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Genetic Engineering and Biotechnology Monitor

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N.B. Special in this issue is an article on biosafety regulations in developing countries by Eduardo J. Trigo and Walter Jaffé, who are both presently at the Technology Generation and Transfer Programme of the Inter-American Institute for Co-operation on Agriculture in Costa Rica.

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A. NEWS AND EVENTS

UNIDO news

Bombay company gives grant to ICGEB

The Bombay Pharmaceutical Firm Wockhardt Ltd. became the first private company to make a major contribution to the International Centre for Genetic Engineering and Biotechnology (ICGEB). This came in the form of a research grant under an agreement signed by Wockhardt Managing Director Habil F. Khorakiwala and UN Industrial Development Organization (UNIDO) Director-General Domingo L. Siazon, Jr.

According to the agreement, Wockhardt Ltd. will contribute up to 50 million Indian rupees, equivalent to more than $3 million, for research at ICGEB's New Delhi laboratory into insulin, tissue plasminogen activator, erythropoietin, hepatitis vaccine and another mutually-agreed upon product during the next five years.

Wockhardt is committed to development of downstream processing and commercialization of these products. Manufacturing will be done by Wockhardt. On behalf of ICGEB, UNIDO will receive royalties from sales in India and abroad. The Organization will carry out these activities in co-operation with the Government of India.

Founded in 1960, Wockhardt won the 1988 Indian National Award for R and D Efforts in Industry. It manufactures and markets bulk drugs, pharmaceuticals and veterinary and dietetic products as well as plant-growth hormones. Operating since 1978, Wockhardt's R and D Unit has a state-of-the-art pilot plant and analytical facilities. (Source: UNIDO Press Release, 15 March 1990)

Regulatory issues

Looser rules tempt genetic engineers East

Western Europe's strict regulations for the field trials of genetically engineered organisms may lead the biotechnology industry to seek alternative testing grounds in countries such as the Soviet Union. This warning comes in a report to be published by a group of scientists from government, academia and industry following their visit to the USSR last September.

The trip convinced the group that the Soviet Union, with its relatively liberal approach to testing the products of biotechnology outside the laboratory, has much to offer the industry. Rod Greenshields, from GB Biotechnology, who led the visit, says it would be cheaper for industrialists to conduct their trials in the Soviet Union, as well as providing a route into a huge potential market. It would also grant the West access to the unexpected scientific excellence which the group found at Soviet biotechnology institutes.

The trip, prompted by the restructuring of biotechnology under President Gorbachev's régime, found that in some cases basic science in this field was ahead of that in the West. Greenshields said the group had been particularly impressed by work on designing genes to be expressed by host organisms delivering useful compounds with therapeutic or industrial uses, such as antibiotics expressed by plant cells.

The group's report says that the European Commission should take into account the possibilities open to the West's biotechnologists in the Soviet Union as the Commission formulates its policies on field tests of genetically engineered organisms and products.

Greenshields says that although the public in the Soviet Union has little confidence in its own biotechnologists, Western scientists are seen as trustworthy. There would be no problem for companies wishing to set up new facilities on Soviet soil, he says. In Western Europe, public opinion, particularly in the Federal Republic of Germany, is such that many companies are deserting the continent to set up facilities in the US.

Environmentalists, now represented in the UK by the newly formed umbrella organization, the UK Genetic Forum, argue that the position adopted by other countries on releasing genetically engineered organisms should not lead to relaxation of rules within the European Community aimed at protecting people and the environment.

Greenshields sees one possible drawback of exploiting the relatively lax régime governing field trials in the Soviet Union: although the trials may be sufficient to satisfy the Soviet authorities, such tests may not be recognized as valid elsewhere. (Source: New Scientist, 20 January 1990)

UK legislation on GMO release

The Royal Commission on Environmental Pollution, in its 13th Report, takes a broad look at the technology and environmental impact of deliberate release of genetically manipulated organisms (GOMs). The report "The Release of Genetically Engineered Organisms to the Environment" says that some present legislation, such as the Health and Safety at Work Act 1974, can be used to control potential hazards but advances in genetic engineering techniques may require more specific statutory controls. The report is available from the HMSO Publications Centre, P. O. Box 276, London SW8 5DT.

