical and Engineering News, 14 July 1986. Copyright 1986 American Chemical Society, Biotechnology Bulletin, Vol. 5, No. 6, July 1986 and Chemical Marketing Reporter, 8 September 1986)

Hormones to sweeten navel oranges

Natural bitterness in the juice from navel oranges may be prevented by feeding orange trees small doses of natural plant hormones known as auxins which work by inhibiting production of nomilin, a compound that is needed to make limonin, which causes extreme bitterness in navel orange juice only hours after it is squeezed. Because of that, only limited amounts of juice from navel oranges can be added to juice products. One attraction of auxins is that they are cheap. Another is that one of the auxins tested at the US Department of Agriculture's Fruit and Vegetable Chemistry Laboratory, 1-naphthalene acetic acid, is

routinely used on apples, pears and grapes. (Extracted from Chemical Week, 17 September 1986)

New grass strain

A Dutch professor of genetics appears to have discovered the gardener's dream, a lawn that rarely needs watering, never needs weeding or fertilizing, and has to be cut only two or three times a year.

According to Jan Weijer, of the University of Alberta, Canada, the super grass also grows in poor soil under most climatic conditions, and reproduces without pollination. It also excretes a natural herbicide.

The grass is based on several varieties of agropyrons, festucus and native peas. It is very dark emerald green and stiff. Weijer has been working with resilient grass strains for more than a decade in connection with high altitude strip mining reclamation projects. Last year, while checking plantings at the university's research farm, he found one plot to be both weed-free and only half the height of adjacent weed-filled plots. But Weijer says that gardeners will have to wait at least six or seven years to see if the discovery will work. It will take this time to build up a commercial seed stock. (Source: New Scientist, 18 September 1986)

Seeds coated with freeze-dried bacteria

A new technique for boosting productivity of tropical pasture land without using fertilizers is being field-tested in Colombia. Scientists from Cornell University's Boyce Thompson Institute for Plant Research, working with scientists at the International Center for Tropical Agriculture at Cali have planted seeds of a tropical forage legume called centrosema that has seeds about the size of shotgun pellets. These seeds have been coated with a vegetable oil containing freeze-dried rhizobia bacteria. In the technique, developed a few years ago at the University of Mississippi, each seed is coated with as many as a million of the nitrogen-fixing bacteria. The idea is that moisture in the soil will reactivate the bacteria once the seeds are planted. (Source: Reprinted with permission from Chemical and Engineering News, 8 September 1986. Copyright 1986 American Chemical Society)

Supergrasses with tropical tendencies

Steve Long and Marion Bingham, of the biological sciences department at Essex University, have provided the techniques needed to identify three good candidates for an EEC research programme energy crop. Long and Bingham have identified 200 species of grasses which photosynthesise as efficiently as tropical species, yet can withstand severe winters. One of the plants grows in north-western Canada, the other in western Europe. Long and his colleagues have developed a way of measuring the efficiency of photosynthesis in the field. They shine a bright light onto leaves and measure the amounts re-emitted as fluorescence. This tells them how much light the plant needs for photosynthesis. In this way Long identified three long-lived, tall perennial grasses, which photosynthesise by the C4 route. The grasses identified by Long are also naturally resistant to herbicides like Atrazine, which will greatly simplify weed control if they are used as energy crops.

Working with another group at Trinity College, Dublin, Long's group is now testing the supergrasses in pilot trials at four sites during the next three years. Two sites have good soils. The other two, in Ireland, are wastelands where ordinary crops cannot be grown. If the supergrasses prove themselves, large-scale trials will follow.

Long's group also provides the technical back-up for an international programme financed by the United Nations Environmental Programme (UNEP). This programme is to study the efficiency of tropical grasslands at trapping carbon dioxide from the air via photosynthesis. (Extracted from New Scientist, 21 August 1986)

New uses for algae

Algae is being used to develop new fertilizers, food supplements, dyes and food colouring, chemicals and luminescent substances. Soil Technologies started selling Microp, an agricultural fertilizer that 'innoculates' soil with several strains of algae that act as benign parasites. Only recently have scientists and biotechnology firms learned to domesticate and cultivate many types of these plants. The main attraction of algae-based fertilizers is that they do not introduce hazardous chemicals into the soil or groundwater supplies. (Extracted from Wall Street Journal, 11 July 1986)

Tree for poor soils

A team from CSIRO (the Australian Government's research organization), led by Glynn Bowen in Adelaide, Australia, has been studying the symbiosis of the Australian native casuarina tree and the bacterium frankia in its roots which helps to fix nitrogen from the atmosphere in the soil. The tree, known as she-oak, can thus thrive in poor soils such as beach sand, salt-marsh, or black cracking clay. The scientists are working to develop a relatively simple inoculation technology. Dr. Bowen believes that an inoculum, mass-produced in the laboratory, is not far off. (Source: Journal of Biotechnica '86, Hannover)

'Fingerprinting' technology to protect silage additives

BioTechnica Ltd.'s 'fingerprinting' technique is a proprietary technique for determining unequivocally the identity of unique organisms. Through its North American office, the company has completed an agreement with the Microbial Genetics Division of Pioneer Hi-Bred International Inc., based in Iowa, covering the use of the technology to fingerprint Pioneer's silage additives, based on Lactobacillus plantarum. Pioneer Hi-Bred is the world's leading producer of hybrid corn and other agricultural seeds. Its microbial genetics interests include silage additives and agricultural probiotics.

Pioneer Hi-Bred expect that the fingerprints will enable them to enforce patent protection of their Lactobacillus strains and to improve the quality of their products. BioTechnica also recently successfully demonstrated its ability to fingerprint plants and is currently discussing the application of the technique in this area with several companies. The company believes that the fingerprinting technique could be used in a number of other ways, helping to identify novel micro-organisms with properties of commercial significance (e.g. antibiotic producers), trace dispersal of micro-organisms or plants in the environment, identify unknown clinical pathogens and assist in quality control. (Source: Biotechnology Bulletin, Vol. 5, No. 7, August 1986)

Food production and processing

Bioreactor for whey processing

Whey as a by-product of cheese production can now be processed by a bioreactor using immobilized enzymes to produce fructose and other valuable products which can be used in food and pharma industries. The pilot reactor operates with

10,000 litres of whey per day and could be used for other biotransformations as well. It has been developed by the Institute for Food Technology at the University of Wuppertal, FRG, in co-operation with Böhm and Alpha-Laval under financial support from the Ministry for Research and Technology. (Source: Journal of Biotechnica '86, Hannover)

Cattle feed from biomass plant to be built

Finnish Sugar will build a plant to make pentose sugars and cattle feed from biomass using Stake Technology's (Canada) know-how. The plant will be the first commercial plant of its kind in the world. The process cooks biomass (wood and oat hulls) on a continuous basis under high pressure for 90-150 seconds to break lignin bonds with cellulose and hemicellulose. The resulting biomass product will be fed directly to cattle or further processed to separate the components. Hemicellulose can then be processed to furfural (used in refining of lube oils) or zylitol (used in drugs and gums). Lignin is used in glues and cellulose can be used in carboxymethyl cellulose, a detergent ingredient. (Extracted from Chemical Marketing Reporter, 14 July 1986)

Australian hydrolyzed milk to curb lactose problems

An Australian dairy factory has become the first continuous producer of milk products acceptable to the vast proportion of the world's population who cannot absorb lactose, a component of milk.