"Proposals for Additional Legislation on the International Release of Genetically Manipulated Organisms" is the title of a consultation paper released by the Department of the Environment, the Welsh Office and the Scottish Office. It proposes ways of augmenting present legislation to cover notification of release, Governmental authorization, and enforcement of the various provisions. (Source: BIOTECHNICA Journal No. 1, 1990)

General

Botanic gardens unite for diversity

A strategy to link several hundred botanic gardens across the world into a global network, thereby making plant conservation more effective, was launched in London in December 1989. The Botanic Gardens Conservation Strategy comes at a time when a quarter of the world's plants are in danger of becoming extinct over the next 25 years. Also, many of the remaining species are likely to show little genetic variation.

Following the model of the World Conservation Strategy, which has underpinned nature conservation over the past decade, this new strategy for plants

ffers a blueprint for conservation in gardens and arboreta in both temperate and tropical countries. There are some 1500 gardens and arboreta around the world, but until now their work has been largely unco-ordinated.

In the past, botanic gardens in tropical countries played a vital part in developing the new crops that nurtured empires - rubber, coffee and oil palm, for example. Today, they are ideal places in which to develop new crops that might be needed as the global climate changes.

The UN Food and Agriculture Organization and the International Board for Plant Genetic Resources already have programmes and facilities for conserving the genetic material of basic crop plants, but there is no equivalent for wild plants. The new programme says that botanic gardens should concern themselves more with species used in medicine, along with fruits, vegetables and spices used on a smaller scale.

Apart from species that provide food, many contain compounds that form the basis of drugs. Morphine, atropine, penicillin and the cancer drug vincristine, all come from plants and many of today's designer drugs were inspired by plant substances. More than 80 per cent of the world's population still uses remedies from natural sources. Some medicinal plants are heavily exploited and need to be conserved, both to ensure that they survive for traditional use and so that scientists can analyse them for their active ingredients.

The secretariat will build a data base to keep track of who is doing what and advise gardens on how best to implement the strategy in their country. The strategy encourages gardens to share the costs of expensive facilities. (Source: New Scientist, 23-30 December 1989)

Wellcome to back genome project

The Wellcome Trust is expected to announce a major grant to the International Human Genome Organization to help to cover the costs of establishing a European office for the organization in London. Wellcome has already said that it is prepared in principle to support the activities of HUGO, set up by the scientific community two years ago to co-ordinate international efforts to sequence the human genome.

HUGO has now applied to the trust, which is funded out of the profits of the Wellcome Foundation, for a grant of £500,000 over three years to cover the administrative costs of a London office. The trustees are meeting on Wednesday to decide how much of this sum they are prepared to provide. (Source: New Scientist, 17 February 1990)

Neurobiology market opportunities

The explosion of small start-up companies hoping to develop new agents to fill in the gaps in our current central nervous system (CNS) drug arsenal is leading to countless opportunities for pharmaceutical, chemical, biotechnology and biomedical companies. These opportunities range from licensing the rights to patented processes, to collaborating in research and marketing agreements.

According to a new 165-page report from Technical Insights, Neurobiology: Exploiting Advances in the Next Biomedical Frontier, the market for drugs targeted at the central nervous system is $1 billion in the United States alone and $3 billion worldwide. With scientific advances being made almost daily, this market is projected to grow to $7.6 billion by the year 2000 in the United States - and three times that amount worldwide.

While breakthrough neurobiology research promises improved drugs for such disorders as schizophrenia, anxiety, Parkinson's disease and epilepsy, the report points up the prospect of drugs to treat many neurological diseases for which no truly effective drug remedies currently exist. These include Alzheimer's disease, multiple sclerosis, Huntingdon's disease and amyotrophic lateral schlerosis (Lou Gehrig's disease), as well as nerve damage to the brain and spinal cord.

When a therapeutic drug application for a disease as devastating as these is submitted, the US Food and Drug Administration (FDA) has given its special priority. The FDA seems to approve biotechnology products - essentially made by the body naturally - faster than it does conventional, synthetic molecules and Technical Insights believes that the FDA will move CNS agents into the marketplace quickly. Details from: Peter Finlay, manager of special projects, Technical Insights Inc., P. O. Box 1304, Fort Lee, NJ 07024-9967 or on +1 (201) 568-4744. Fax: +1 (201) 568-8247. (Source: Biotechnology Bulletin, Vol. 9, No. 1, February 1990)

Growth factors: impact on wound dressing markets

When growth factors are approved for use, markets for wound dressings for skin ulcers will be greatly affected by the manner in which growth factors are used - according to a new Technology Management Group report, Worldwide Markets for Wound Dressing: The Impact of Growth Factors on Markets for Treatment of Skin Ulcers and Other Conditions.

Markets for synthetic wound dressings in 1990 are currently worth about $470 million worldwide. This figure covers polyurethane-based dressings and other polymer dressings, hydrocolloids, gels (including hydrogels), chitin and other materials. These markets could grow to as much as $688 million by 2000.

Skin ulcers include pressure sores (decubitous ulcers), venous stasis ulcers (leg ulcers) and diabetic ulcers. These markets are estimated at $220 million in 1990 and could grow to $383 million by 2000. Markets for burn, surgical healing and other dressings are expected to grow slightly - and are thought unlikely to be affected within 10 years by growth factor products.

Within the next decade, says Technology Management Group, growth factors will be approved for treatment of skin ulcers. At least 75 companies are involved in this area worldwide. The resulting products will be used in a variety of ways.

Dressings will be used without growth factors. Growth factors will be applied topically both with and without dressings. Materials will have growth factors incorporated into them. This will enable treatment of wounds on a highly specific basis, depending on wound characteristics. Details of the 4-issue TMG review, priced at $3,200.00, from: Technology Management Group, 25 Science Park, New Haven, Connecticut 06511, USA or on +1 (203) 786-5445; Fax: +1 (203) 786-5449. (Source: Biotechnology Bulletin, Vol. 9, No. 1, February, 1990)

European consumer self testing growth

Sales of self testing diagnostic kits and reagents in Western Europe grew in 1989 by 12 per cent over 1988 levels to total over $300 million. This is one of the conclusions of a new report from European Business Associates (EBA), Consumer Self-Testing in Europe - 1989.

Among the pressures driving the growth of the self testing market, EBA mention the following: (1) a general and increasing trend in the population to accept more responsibility and involvement in their own health care needs; (2) pressures on Governments to reduce or limit ever-increasing health care expenditures; (3) a general aging of the population with resultant changed demands for the monitoring of chronic illnesses which lend themselves more easily to consumer monitoring and self testing; (4) economic and social pressures which result in women delaying starting a family to later ages, so creating greater demands for pregnancy tests and fertility tests; and (5) the continuing advent of new, simpler, easier-to-use and sensitive test presentations which are making home testing easier.

Future developments in the self testing market in Europe depend to a significant extent on governmental and professional attitudes, as well as on reimbursement policies. But EBA project that the market for existing products alone will have grown to $421 million by 1994. Details of the report, priced at $1,250.00, from: European Business Associates Sarl, 22 rue Dernier Sol, L-2543 Luxembourg or on (352) 49 59 75. Fax: (352) 40 35 07. (Source: Biotechnology Bulletin, Vol. 9, No. 1, February 1990)

Scientists use US space shuttle and Soviet space station to crystallize proteins

Protein crystals grown in the near-zero gravity of earth orbit are proving far superior to earth-grown crystals, according to the principal investigator who set up the experiments on the space shuttle Columbia. Coincidentally, an American company has been testing similar equipment for crystallizing proteins in outer space on the Soviet space station.

Charles E. Bugg, who heads the Centre for Macromolecular Crystallography at the University of Alabama, said that one of the companies involved in the Columbia experiments, E. I. du Pont de Nemours & Co., Wilmington, Del., again achieved a "very dramatic result" with its protein, isocitrate lyase.

Protein crystals grown in a near-gravity-free environment have certain advantages over those grown on earth. Because they do not sink to the bottom of the container, they are continuously bathed on all sides by growth medium. Also, gravity creates convection currents that can result in formation of many crystals. These are either too small to conveniently determine the protein structure by X-ray crystallography or they grow into one another with resulting deformities.

Twenty-three groups flew 24 different proteins on Columbia's record breaking 11-day orbital flight STS 32, which ended 20 January, compared to 11 on the 1988 mission. Du Pont's other compound on board the shuttle, cyanobacterium photosystem I complex, did not crystallize.

Similar crystal-growing experiments are now underway on the Soviet space station, Mir, in co-operation with Payload Systems, Inc. (PSI), Boston. Meredith McClintock, manager of business planning at Houston-based Space Systems Inc., parent company of PSI, said the American protein and equipment were launched into space from the Cosmodrome in Khazakstan on 20 December, and activated on Mir on 23 December.

The space station offers a major advantage compared with the shuttle. Instead of a short-duration experiment, the crystals have a much longer time to grow. This is necessary for the majority of the proteins. Only a few hundred of the thousands of useful proteins have been successfully crystallized on earth to date.