Production of hydrolyzed milk, in which most of the lactose is broken down into digestible sugars, started at the Drouin Co-operative Butter Factory near Melbourne in June 1985.

Although the principle of milk hydrolysis has been known to scientists for years, the Drouin factory is the first to put the process into continuous commercial production. This follows four years of research and development in Australia of a laboratory technique invented by Sumitomo Chemicals in Japan.

The first litres of hydrolyzed milk to flow from the Drouin plant represented a potential boon to the Australian dairy industry and to third world populations who have until now been unable to consume milk products.

The widespread incidence of lactose intolerance in third world countries has traditionally denied a great proportion of the world's poorest people access to a ready source of nutrients and calcium. It has been estimated that up to 90 per cent of the world's adult population suffers from some degree of lactose intolerance.

Lactose is a simple carbohydrate, often called milk sugar, which exists almost exclusively in milk or milk products. Human breast milk has the highest lactose content of all mammalian milk.

Before lactose can be absorbed by the body it must be broken down by the lactose enzyme in the inner lining of the small intestine. It is the common failure of the adult body in non-Caucasian races to produce this enzyme which causes lactose intolerance. In groups such as the Australian Aboriginals, American Indians, Chinese, Japanese, Vietnamese and Arabs, the incidence of lactose malabsorption is as high as 95 per cent.

About half of people affected by lactose malabsorption will develop diarrhoea, abdominal cramps, distension and flatulence after drinking milk.

As dairy foods are an important source of calcium, riboflavin, protein and vitamin A, scientists have long been searching for a way to make milk products acceptable to people whose lactase levels are insufficient. Research into this area has been given a high priority by several Australian authorities, including the Australian Commonwealth Scientific and Industrial Research Organization (CSIRO) and the Australian Dairy Corporation.

Milk hydrolysis is, put simply, the process of carrying out the first step of digestion in the factory by breaking the lactose down into its component sugars, glucose and galactose. This is achieved by introducing the lactase enzyme to the milk in the production stage.

Previous production of hydrolyzed milk involved mixing quantities of the enzyme with the milk. This process was extremely expensive because of the high cost of the enzyme, which was not retrieved, and because it did not allow continuous production. Also, supplies of the lactase enzyme were sometimes impure.

The new continuous approach used at the Drouin Co-operative Butter Factory is considered more economical, resulting in products costing about a third of those produced by earlier methods.

At Drouin, the enzymes are chemically "tied" to thousands of glass beads in a column through which the milk passes, breaking down about 75 per cent of the lactose present and making the end product digestible to lactose-intolerant people. The beads need to be replaced only every two years, reducing the amount of enzymes needed in the process and reducing the cost.

The proportion of lactose broken down can be controlled by the flow rate of the milk through the hydrolysis column.

The plant is producing 4,000 litres (880 gallons) of hydrolyzed milk an hour. Milk products expected to result from the new process include skim and whole milk, skim milk powder, yoghurt, ice cream and syrup.

One side-effect of milk hydrolysis is that the breakdown of lactose into glucose and galactose makes the end product sweeter than untreated milk. In fact, it is estimated that hydrolyzed milk is as sweet as normal milk with 2 per cent sucrose added.

This extra sweetness without added sugar means hydrolyzed milk has great potential as a diet product.

The head of the unit processing group at CSIRO's dairy research laboratory in Melbourne, Dr. Greg Zadow, says hydrolyzed milk products have been tested successfully in Kuala Lumpur and Singapore, where the incidence of lactose malabsorption is high.

He says the process will open up many markets for dairy products in South East Asia, and will make possible a reassessment of the importance of dairy products in foreign-aid packages. (Source: Australian Information Service)

Enzymes recovery on the way

The industrial enzymes business may be back on the road to recovery after the serious setbacks of the last couple of years. According to Alastair Kilgour, analyst with Morgan Grenfell, industrial enzyme producers like Novo and Gist brocades, the Dutch company and number two in the market, are failing even to earn returns of

5 per cent on sales with some products making a loss. Business has been particularly bad in starch enzymes which are used to produce high fructose corn syrup. A price war has raged in the US since 1[illegible]

Although there is some optimism for the short term, thanks to the possibility of price increases and some volume gains, the longer term outlook is mixed, in Kilgour's view. It is estimated that starch enzymes will experience annual volume growth of some 5 per cent for the next two years, which will translate into sales growth of up to 10 per cent if higher prices stick. (Extracted from European Chemical News, 7 July 1986)

Biotechnology in food production and processing by Prof. Dr. Dietrich Knorr, Professor of Food Processing and Biotechnology, and head of the Biotechnology Group of the Department of Food Science, University of Delaware, Newark, DE, USA

The recent discussion surrounding the "ice minus bacteria" (Pseudomonas syringae) and the production and utilization of fuel alcohol, as well as the worldwide attempts to increase resistance against pesticides, exemplify the impact biotechnology will have on the agricultural production of food and feed material.

Interestingly there is much less public debate on the impact of biotechnology on the processing of food. This is even more surprising if one considers that the food industry is the oldest and largest user of biotechnological processes and products thereof. Estimates of the biotechnology based food industry are around US$250 billions which almost equals the total annual sales of the US food processing industry. Out of this more than 10 per cent account for alcoholic beverages with projected increases from 27×10^9 in 1982 to 40×10^9 in 1990. (1)

Alcoholic beverages are also besides vinegar, sourdough and cheese production, the most prominent examples of the fact that biotechnology has been practised for more than 8,000 years. Meanwhile there are about 2,000 varieties of cheese around the world (2) and members of the Committee on Biotechnology of the German DECHEMA (3) estimated that in 1990 only 20 per cent of the products known in 1982 will be on the shelves of the supermarkets and that many of the new products will be of biotechnological origin (about 8,000 food items have been identified in an average sized US supermarket). Hopefully these few examples illustrate the magnitude and importance of the biotechnology based food industry.

The role of biotechnology in food processing is manifold and can be organized in (1) raw material production, (2) raw material modification and improvement, (3) raw material preservation, and (4) production of food additives or production/processing aids. Currently emphasis in raw material production is directed towards increasing productivity through improved efficiency of nutrient use and conversion, or through improved stress resistance and towards identifying new food sources. Much emphasis is on plant foods, because plant products from fewer than 30 plant species provide worldwide more than 90 per cent of the human diet. (4) For example extensive work is under way to fix atmospheric nitrogen, micro-algal mass culture production has been explored over the past 30 years, controlled environment agriculture (i.e. aquaculture, hydroponics) is carried out on an industrial scale, and the use of cultured plant cells is being considered for food production. (5) In addition the improvement of crop species through regulation of endogenous genes, the transfer of DNA from one species to another and photosynthetic efficiency are being sought. (4) However, animal products provide annually over 56 million tons of edible protein; marine food products are gaining increasing importance and the use of single cell proteins (SCP) has been stressed over and over again. Consequently many efforts also exist in these areas with emphasis on improvements in the reproductive efficiency of livestock and improvement of animal breeds. SCP for use as a protein source in food and animal feeds is produced on a large scale (6) and solid-state fermentations for food production (i.e. mushrooms) are carried out industrially. Modification and improvement of raw material can be applied to convert raw material, to increase stress resistance and to improve functional and nutritional quality. For example polymeric carbohydrates may be removed or included in the product (i.e. dietary fibre) or be converted to other products (i.e. sugars). Work on the improvement of functional properties such as colour, flavour and texture of raw material and on the increase of essential nutrients in plants (i.e. by reducing undesirable constituents) is being conducted. (7) Raw material preservation by biological processes is essential to the food production and food processing industry. Here the production of silage, the fermentation of coffee and cocoa beans and the oxidation (commonly called "fermentation") of tea as well as the preservation of any food or feed-related biomass via bioconversion are typical examples.