Another flight on Mir is planned at the end of 1990 or early in 1991 to refine the methodologies and introduce proteins from Space Systems' clients. Future flights planned for 1991, 1992 and 1993 will further refine the methodologies and, with luck, increase client crystal yields. (Source: McGraw Hill's Biotechnology Newswatch, 5 February 1990)

Union of biological and biomedical organizations founded

Eight European organizations concerned with biological and biomedical research have formed a new Union, the European Union of Societies for Experimental Biology (EUSEB), to strengthen and integrate biological sciences in the European region. Organizations supporting the Union cover biochemistry, cell biology, developmental biology, molecular biology, neuroscience, pharmacology, physiology and toxicology.

EUSEB's first president will be Prof. Hamish M. Keir, head of the Department of Biochemistry, University of Aberdeen and immediate past chairman of the Biochemical Society.

The other principal elected officers are vice-president, Prof. Guy Dirheimer (Strasbourg); secretary-general, Prof. Rodolfo Paolette (Milan); and treasurer, Prof. Stefan Silbernagl (Wurzburg). Details from: Prof. Keir at Department of Biochemistry, University of Aberdeen, Marischal College, Aberdeen AB9 1AS, Scotland or on 0224-645908. (Source: Biotechnology Bulletin, Vol. 8, No. 12, January 1990)

B. COUNTRY NEWS

Argentina

Potato growers in Argentina armed with viral DNA probes

As of February 1990 onwards Argentine potato farmers will be using a service which will inform them within 48 hours if their crops are infected by any of four viral pathogens: potato virus X or Y, leaf-roll virus or spindle-tuber viroid. The grower simply samples the plant by squashing a bit of leaf, steam or tuber onto a blotting membrane. A reference laboratory at Industrias Quimicas Almidar SA (IQA) in Buenos Aires telephones the results in return. By mid-year, IQA's Bio-Almidar unit plans to make available a field-test version of its laboratory nucleic-acid hybridization probes. With this farmers will be able to spot pathogens in as short a time as six hours.

The test kits will cost $150 to $180, and include enough material to assay 100 times for each of the four viruses. Bio-Almidar is currently in early-stage negotiations with US and European companies, to adapt their assay to locally important

viral types. High yield in potatoes depends on the absence of pathogens in the seed stock. Bio-Almidar reports that its biotin-labelled DNA probes are up to ten times more sensitive than conventional ELISA assays, detecting as little as 0.6×10^{-12} g of the viruses.

In the future they plan to combine several probes, corresponding to different viruses, in the same assay, as detection is not affected by the presence of non-complementary probes. Bio-Almidar has filed what it calls "very comprehensive" patent applications on the probes in its home country, the USA and Europe. (Source: McGraw-Hill's Biotechnology Newswatch, 19 February 1990)

Australia

Melbourne aims to establish genetic research centre

Plans are expected to be approved by the State Government of Victoria, Australia, to establish a centre in Melbourne for R & D in genetic engineering and biotechnology. At an investment of A$70 million, the centre will comprise three new institutes carrying out research into molecular biology, drug and vaccine development, disease resistant crops and genetically modified animals.

Due to be completed by 1995, the centre-piece biomolecular research institute is projected to cost A$40 million and will be fully equipped to conduct research into new drug design and to initiate a major anti-viral research programme to investigate AIDS, hepatitis and some forms of cancer. Details from: Office of Investment, Department of Industry, Technology and Resources, 228 Victoria Parade, East Melbourne 3002, Australia. (Source: Biotechnology Bulletin, Vol. 9, No. 1, February 1990)

Double blow for blowflies in Australia

Australian scientists are to test a new method of controlling the blowfly (Lucilia cuprina), an agricultural pest of sheep which costs farmers A$200 million a year, through the release of blowflies that have been genetically manipulated in a unique way.

Scientists at the Commonwealth Scientific and Industrial Research Organization (CSIRO) will release 700 million blowflies during the summers of 1990 and 1991 on the remote Furneaux group of islands north of Tasmania. Each male fly will deliver a double genetic blow. A sex-linked translocation will cause a high frequency of sterility in the male line while several other genetic mutations will bring about blindness in the female line.

According to Rod Mahon, senior research scientist within the Division of Entomology at the CSIRO, the Furneaux experiment is the first use of genetic manipulation to suppress an insect population. In the ongoing screw-worm eradication programme in Texas and Florida the continuing release of infertile males is necessary.