The production of additives and production/processing aids via biotechnological processes results in a vast variety of products including vitamins (i.e. B_2, B_{12}, C, D), fatty acids and other organic acids (i.e. citric acid), flavours (i.e. vanilla) amino acids (i.e. phenylalanine, aspartic acid), enzymes (i.e. amylases, proteases, glucose, isomerases, pectinases, lipases) and polysaccharides (i.e. xanthan gum, chitosan).

Polysaccharides can be commonly derived from algae or botanical sources and are traditionally used in the food industry as stabilizers and thickeners. More recently they are also utilized for the micro-encapsulation of flavours, immobilization of enzymes, as well as in food process waste management. (8) They are now being produced commercially through microbial processes and recently advances have been made towards control and manipulation of the biosynthesis of microbial polysaccharides thus offering the potential to affect the structure and form of the final polysaccharide product. (9) The classic example of the impact that biotechnology can have on the production of a food ingredient is the development of the high fructose corn syrup (HFCS) technology. It involves the application of two amylases and glucose isomerase to effect liquidation and subsequent saccharification of cornstarch to yield a mixture of fructose and glucose. HFCS is about as sweet as sucrose syrup of the same solids content and its use has risen from almost nonexistence in 1970 to 16.4 per cent of the US per capita consumption of nutritive sweeteners 10 years later. (10)

Biotechnology in food processing can significantly alter the composition, quality and functionality of food items. It provides tools and methods for (1) product modification, (2) product preservation, (3) processing methods, (4) product characterization, safety and quality control, and (5) waste treatment and utilization.

Applications of product modification include proteins, polysaccharides, fats and oils. Meat

tenderization with proteases is one example of a large-scale application of enzymatic hydrolysis to modify food functionality. The enzymatic modification of olive oil and stearic acid to a fat similar to cocoa butter or the enzymatic modification of limonoid bitterness in citrus products to improve flavour are promising and potential product modification techniques. (11)

Product preservation via classical biotechnological processes reaches from the preservation of food from plant origin (i.e. cabbages, olives, fruits, soya) to that of animal origin (i.e. dairy products, meat products, fish). (12) Even the production of alcoholic beverages from various fruits can be considered as a food preservation process. Currently much emphasis is on the enhancement of the efficiency of micro-organisms used in food fermentation industries, especially on the genetic manipulation of starter cultures. (13) Processing methods such as separation methods, which account for roughly one third of the approximately 150 to 175 unit operations involved in food processing, are critical for food quality, functionality and safety. In addition to unit operations based on mechanical or physical modes of operation, biologically based ones could be introduced to categorize for example the extensive use of pectinases to enhance the processing of liquid fruit and vegetable products. (14) Non-lipolytic enzymes have been used to improve the extractability of oil from seeds. (15) In addition the use of dense gases (16) such as supercritical carbon dioxide is becoming increasingly important for the extraction of "natural" ingredients or for the de-alcoholization of beverages. Furthermore immobilization methods such as immobilization of enzymes or entrapment of microbial or plant cells provide effective means to ease the separations of biocatalysis and the desired products.

Product characterization, quality control and product safety are important parts of a food processing operation. Besides the use of traditional methods to ensure quality and safety of foods and to identify food components, the increasing number of analytical methods involving enzyme reactions as well as the developments in bioselective electrodes (17) will gain acceptance in the food industry. In addition the potential of tissue culture and genetic methods for nutrient and toxicity assessments as well as the developments of freshness indicators (i.e. via monoclonal antibodies) are important potential aspects in the area of food safety.

Treatment and utilization of food process wastes is an increasing problem because of the large volumes involved which create a disposal as well as a pollution problem. Whey, the liquid that results from the separation of curd during the processing of cheese, contains about one per cent protein and 5 per cent lactose. For example, 20 million metric tons of whey accumulate annually in the US alone of which approximately 50 per cent are disposed of in industrial or municipal waste treatment operations. (18) This provides a major challenge for the biotechnologists to identify effective uses for the bioconversion of these waste products such as enzymatic hydrolysis of lactose. (19) The rapid solution of the problems of food processing and agricultural wastes has recently been identified as a specific R&D recommendation by the Economic Commission for Europe (ECE) of the United Nations. (20) Bioconversion of food processing waste also includes the use of starch substrates. The "Symba" process for example utilizes a symbiotic culture of two yeasts to convert potato starch into SCP. The application of molasses or corn steep liquor as substrates are other examples of waste utilization. Even the production of vinegar from "waste" wine can be placed into this category. (21) Finally the anaerobic digestion of food wastes to provide methane needs to be mentioned. (22)

References

(1) Science, 229, 1224, 1985.

(2) Sci. American, 252, (5), 66, 1985.

(3) Biotechnologie 82, Dechema 1982.

(4) J. W. Rosenblum, Agriculture in the twenty-first century, Wiley 1983.

(5) Science 219, 671, 1983; ibid. 229, 1224, 1985; Enzyme Miro Technol, 7, 474, 1985; Food Technol. 39 (10), 124, 1985.

(6) Science 219, 740, 1983.

(7) Food Technol. 38(2)120, 1984; Science 221, 949, 1983; Experientia, 39, 687, 183.

(8) Food Technol. 38(1), 85, 1984.

(9) High Technol. 5(2)66, 1985; Bio Technol. 1, 778, 1983.

(10) Food Technol. 37(10), 85, 1983; ibid. 37(10)66, 1983.

(11) US patents 4, 447, 456; 4, 485, 172; 4, 485, 173.

(12) Reed, G., Biotechnology, Vol. 15, Verlag Chemie, 1983.
A. H. Rose, Industrial Microbiology, Butterworth, 1961.

(13) S. E. Gilliland, Bacterial starter cultures for foods, CRC Press, 1985.

(14) Process Biochem 20(3), 75, 1985.

(15) J. Am. Oil Chem. Soc. 60, 476, 1983.

(16) Naturwiss. 71, 181, 1984.

(17) J. Biotechnol. 3, 1, 1985.

(18) J. H. Green and A. Kramer, Food processing waste management, AVI, 1979.

(19) Process Biochem. 20(1), 2, 1985.

(20) Symposium on the importance of biotechnology for future economic development, UN, ECE, 3-7 June 1985, Szeged, Hungary.

(21) Rehm, H. J., Industrielle Mikrobiologie, Springer 1967.

(22) D. A. Stafford et al., Methane production from waste organic matter, CRC Press, 1984.

This article first appeared in the Biotechnica Newsletter of the Messe-AG, D-3000 Hannover 82, Federal Republic of Germany.

Chemical applications

Adhesive production gene isolated

Dr. J. Herbert Waite of the University of Connecticut Medical School in Farmington, USA, has deciphered the chemical structure of the adhesive that enables mussels to form a life-long attachment to rocks. The genetic code used by mussels to synthesize the substance has been determined by Genex Corp. (Rockville, Md.), making possible the use of a yeast or bacterium for its commercial production. The powerful adhesive would have many biological applications, including re-attaching broken teeth and reconnecting broken bones. (Source: Genetic Engineering News, September 1986)

Biotechnology company has microalgae source for a higher fatty acid

Cyanotech Corporation, Woodinville, Washington-based specialty producer of high-value products from microalgae, says it has successfully developed an algal source for eicosapentaenoic acid (EPA) which would make purification of the acid far simpler.