In a small trial using the genetically manipulated blowflies, mutations were still present in the population nine months after the release of males had ended. The blowflies are released from the air so a reasonably high density of sheep per hectare is needed to make the system cost-effective.

The Lucilia blowfly was introduced to Australia, probably from South Africa or India. It is, according to Mahon, extremely well adapted to living on live sheep and can rapidly develop resistance to insecticide as it undergoes 6-10 generations a year. (Source: Nature, Vol. 343, 8 February 1990)

Marine biotechnology

The Department of Industry, Technology and Commerce released a Report of the Review Committee on Marine Industries, Science and Technology in Australia in early 1989. The Report entitled Oceans of Wealth? is some 188 pages long and covers all aspects of the marine industries including shipbuilding, construction of ports, defence, as well as environmental and biotechnological opportunities. One of the recommendations is for follow-up meetings on marine biotechnology. A marine outlook conference may be held in mid-year and this may include discussions on marine biotechnology. In view of the importance of the seafood industries in the Asia-Pacific region relative to that and the rest of the world, it is felt important that Australia looks to the types of contributions that it can make in marine biotechnology. (Source: ABA Bulletin, Vol. 5, No. 1, February 1990)

Roche forms malaria vaccine duo

Roche Products, the Australian affiliate of Switzerland's Hoffmann-La Roche, is stepping up efforts towards a malaria vaccine by teaming up with Melbourne-based Saramane, an organization founded four years ago specifically for malaria vaccine development.

Malaria is a serious public health problem, but to date a vaccine has proved elusive because the life cycle of the malaria parasite comprises several stages. In recent years research has concentrated on producing the specific proteins present on the surface of the different stages of the malaria parasite and on developing potential malaria vaccines from these antigens.

Previous work by Roche and Saramane is complementary. The Australian scientists have identified various antigens of the merozoite stage (the blood cell stage of the parasite) and tested them in animals as potential vaccines, while Roche has synthesized certain antigen structures from the surface protein of the sporozoite stage (the stage of the malaria parasite which is injected into the bloodstream with the mosquito bite) and shown that this vaccine induced partial immune protection in human volunteers.

The collaborative venture is expected to lead to the development of a malaria vaccine consisting of several antigen components for increased effectiveness. But Roche concedes that in spite of progress in identifying parasite antigens there are still numerous problems to solve and several years of R & D will be necessary before a vaccine can be launched on the market. (Source: European Chemical News, 1-8 January 1990)

Government grants for biotechnology
(From Press Release by DITAC)

An environmentally friendly fungus which produces natural insecticides and could improve Australian wheat yields by up to 40 per cent, and new wide-ranging drug technology, are among six biotechnology grants worth more than $3.6 million announced by the Federal Government. The drug technology project could aid in the discovery and testing of new drugs to assist in the treatment of many illnesses, including lung cancer, hypertension, psychiatric disorders and arthritis. Other potential outcomes from the biotechnology projects

are a high nutrition lucerne, new enzymes for industrial and medical uses, a new biological process for producing gums for the food industry and chicken vaccines. Details of the grants are given below.

Research organization: Biotech International Limited and the University of Western Australia.

Commercial collaboration: Biotech International Limited.

Project description: Within three years, field trials will have commenced into a novel use of fungus in agriculture. Previously, fungus infections in the roots of crops meant either reduced yield or total crop failure. Biotech International Limited and the University of Western Australia have been growing wheat with a fungus that does the opposite. It increases grain yield by up to 40 per cent. This research involves genetically engineering the fungus so that it produces natural insecticides. When the engineered fungus infects a plant, insecticides will be released into the leaves. Any insect, pest which tries to eat the plant will die or be repelled. The insecticide, however, is totally harmless to humans or animals.

If this project is successful, the technology developed will pave the way for a vast range of applications in agriculture, horticulture and forestry. The benefit to Australia will not only be increased export earnings from better farm production, for as world leaders in this new technology, the knowhow itself will earn valuable export earning.

Amount: $650,000 over three years.

Research organization: CSIRO Division of Plant Industry.

Commercial collaboration: Riyate Pty. Ltd. (trading as Agtech Promotions and Seedco).

Project description: The grant will fund work aimed at the improvement of the nutritional value of lucerne by genetic engineering. Lucerne is an important seed, pasture and fodder crop in Australia. Success in this project will lead to the production of lucerne hay with value added in two ways. Firstly, by genetic engineering, new genes which code for proteins of unusually high nutritional value for livestock will be transferred into lucerne. A further benefit will be derived as the resulting improved lucerne will be baled by a new process under patent to one of the commercial collaborators.

At present, half the total lucerne seed is exported, while only a small proportion of lucerne fodder is of sufficient quality to export. Not only is there room for greater efficiency in the domestic market but a large potential export market exists for baled lucerne hay of high nutritional quality.

Amount: $590,000 over three years.

Research organization: CSIRO Division of Biotechnology.

Commercial collaboration: Peptide Technology Limited.

Project description: The world market for enzymes in industry and for medical application is expanding rapidly with a predicted market size of approximately A$7 billion p.a. in the year 2000. The primary aim of the project is to produce new enzymes for use by Peptide Technology Ltd. This company is a world leader in the latest process of enzymatic peptide synthesis and requires the enzymes to help solve production problems and allow greater flexibility in manufacturing.

The enzymes produced, as well as meeting Peptide's requirements, will have many other potential uses. The general commercialization and other applications will be investigated by Burns Philp and Company Limited, who are one of Australia's major user/importer of enzymes. The experience and expertise gained in carrying out this project will be available for developing enzymes for other industrial and/or medical applications as the need arises.

Amount: $567,000 over three years.

Research organization: CSIRO Division of Food Research.

Commercial collaboration: Tridan Limited/Bunge (Australia) Pty. Ltd.

Project description: CSIRO Division of Food Research, Tridan Ltd. and Bunge (Australia) Pty. Ltd. are to produce natural products by novel fermentation techniques for food and other industries. The results of this project will enable replacement of imports of certain industrial products (value in excess of $10 million.) It will also allow development of export markets for these products for which there is a total world value of more than $500 million p.a.

Amount: $437,000 over three years.

Research organization: Garvan Institute of Medical Research.

Commercial collaboration: Pac Bio Ltd.

Project description: New drug discovery using cloned target molecules.

Project aim: Research being funded in the human pharmaceuticals field may be applicable to many drug discovery programmes. The success of this research would provide a significant opportunity to develop the local pharmaceutical industry, by sale and licensing of new drugs, both in Australia and overseas.

Many currently used drugs work by virtue of their actions at receptor molecules on the surface of cells. This project aims to isolate and characterize new cell surface receptors for which clinically useful drugs have not yet been obtained. These receptors will then be used for the design and screening of new drugs for treatment of a wide variety of diseases such as hypertension, lung cancer, psychiatric disorders, arthritis, etc. Because the candidate drug will be identified by its ability to interact with a specific receptor, it should be devoid of significant side effects, a problem with many current drugs.

Amount: $750,000 over three years.

Research organization: CSIRO Division of Animal Health.

Commercial collaboration: Arthur Webster Pty. Ltd.

Project description: Australian researchers have led the world in discovering many of the hormones that control the development of the immune system and disease resistance in mice and humans. CSIRO Division of Animal Health and Arthur Webster

Pty. Ltd. have been granted $650,000 in a joint project to identify and produce these hormones from the chicken and deliver them safely and effectively to day-old chickens.

This development would significantly enhance the chicken's disease resistance. Some of these hormones will also enable the chickens to respond more effectively to a range of protective vaccines at a younger age. Each year over 10 billion chickens are hatched world wide, 5 billion in the USA alone. Given these statistics, even at a cost of 1c per treatment, returns in excess of $20 million are expected from sales in the USA, Europe, Asia, Japan and Australasia.

Amount: $603,400 over three years. (Source: ABA Bulletin, Vol. 5, No. 1, February 1990)

Canada

Genetic predisposition to disease

Genetic diseases account for more than 20 per cent of all admissions to Canadian hospitals. Moreover, it is estimated that at least one in ten Canadians alive today will suffer disease or impairment due to individual heredity.

For this reason, the Canadian Science Council in 1987 initiated a major study on the policy implications of genetic predisposition to disease. The Council believes that a better understanding of genetic predisposition to disease is central to preventive health care.

Under the chairmanship of Council member Dr. Charles Scriver, the study committee refined its general objectives and provided direction to five sub-committees. These sub-committees were set up to identify and address policy concerns in the areas of medical education, health care economics, statistics, ethical and legal aspects, and the general status of the underlaying science and technology.