EPA, a C_{20} polyunsaturated fatty acid with five double bonds that is found in certain fish oils, is believed to be effective in reducing risk of heart disease and in preventing or even reversing formation of atherosclerotic plaques in the arteries.

Several fish oil products containing EPA are currently available in the marketplace; however, fish oils containing EPA also contain other fatty acids with closely similar chemical structures, complicating the separation and purification. According to Cyanotech, its algal source contains no closely related fatty acids, meaning EPA purification would be much easier.

Also, the company says its microalgal EPA product is essentially free of cholesterol and undesirable fatty acids and has no "fishy" odour. Large-scale culture ponds and processing facilities operated in Kona, Hawaii, allow the company to mass produce microalgae so that any desired quantity of EPA can be produced, Cyanotech says.

The company has been producing EPA in pilot facilities at Woodinville, but now wants to mount a commercial-scale operation at the Hawaiian site. Cyanotech plans to produce algal EPA in two forms: first as a dried algal powder containing approximately 10 per cent EPA for over-the-counter sale as a health food, and, second, as a purified oil containing at least 75 to 80 per cent EPA. (Source: Chemical Marketing Reporter, 9 June 1986)

Energy and environmental applications

Coal tar clean-up

Biotechnology is to be used to clean up land polluted by coal tar. The US company, Cambridge Analytical Associates, has started preliminary trials of its clean-up process which uses bacteria at a New England utility site.

The trial, which is restricted to a one-acre site, will, if successful, be followed by a larger operation next year. (Source: European Chemical News, 22 September 1986)

Technology: in situ bioreclamation

Of the broad group of hazardous waste treatment technologies under development in the US, one of the most exciting, and controversial, is in situ bioreclamation - in which micro-organisms are stimulated with nutrients and oxygen to degrade organic contaminants in groundwater and soil. But, for example, biodegradation has not been effective in detoxifying halogenated chemicals such as carbon tetrachloride, vinyl chloride, polychlorinated biphenyls and dioxins.

In situ biodegradation has been successful for years in treating petroleum hydrocarbons, principally gasoline and fuel oil. And, say its proponents, in situ performance against a whole host of aliphatic and aromatic chemicals has been demonstrated in the laboratory. Now, they insist, in situ bioreclamation systems are working in the field and cutting costs handsomely.

Bioreclamation specialists emphasize that every remedy for contaminated soil and groundwater must be site specific. The problems of dealing with subsurface pollutants are so complex, they say, that the solution invariably will be a combination of technologies.

Site specificity and complexity make drawing conclusions chancy, even from documented field experience.

There are three basic in situ biodecontamination techniques:

- Pumping water from the aquifer to form a cone of depression in the water table, from which free, insoluble contaminants can be pumped;
- Adding nutrients and oxygen to groundwater and, through infiltration galleries, to the layers of soil that contain contaminants but are not saturated with them - the "unsaturated zone";
- Hydraulically moving the water table up or down to wash or biodegrade contaminants from the unsaturated zone.

Engineers and bioreclamation executives disagree on the technology's effectiveness for several reasons. One briskly debated area is the effect of soil hydrology on biodecontamination.

Microbiologists respond that nutrients and oxygen will follow paths taken by contaminants. If a formation is impermeable to remedial fluids, it is also likely to be impermeable to contaminants. Although in situ biodegradation does not work for all halogenated aliphatic chemicals, research is under way. Stanford University's (Stanford, Calif.) Perry McCarty, professor of civil engineering, says compounds with two or more chlorine atoms can be transformed anaerobically in the laboratory through reductive halogenation. He adds a primary substrate - acetate, methanol or isopropanol - to increase the concentration and activity of methane-forming bacteria. However, there is a caveat to this approach, in that the final product of reductive halogenation can be a known carcinogen, such as vinyl chloride. To biodegrade such end products would require aerobic conditions, the reverse of the environment required for successful biodegradation in the first place. Nevertheless, the anaerobic/aerobic strategy may be the only way to handle some chlorinated aliphatics biologically.

Researchers at the Kerr laboratory have discovered that if they add to the soil aerobic organisms that grow on aliphatic hydrocarbons such as natural gas or propane, they can degrade a variety of chlorinated solvents, including trichloroethylene, dichloroethylenes, certain trichloro- and dichloroethanes, chloroform and ethylene dibromide.

A Stanford scientist reports success with anaerobic transformation of aromatic hydrocarbons by bacteria in aquifers. This flies in the face of previous evidence that aromatic hydrocarbons can be degraded only under aerobic conditions, in the presence of molecular oxygen.

What such conflicts demonstrate, say those involved with a multitude of technologies, is that in situ bioreclamation is still in its nascent stages. (Extracted from Chemical Week, 20 August 1986)

Industrial microbiology

Detergent enzyme plant start-up

A joint venture between West Germany's Henkel and Biochemie of Kundl, Austria, has started production of detergent enzymes at its new plant at Kundl in the Tyrol.

Initially, the new plant will allow Henkel to meet around two-thirds of its enzyme requirements. Previously, the company purchased all its raw enzymes from three outside manufacturers, Novo Industri, Gist-brocades and Miles.

Henkel and Biochemie, a Sandoz subsidiary, also plan to co-operate in R&D, with an eye towards developing "tailor-made" enzymes for specific uses in detergents. According to Henkel "it is conceivable" that lipases and hydrolases will be developed as detergent enzymes in future.

The two companies say they are looking at the US market. There currently only 15 per cent of all detergents contain enzymes, compared with 85 per cent in Europe. (Source: European Chemical News, 14 July 1986)

Industrial equipment

Biotechnology takes its place in schools

Pupils at 80 selected schools in the north and south-east of England will get a chance to run sophisticated biotechnology experiments in specially designed mini-fermenters. The schools are taking part in a scheme sponsored by the Department of Trade and Industry (DTI) which aims to promote biotechnology in schools, and to assess the equipment and the curriculum that such a course would require. If the trial is successful, the DTI could support a larger scheme to assist all schools to purchase a fermenter.

The fermentation industry is the third largest industrial sector in the country. However, the high cost of equipment, the sensitivity of the techniques involved, and its interdisciplinary nature have effectively excluded biotechnology from the syllabus in all but a few favoured schools.

Geoffrey Holt and Alan Bull of LH Bioprocessing, a biotechnology research and development company based at the University of Kent, together with Mike Bushell from the University of Surrey, set out to develop a small bench-top fermenter for the classroom which had to mimic the technology applied in industrial fermenters as well as be easy to operate in the most rudimentary school biology laboratory. It also had to be relatively cheap and safe. The body of the fermenter has a capacity of one litre, and is constructed of heatproof glass. It is designed so that it will fit into a pressure cooker for easy sterilization.

Perhaps the most exciting feature of the fermenter is a computer programme, written by Michael Bushell, which allows the information from the probes to be hooked up to a BBC microcomputer. All the variables are sampled regularly, and displayed on a colour monitor. The student can key in the desired temperature, which is then regulated automatically. So the student can control a crucial variable, see the progress of an experiment and have a permanent record for later analysis. This represents the state-of-the-art in monitoring and control of fermentation processes, and was introduced only comparatively recently by industry.

The hope is that the DTI will initiate a scheme to assist every school to buy a fermenter. (Extracted from New Scientist, 21 August 1986)

Equipment for large-scale biotechnology production

Pharmacia and Alfa-Laval have finalized the details of a 45/55 joint venture that will make equipment for large-scale biotechnology production. A first order has already been received from Australia's Commonwealth Serum Laboratories for the planning of a blood plasma processing facility. (Source: European Chemical News, 7 July 1986)

E. PATENTS AND INTELLECTUAL PROPERTY ISSUES

Genentech faces hGH patent suit

Genentech is being sued by Hoffmann-La Roche and the Hormone Research Foundation (HRF). The suit, filed in the federal district court in San Francisco, alleges that the manufacture and sale of recombinant human growth hormone (hGH) infringes an HRF patent for which Roche received an exclusive licence in 1982. Genentech is expected to defend its own position successfully.

Granted in 1971 to Dr. C. H. Li of the University of California, the patent covers the chemical synthesis of hGH. Hoffmann-La Roche and HRF claim that the synthesis clause in the patent also covers the manufacture of hGH by recombinant means. Genentech is defending its position claiming that, as recombinant techniques had not been developed at the time of the patent award, Roche and HRF's claim is not valid. (Extracted from European Chemical News, 22 September 1986)

Genex patents novel antibodies

Genex, the US biotechnology concern, has filed patent applications relating to the design and production of novel single chain antibodies developed using its protein engineering technology. The hybrid molecules are unlike conventional antibodies as they are expected to be manufactured in genetically-engineered micro-organisms.

Other possible advantages of single chain antibodies include anticipated smaller size, greater stability and significantly reduced cost. The smaller size of the proteins may reduce the body's immune reactions and thus increase safety and efficacy of therapeutic applications.

Once widely available, single chain antibodies may revolutionize the use of antibodies in diagnosis, therapy, sensing devices and separations technology. Genex intends to commercialize its single chain antibodies in collaboration with various corporate partners for defined uses and markets. (Source: European Chemical News, 15 September 1986)

Gamma interferon patented in Germany

Biogen claims to have received a patent in the Federal Republic of Germany to use gamma interferon

in the treatment of rheumatoid arthritis and expects to have a product on the market by the end of the year. The patent was granted to Biogen's German affiliate Bioferon Biochemische Substanzen GmbH. Biogen has sought similar worldwide patent protection for gamma interferon.

The company claims its gamma interferon represents the first biotechnology product to enter the anti-arthritic market. It follows Biogen's alpha interferon which is marketed by Schering- Plough and went on sale last year.

In addition to treating rheumatoid arthritis, Biogen's gamma interferon product is undergoing clinical testing for the treatment of renal cell (kidney) cancer and other cancers in the US, Europe and Japan. (Extracted from Chemical Marketing Reporter, 19 May 1986)

Patent sought for alga that secretes hydrocarbons

The University of California (Berkeley) is seeking a patent for an alga that secretes hydrocarbons throughout its growth period. Other algae that have been studied secrete hydrocarbons only after reaching maturity. The new strain of Botryococcus braunii contains hydrocarbons in excess of 30 per cent of its dry weight. The alga can be easily harvested from ponds since it grows in fairly large colonies on the surface. Other algae that secrete hydrocarbons are difficult to harvest, since they remain in suspension. The algae can be forced to secrete oil when a pressure of 2-5 psig is applied and can subsequently be returned to the pond. Some 97 per cent of the oil, which contains long-chain hydrocarbons, can be catalytically cracked to form transportation fuels such as diesel oil, gasoline and aviation-grade fuel. The university hopes to commercialize the alga for fuel production. (Extracted from Chemical Engineering, 18 August 1986)

Interleukin-2 patent

Interleukin-2 Inc. claims the European Patent Office has approved its patent covering a proprietary process for the manufacture of interleukin-2. According to the company, the European patent covers Interleukin-2's technology in the UK, France, Federal Republic of Germany, Switzerland, Austria, Italy, Sweden, Holland and Liechtenstein. (Source: Chemical Marketing Reporter, 8 September 1986)

Two biotechnology companies in dispute over an anticancer drug patent

Amgen (Thousand Oaks, Calif.) is suing Cetus (Emeryville, Calif.) in an attempt to invalidate the latter's US patents on interleukin-2 (IL-2). Amgen asserts that its IL-2 does not infringe on the Cetus patents and asks the court to consider the scope of those patents. Amgen filed suit after it received a report that Cetus was preparing to sue Amgen for patent infringement. Amgen claims its genetically engineered mutein product is chemically different from Cetus', in that it has an aniline unit in position 125 of the amino acid sequence, where the Cetus product has cerine. Cetus' IL-2 is already in late Phase II trials in the US. Amgen has completed Phase I trials. (Extracted from Chemical Week, 3 September 1986)

Enzo Biochem licenses technology from Yale

Enzo Biochem has obtained an exclusive license from Yale University for a new polymer technology that offers a 10- to 100-fold increase in signal amplification over current nonradioactive methods. Enzo Biochem says the system can be applied to development of a broad range of novel therapeutic and diagnostic products. Enzo also has received an option for the extension of its original license from Yale - for the inventions used in the development of Enzo's proprietary nonradioactive DNA probe technology - to the life of the patents issued from the five years now remaining on the original license. (Source: Reprinted with permission from Chemical and Engineering News, 18 August 1986. Copyright 1986 American Chemical Society)

F. BIO-INFORMATICS

A new OECD report on biotechnology: "Recombinant DNA safety considerations"

A decade after the international scientific meeting of Asilomar (USA) on the potential risks of recombinant DNA organism laboratory manipulations, this report just published by OECD represents a new landmark in the history of biotechnology.

After three years of difficult and intensive work, high-level experts from OECD countries have overcome initial differences of opinion and reached an international consensus on scientific criteria for the assessment of potential risks associated with the use in industry, agriculture and the environment, of the recombinant DNA technique. This is the best known of the new biotechnology techniques.

Thus, a large number of countries have agreed on the principles to be applied for the safe development of a new and complex technology from its very beginning.

With the emerging commercial applications of biotechnology and its prospects for agriculture and the environment, the task of the experts was to determine whether the large-scale use of recombinant DNA organisms raised additional risks as compared to their construction in the laboratory or indeed compared to traditional organisms which industry has been employing for a long time.

The largely positive assessment of the experts and the scientific criteria established will help to develop the recombinant DNA technique and thus to reap the benefits it is expected to bring in different sectors of economic and social life as well as to protect health and the environment. The report constitutes a first step towards the establishment of international guidelines and the harmonization of policies concerning safety in this area.

The experts' recommendations have been adopted by the Council of the OECD, which shows the willingness of Member countries' Governments to commit themselves to a common approach to safety problems.

The report:

- Analyses the different biotechnology applications in industry, agriculture and the environment and emphasizes the important benefits they may bring to humanity.

- Considers that in general the risks associated with recombinant DNA organisms are primarily of the same nature as those occurring in the case of classical organisms.

- Establishes an important distinction between industrial applications (contained) and agricultural and environmental applications (non-contained).

- With reference to industrial applications, considers that the large majority of them will require only minimal safety measures as industry utilizes essentially low-risk organisms. These measures will be known internationally as GILSP (Good Industrial Large-Scale Practice).

- With reference to agricultural and environmental applications, advocates a provisional strategy, namely an independent case-by-case evaluation, since generally applicable international guidelines are still premature.

- Identifies detailed scientific parameters for the risk evaluaton of different types of applications.