Among the goals of the study is the intention to document the impact of genetic disease on the health of Canadians; to review available and anticipated technologies and identify their potential benefit and harm; to consider the associated ethical, legal, monetary, and human resource problems; to develop policy recommendations; and to foster better awareness of the role of genetic predisposition in health care.

Collection and analysis of the information are now almost complete. The preliminary findings were discussed with government planners in June 1989. (Source: Biotechnica Journal No. 1, 1990)

European Community

EC imposes controls on biotechnology companies

Biotechnology companies in the European Community will be subject to important new controls following the formal adoption of two directives in Brussels by environment ministers.

The measures introduce regulations - notably an obligation to carry out an environmental risk assessment - for activities where organisms obtained by altering the genetic material of bacteria, plants or animals are involved. One covers situations in which they are intended to be kept under physical containment, the other in which they are intended to be used in the open environment.

The directives lay down harmonized approval procedures to be followed ahead of experimental work, industrial production or the marketing of products throughout the EC. They are based closely on a model developed by the OECD. (Extracted from Financial Times, 23 March 1990)

EC biotech plea

Europe is in danger of falling behind the USA and Japan in biotechnology, a group of seven major companies in the field warned recently. The European Commission should give priority to a coherent biotech policy, the group said in a paper, addressed to the Commission.

1990 is seen as a pivotal year for Community biotechnology policy, according to Peter Doyle, ICI's research and technology director and chairman of the Senior Advisory Group on Biotechnology within the European Chemical Industry Federation (CEFIC). Feruzzi, Hoechst, Monsanto, Rhône-Poulenc, Sandoz and Unilever are also members of SAGB.

The group calls for the establishment of a clear products registration system, based on safety and quality criteria. Research and development, patent protection and the establishment of a single market for biotechnology processes and products should also figure in EC policy.

The establishment of an effective biotechnology policy is closely connected with development of the industry, the group warned. European talent and investment is already "emigrating to more favourable political environments", according to SAGB.

The EC is currently considering two directives on the release of genetically manipulated organisms. The directives would apply strict rules to the release of GMOs both for academic and commercial applications. (Source: Chemistry and Industry, 19 February 1990)

Invitation to STEP programme

The EC Commission has published a call for proposals to be submitted not later than 30 March 1990 for participation in the STEP programme (science and technology for environmental protection). The budget for the programme is ECU 75 million. The programme covers nine broad research areas:

1. Environment and human health
2. Assessment of risks associated with chemicals
3. Atmospheric processes and air quality
4. Water quality
5. Soil and ground water protection
6. Ecosystem research
7. Protection and conversion of the European cultural heritage
8. Technologies for environmental protection
9. Major technological hazards

This call for proposals covers the research areas 7, 8 and 9. Research for areas 1 and 2 will be invited at a later date. The invitation for the areas 3 through 6 has been published earlier with deadline 29 December 1989. Details may be had from:

Commission of European Communities
Directorate-General for Science,
Research and Development
SIEP Programme, Directorate XII/E-1
75 rue Montoyer
B-1040 Brussels
Telex: 21877 COMEU B
Telefax: 00322-236-3024
(Source: Biotechnica Journal No. 1, 1990)

Programme ECLAIR

The Community programme for encouraging agro-industrial research (ECLAIR) experienced a rapid take-off with the selection of 23 co-operation projects which will receive financing from the Commission.

These projects cover all the steps in the agro-industrial chain, including industrial applications and new commercial uses. Among the participants are businesses, universities, research institutes and even agricultural co-operatives.

The programme ECLAIR adopted at the beginning of 1989 is financed at 80 million ECU to encourage pre-competitive research in the agro-industrial field. The EC Commission co-finances the projects on an equal footing with the partners. (Source: Biotechnica Journal No. 1, 1990)

EC human genome programme

The EC Commission has revised its proposal for a 15 million ECU research programme on "Human Genome Analysis" (Document COM(89) 532). The revised proposal, modified in the light of the European Parliament's amendments to the original version, has been passed to the Parliament for second reading. Information from Dr. Tony Dickens at the EC Commission (00322-235-0032) (Source: Biotechnica Journal No. 1, 1990)

BRIDGE programme adopted

The specific research and technological development programme in the field of biotechnology BRIDGE (1990 to 1994) was adopted by the Council on 27 November 1989. Within this programme funds amounting to 100 million ECU will be available for contract research (76.5 MECU), training activities (12 MECU), COST and other concertation activities (11.5 MECU). The contract research funds include pre-normative research, cell biology, enabling technologies and information infrastructure. (Source: Biotechnica Journal No. 1,1990)