"Recombinant DNA Safety Considerations", safety considerations for industrial, agricultural and environmental applications of organisms derived by recombinant DNA techniques, 69 pages, OECD, Paris 1986. ISBN 92-64-22857-8. Available from OECD Sales Agents. (OECD Press Release, 16 October 1986)

Biotechnology market opportunities

Research in biotechnology is beginning to pay off, according to Bio-Market Opportunities, a study published by Technical Insights Inc. By 1990, it forecasts, the US market for human interferons should reach $600 million-$800 million. By 1995, the market for interleukin-2 (IL-2) and other lymphokines could reach $1.8 billion. The 94-page report has 15 sections focusing on bio-markets ranging from human recombinant DNA vaccines, lymphokines and interferons to herbicide-resistant crops and animal growth hormones. Price $248 (US) or $278 (overseas), obtainable from Dept. GTPR86, P.O. Box 1304, Fort Lee, NJ 07024, USA or on (201) 568 4744. (Source: Biotechnology Bulletin, Vol. 5, No. 6, July 1986)

EC Concertation Unit for Biotechnology in Europe

CUBE, the European Commission's Concertation Unit for Biotechnology in Europe, is to monitor strategic developments in biotechnology worldwide, make recommendations on Community strategy, promote information between member countries and facilitate the co-ordination of activities within the Commission itself. CUBE was formally set up in February 1984, to help implement the recommendations from the FAST team (Forecasting and Assessment in Science and Technology). Some of CUBE's specific activities include providing the secretariat for the Commission's Task Force on biotechnology with information, providing representation and advice in international fora and conferences, and commissioning study contracts.

A particular interest of CUBE has been the application of computing to biotechnology. Together with the Commission's Information Technologies and Telecommunications Task Force a study of bio-informatics "IT for BT" has been set up. Ten contracts hve been agreed so far. CUBE may be contactud for details at DGXII, rue de la Loi 200, 1049 Brussels, Belgium, Tel. 2350749.

"Biotechnology and Microbiology in Australia"

The first comprehensive, market-oriented report of biotechnology and microbiology in Australia today is now available.

A package containing information on Australian biotechnology and microbiology in easy to understand language including who is doing what and where, opportunities, overseas competition, market trends etc. One of the key objectives of this information package is to identify areas of commercial potential in Australian research and development and put these advances into a commercial perspective. Biotechnology and Microbiology in Australia criticizes certain aspects of the industry. It also further highlights likely Australian problems with the benefit of overseas experiences, chiefly in the USA and Japan.

This information package contains:

1. Market survey:

   a far-reaching analysis of products, services and market opportunities.

2. Information data base:

   complete indexed compendium of relevant R&D.

   description of Australian companies active in bictechnology (Main Board, Second Board and Private).

   Australian biotechnology patents granted.

   competitor companies in Japan, South-East Asia and New Zealand.

As an optional extra, the complete R&D data base, (including 1,095 researchers identified and listed), plus companies, government departments and relevant organizations is now available on computer floppy disc.

The price of the book, plus air mail is US$378, that of the computer disc, dBASE III users only, US$741. Further information can be obtained from the publishers, Science Focus, Division of Rendex Industries P/L, 131 Canterbury Road, Toorak, Victoria 3142, Australia.

Recombinant DNA methods for teachers

Secondary school teachers will be exposed to new knowledge and teaching methods involving recombinant DNA through a project initiated by Cold Spring Harbor Laboratory and Citibank, USA. A specially designed van carries all the equipment needed for up to 36 teachers to perform experiments that culminate in production and analysis of recombinant DNA molecules. Appropriately named "Vector", the mobile DNA laboratory will be used in a five-day course, "Recombinant DNA for Beginners", that will be given at seven locations around the USA. (Source: Reprinted with permission from Chemical and Engineering News, 23 June 1986. Copyright 1986 American Chemical Society)

The biotechnology of malting and brewing, by James S. Hough, Adrian Brown Professor of Brewing Science and Industrial Biochemistry and Director of the British School of Malting and Brewing, University of Birmingham.

This book gives a clear, concise account of malting and brewing processes and the science on which they are based. There are chapters about barley and the malting of the grain, about water, hops, and yeasts and bacteria as well as descriptions of fermentation and post-fermentation processes. The techniques of production of high-quality beers are also described. The whole description is placed within a biotechnological context: modern developments and the wider significance of the bacteria that commonly contaminate beer are carefully examined. Price:

£20. Cambridge Studies in Biotechnology 1. Published by Cambridge University Press, The Edinburgh Building, Shaftsbury Road, Cambridge CB2 2RU, United Kingdom.

Biotechnology and wastewater treatment, by C. F. Forster, Department of Civil Engineering, University of Birmingham.

The aim of this book is to provide the biotechnologist with the fundamentals of wastewater treatment technology. Although the art of sanitation is several thousand years old, sewage treatment is relatively recent and the book describes both the basic biological concepts and industrial practices. Problems of pollution are given attention and recent developments in control are discussed. Reactor types, aeration, the handling and disposal of sewage sludge and the anaerobic treatment of effluents are among the topics dealt with. The particular problems of developing countries are included and the challenge of biotechnology is made apparent. Price: £35. Cambridge Studies in Biotechnology 2. Published by Cambridge University Press, The Edinburgh Building, Shaftsbury Road, Cambridge CB2 2RU, United Kingdom.

Economic aspects of biotechnology, by Andrew J. Hacking, Tate & Lyle Group Research and Development, Reading.

Both macro- and microeconomic aspects of biotechnology are discussed in this book. It explains economics and accounting procedures from first principles and assumes no prior knowledge of these areas. The author works on developing new biotechnological projects. He draws extensively on his own experience and brings together the factors which determine commercial reasoning towards biotechnology in areas such as markets, project selection, costing and capital investment. His subjects include market analysis, fermentation, enzyme technology, genetic engineering and many others. Price £35. Cambridge Studies in Biotechnology 3. Published by Cambridge University Press, The Edinburgh Building, Shaftsbury Road, Cambridge CB2 2RU, United Kingdom.

ACS helps swell the tide of on-line data bases

At the end of September 1986 the American Chemical Society (ACS) launched a computerized data service called Chemical Journals Online (CJO), allowing personal computer users in the USA, Federal Republic of Germany and Japan to read the full texts of ACS's 18 research journals. The service joins a swelling tide of chemically related on-line data bases in the past several years which allow subscribers to retrieve information instantaneously on technical, business, environmental, legal and legislative matters. For those who are uncertain about which on-line service to use, there are even data bases on data bases.

The CJO service is typical of many of the new on-line data bases. Computer users with modems will be able to tap into the system with a local phone call through such telecommunications networks as Dialog, CompuServe and Tymnet. For fees ranging from $50 to $3,000, they will then have access to the full texts of about 45,000 articles going back to 1982. Although the system does not go back very far, the full-text capability should prove valuable to subscribers.

Locating an article with CJO will be possible by answering questions posed by the system when the user logs on. By specifying such information as publication date, journal title, volume and issue, author, the particular chemical name and the registry number of the chemical listed in ACS's Chemical Abstract Service (CAS) - either alone or in combination - subscribers will be able to rapidly locate the paper they are looking for. Users of ACS's CAS Online service, which provides abstracts of papers, will be able to get the full texts of the articles by switching on line to CJO.

The new CJO programme will be part of a scientific and technical data network called STN International. A data-pooling venture between ACS in the US and scientific societies in the Federal Republic of Germany and Japan, STN allows subscribers of on-line services or members in any of these countries to gain access to the data bases of participating societies in the other countries. Another plus for the new system will be software that makes it easier to use than a similar ACS system that existed several years ago. While CJO will be confined initially to ACS journals, the system will be expanded to include chemical journals of other publishers. (Extracted from Chemical Week, 24 September 1986)

EEC bio-informatics programme

Within the new Framework Programme of Technical R&D 1987-1991 the European Economic Commission proposes a specialized programme on "Bio-informatics: Collaborative European Programmes and Strategy (BICEPS)". Designed by the CUBE office (Concertation Unit for Biotechnology in Europe) the new programme concentrates on the information problem in biotechnology.

At present the EEC supports research in bio-informatics in the following projects: image processing of gels, advanced software for production modelling, expert systems and the development of cell culture data banks. In addition, new information sources will receive start-up funds.

Preparatory studies are now being launched to look at the potential for the Commission's support in the areas of biosensors, biochips, and advanced clinical applications in instrumentation and communications. Copies of new studies may be obtained from CUBE (DG XII, EEC, Brussels, Belgium):

- Knowledge-based facilities for information retrieval, and
- Biomolecular modelling in the European Community.

BICEPS will make its first report in September 1986 and new projects will hopefully start in 1987 - one would be a European BIONET - the on-line supply of DNA and RNA sequences.

BICEPS addresses both the medical informatics and bio-informatics needs:

1. Medical informatics

A further improvement of health care and better economics of providing it depends on progress in numerous domains. One of the opportunity areas for progress builds on the consequent exploitation of the potential of IT&T. Their application in various functions can ring very significant improvements in quality, availability and cost-effectiveness of medical care.

2. Bio-informatics

A major part of the medical expenses is associated with pharmaceutical products and medical research. In this domain there is strong dependence of progress in biotechnology and medical research with bio-informatics.

For 1987 a definition phase is envisaged preparing the main programme foreseen to be implemented in 1988. This will permit a precise formulation of the work offering the greatest advantage of Community scale and being complementary to work carried out on the Member State level. (Source: Journal of Bio-Technica '86, Hannover)

New computer programme

Biosym Technologies (San Diego, CA) has introduced a computer programme for molecular simulation and analysis. The new Discover programme facilitates the co-ordination of molecular properties with structure. It is being used in biotechnological, pharmaceutical and agricultural chemical applications. (Extracted from Chemical Week, 20 August 1986)

DNA databases are swamped

In the four years since they were established, the major DNA databases, located at the Los Alamos National Laboratory in the United States and the European Molecular Biology Laboratory (EMBL), Heidelberg, have grown in size by some 25 times, and the rate of increase in production of DNA sequence information could almost double the size of the databases by June 1987, at which time the initial $3.5 million, 5-year contract for the US facility comes to a end. The National Institutes of Health recognizes that it will have to find significantly increased resources when it awards a new contract for the continuation of the US database because the Los Alamos operation, known as GenBank, has simply been unable to cope with the volume of sequence information coming through the journals. The facility faces a large backlog of sequences that are yet to get into the database, some of which go back as far as two years. For instance, only 19 per cent of the sequences published in 1985 are in GenBank.

This effort to catch up includes hiring more people to enter the information. The principal tactic, however, is to cut back on annotation of the sequences, which to some extent diminishes the value of the database. Annotation involves the indication of start and stop positions in a gene, intron and exon boundaries, the location of enhancers, and the addition of other relevant biological information. The assembly of these data has so far been done by technically qualified database personnel, who comb through the source paper and other relevant publications.

GenBank shares the job of collecting sequence information with the EMBL, and the two databases then pool their information. The EMBL facility, like GenBank, found itself flooded with data, but for a number of reasons has already been able to clear up much of its backlog. Not only did the EMBL database have a 6-month jump on GenBank in beginning the data-collection job, starting in April 1982 as against GenBank's October, but it also initiated its crash catch-up programme a year earlier than GenBank.

GenBank and EMBL are collaborating closely to find ways of getting sequence information into their databases more rapidly and efficiently. For more than a year GenBank has been writing directly to authors of sequences, asking for annotation details in standard format. The response has been poor, about 30 per cent. Even fewer authors take the opportunity of submitting their information on a floppy disc, which method greatly facilitates input to the database. In fact, authors might soon find that having their sequence on the databases will be the only way of making their work public, as journals become reluctant to occupy page upon page of their publications with virtually unreadable sequences. Also important is the basic handling of data, especially the melding of related information, which currently is enormously time-consuming. (Extracted from Science, Vol. 232, 27 June 1986)

Grant awarded to develop computer system for protein engineering

School of Pharmacy researchers at the University of California (San Francisco) have received a $4.39 million, three-year grant from the Federal Government to develop a new computer system called the Macromolecular Workbench. The system can help predict the three-dimensional structure of proteins which, in turn, will enable scientists to determine how proteins act, how drugs and other chemicals interact with proteins and how to engineer new proteins. (Source: Genetic Engineering News, September 1986)

Information in biotechnology is becoming an increasingly valuable commodity, and a number of start-ups have been formed to address this need. Bioindex from Technical Communications (Lafayette, CA) monitors the literature to track some 400 biotechnology therapeutic projects. Four files - organized by developing company, product type, specific product, or products being developed without partners - are available. The price of $875 includes the current issue plus five bi-monthly updates. To keep up with the biotechnology companies themselves - over 800 of them - Oryx Press (Phoenix, AZ) and Cetus Corp. (Emeryville, CA) will publish a bi-monthly directory service called BioScan. A subject index, company cross-reference index, investor index, and geographic index will allow easy access to the information. The price of $424 (in the US) is for the first issue (October 1986) and the first five bi-monthly supplements.

As for on-line information acquisition, BioSciences Information Service (Biosis, Philadelphia, PA) and Information Access Co. have ended their joint production of the BioBusiness database due to production incompatibilities. BioBusiness will now be produced (without interruption) by Biosis alone. (Extracted from Bio/Technology, Vol. 4, June 1986)

New molecular simulation programme

Discover is a new computer programme for molecular simulation and analysis, developed by Biosym Technologies of San Diego, CA. It is designed to facilitate the study of structure-related properties of both large and small molecular systems. The simulation programme has been under development at Biosym since 1984 under the direction of Dr. Arnold Hagler, the company's chief scientific officer and co-founder. (Biotechnology Bulletin, Vol. 5, No. 8, September 1986)

GENEUS computer programme

Researchers at the Unit for Applied Cellular and Molecular Biology at the University of Umea in Sweden have developed a genetic engineering computer software package which is comparatively cheap and easy to handle. It contains data from EMBL and is directly adapted for VAX computers. The system has self-checking programmes as well as auxiliary information. Petter Gustafsson hopes to adapt the computer package also to small computers. (Source: Journal of Biotechnica '86, Hannover)

Princeton scientist speeds up gene identification process

Princeton University computer scientist Daniel P. Lopresti has developed a computer chip which, when plugged into a personal computer,

compares selected genes with a database of known genes up to 300 times faster than a minicomputer. The chip could make the search for the genetic roots of cancer and other diseases much simpler. (Source: Genetic Engineering News, September 1986)

G. MEETINGS

13 to 15 January 1987
The New York Academy of Sciences Conference on Biological Approaches to the Controlled Delivery of Drugs, Marriott Marquis Hotel, New York City, USA. Further details from Conference Department, The New York Academy of Sciences, 2 East 63 Street, New York, NY 10021

26-28 January 1987
The Second Annual New Orleans Conference Bio/Technology, The New Orleans Marriott, New Orleans, USA. For information on registration please contact Diana Berger, Conference co-ordinator, Bio/Technology, 65 Bleecker Street, New York, NY 10012

24 to 28 March 1987
BIOEXPO 87, to be held in Paris at the Parc des Expositions, Porte de Versailles. BIOEXPO is organized by ADIP (Association for the Development of the Pasteur Institute), the BIOFUTUR group and SEPPI, in association with Genetic Engineering News (published by Mary Ann Liebert Inc., New York), under the patronage of the French Ministries of Industry, Agriculture, Research and Higher Education. Its Organizing Committee is chaired by Professor Raymond Dedonder, Director of the Pasteur Institute, Professor Pierre Douzou, President of the "Essor des Biotechnologies" Mobilizing Programme, and Professor François Gros, of the Collège de France. Further information from Association pour le Développement de l'Institut Pasteur (ADIP) BIOFUTUR/SEPPI and BIOEXPO/SEPPI, 8 rue de la Michodière, 75002 Paris, France, Tel.: (1) 47 42 92 56, Telex: 211897 F TECEXPO

26-28 May 1987
The National Institutes of Health and the Institut Pasteur announce a Centenary Symposium on the Impact of Molecular Biology on Biomedical Research. The meeting will take place at the National Institutes of Health, Bethesda, Maryland in the Masur Auditorium. Further details from Ms. Wendy Walker, Courtesy Associates, 655 15th Street, N.W., Suite 300, Washington, DC 2005, USA. Telephone: (202-639-5180) (9 a.m.-6 p.m.), Telex: 440487 COURTEST

28 June - 2 July 1987
Frontiers in Bioprocessing, Boulder, Colorado, USA. A conference sponsored jointly by:

- Center for Chemical Engineering, National Bureau of Standards - Boulder, Colorado
- Bioprocessing and Pharmaceutical Research Center - Philadelphia
- Center for Separation Science - University of Arizona.

For additional information contact:
Dr. Subhas K. Sikdar, National Bureau of Standards, 325 Broadway, Boulder, CO 80303, USA, Tel.: (303) 497-5232

15-17 September 1987
Separations for Biotechnology, Reading, UK. Further details from Society of Chemical Industry, 14/15 Belgrave Square, London, SW1X 8PS

22 to 24 September 1987
Termin der BIOTECHNICA '87, Hannover, Federal Republic of Germany. Further information from Dipl.-Oec. Bernd A. Diederichs (0511) 89 27 20, Dipl.-Oec. Martina Scharnhorst (0511) 89 27 20

5-9 October 1987
Centenary Symposium of Institut Pasteur, Paris, France, on Molecular Biology and Infectious Diseases. Further details from Institut Pasteur, 28, rue du Docteur Roux, 75724 Paris, Cedex 15, Telex: PASTEUR 250 609 F, Tel.: 16 (1) 45 68 80 00

6-8 October 1987
The First International Symposium on Bio-Processing Safety Standard Guidelines and Practices to Insure Worker Safety in the Bio-Processing of Industrial Chemicals, Foods, and Waste Products, in Washington, DC, USA. Further details from Joyce Barton, ASTM, 1916 Race Street, Philadelphia, PA 19103, USA, Tel.: (215) 299-5400, TWX: 710-670-1037.

UNITED NATIONS INDUSTRIAL DEVELOPMENT ORGANIZATION

UNIDO MAILING LIST QUESTIONNAIRE

Code 503

Genetic Engineering and Biotechnology Monitor

To be considered for inclusion on the UNIDO Newsletter mailing list, please complete questionnaire and return it to:

UNIDO MAILING LIST, INDUSTRIAL INFORMATION SECTION,

P.O. BOX 300, A-1400 VIENNA, AUSTRIA

	Type or print clearly (one letter per box) and leave a space between each word
NAME (underline family name)	
TITLE OR POSITION	
ORGANIZATION	
STREET AND No. (or P.O. Box)	
CITY AND STATE OR PROVINCE	
COUNTRY	

PLEASE DO NOT WRITE IN THESE SPACES

S/A ☐ DISP. CODE ☐ COUNTRY ☐☐☐

CITY ☐☐☐☐☐☐☐☐☐☐☐☐

T TYPE OF ORGANIZATION: Identify below the type of organization to which you belong, checking the box(es) as appropriate (e.g., for a research centre at a university, boxes 20 and 23 would be applicable).

01	☐	UN, specialized agency or other UN body	12	☐	Trade centre or association	23	☐	Research centre/laboratory
02	☐	Other intergovernmental organization	13	☐	Professional association/learned society	24	☐	Library/documentation centre
03	☐	International non-governmental organization	14	☐	Bank or financial institution	25	☐	Information centre
04	☐	UNIDO National Committee	15	☐	Industrial enterprise	26	☐	Publisher
05	☐	Embassy or Mission to UNIDO	16	☐	Public utility	27	☐	Bookseller
06	☐	Government body for development aid	17	☐	Trading concern	28	☐	News agency/press
07	☐	Ministry for industry	18	☐	Engineering organization	29	☐	Radio and television
08	☐	Other governmental department	19	☐	Consultant			
09	☐	Non-governmental aid agency	20	☐	University			
10	☐	Chamber of industry or commerce	21	☐	Vocational or technical institute/school			
11	☐	Manufacturers' association	22	☐	Industrial training or productivity centre			

F FIELD OF INTEREST: Check the appropriate box(es) which reflect your *main* field(s) of interest:

MANUFACTURING INDUSTRIES – PLANTS, PROCESSES AND PRODUCTS								
001	☐	Food processing	017	☐	Electrical machinery	030	☐	Industrial legislation
002	☐	Beverages	018	☐	Transport equipment	031	☐	Industrial property
003	☐	Tobacco	019	☐	Precision instruments	032	☐	Transfer of technology (licensing)
004	☐	Textile and garment	020	☐	Agricultural machinery	033	☐	Industrial research and development
005	☐	Leather	NON-MANUFACTURING INDUSTRIES AND PROJECTS			034	☐	Standardization
006	☐	Wood processing				035	☐	Industrial organization and administration
007	☐	Pulp and paper				036	☐	Industrial co-operatives
008	☐	Petrochemical and plastics	021	☐	Mining and quarrying	037	☐	Industrial information and documentation
009	☐	Industrial chemicals and fertilizers	022	☐	Utilities (including power plants)	038	☐	Industrial promotion
010	☐	Pharmaceuticals and other chemical products	023	☐	Public services (transport, communications, tourism)	039	☐	Industrial training
011	☐	Rubber	024	☐	Construction (civil engineering) projects	040	☐	Industrial management
012	☐	Non-metallic mineral products and building materials	SUPPORTING INDUSTRIAL ACTIVITIES			041	☐	Industrial consulting services
013	☐	Iron and steel				042	☐	Development of small-scale industries
014	☐	Non-ferrous metal				043	☐	Industrial estates
015	☐	Fabricated metal products	025	☐	Industrial planning and programming	044	☐	Appropriate technology
016	☐	Machinery	026	☐	Industrial policies			
			027	☐	Industrial financing and investment promotion			
			028	☐	Promotion of export-oriented industries			
			029	☐	Industrial development surveys			

LANGUAGE: Indicate below in which language you wish to receive the NEWSLETTER

ENGLISH ☐ FRENCH ☐ SPANISH ☐ RUSSIAN ☐