Agricultural resources programme

The EC Commission published its revised proposal for a specific research and technological development programme in the field of competiveness of agriculture and management of agricultural resources in the Official Journal No. C 284, 10 November 1989, p. 2. This programme is planned to finance research at a total amount of 55 million ECU in four sectors:

1. Conversion, diversification, including extensification of production, reduction of costs and protection of the environment;

2. Product quality, new uses for traditional products, and aspects of plant and animal health;

3. Socio-economic aspects and specific actions for all regions in the Community lagging behind in development; and

4. Methods and services to disseminate agricultural research information particularly from this programme. (Source: Biotechnica Journal No. 1, 1990)

EC programme FOREST

The EC Commission has started the FOREST programme for R & D in renewable raw materials. The programme is designed to increase available forestry resources and improve the quality of raw materials in keeping with economic and environmental requirements. Secondly, it is aimed at improving the international competiveness of EEC forest industries and to facilitate the rational use of forest products in the EEC.

FOREST will cover three broad areas of research:

1. Forest resources including tree improvement and breeding

2. Wood technology including processing technology

3. Pulp and paper manufacturing

The programme will be implemented by cost-shared contracts and co-ordinated activities under a 12 million ECU budget. (Source: Biotechnica Journal No. 1, 1990)

Federal Republic of Germany

Scientiscs demand right to genetic research

More than 2,000 Federal Republic of Germany molecular biologists and other scientists published a declaration in Bonn calling for legal guarantees of their right to perform research using recombinant DNA, and for legal safeguards against the misuse of genetic information. The declaration comes as the Federal Republic of Germany Parliament begins its final debate of a new law to regulate genetic research.

The declaration states that recombinant DNA is an "indispensable tool" for all areas of modern biology, and is used in over 800 research institutes in the FRG alone. It calls on the federal and regional governments to guarantee the continued development of genetic technology in the FRG. It states that safety guidelines such as those used by the Federal Republic of Germany research ministry are adequate, and that further restrictions on genetic research as a whole will not add to safety.

The declaration was drafted in response to public calls to strictly regulate, or even prohibit, genetic manipulation as such. Public opposition has blocked several planned industrial installations using biotechnology. This has encouraged some FRG companies to plan their new facilities in other countries.

Scientists are afraid the opposition will spread to research. The declaration calls for the regulation of basic and applied genetic work to be tied to the potential risk of particular manipulations. It says the release of genetically-modified organisms should be approved case by case. In response to public anxieties that have been attached to genetic research in the FRG, the scientists "categorically renounce" the alteration of inheritable characteristics in humans. They request guarantees that research on the human genome will not infringe medical confidentiality, and that "knowledge of the genotype remains the exclusive right of its bearer". (Source: New Scientist, 27 January 1990)

Gene law timetable "hasty"

The Federal Health Ministry hopes to push its new "framework law" regulating genetic engineering through Parliament and into effect by July, despite considerable delays which have threatened its early passage.

The legislation was originally set to be in place by January 1991. However, the timetable was brought forward, following the suspension of Hoechst's permit for a genetically engineered human insulin plant at Frankfurt last November. According to the court ruling, the states have no basis for awarding permits before passage of pertinent legislation.

The revised timetable has been widely criticized as hasty, especially as a number of changes need to be made to the bill.

Last October, the upper house criticized the fact that the bill only mentioned work with gene-spliced material and did not regulate approval of production plants. The chamber of states insists the states should have responsibility for approving facilities.

Other points of controversy centre on the participation of scientists critical of genetic engineering in the central committee on biological safety. This is the body that advises the Federal Government on the public hearing requirement for new products, worker protection, waste disposal and wastewater discharge.

Legal experts in the lower house have complained that the Federal Government wants to regulate too many points outside Parliament. The chemical industry wants to see the public hearing requirement limited only to high-risk projects. (Source: European Chemical News, 5 February 1990)

The FRG bows to pressure over gene research

The FRG's proposed new "gene law" has passed through the committee stage in the Bundestag with fewer changes than scientists had feared. It is now expected to be in force by July, although it will still come under attack from the Greens, who say that it will not protect the environment and is contrary to the FRG constitution.

The law permits research and commercial activities involving genetic engineering under certain defined conditions. There is immense pressure in the FRG, both from industry and from public interest groups, to have some law on genetic technology.

During parliamentary hearings last month, representatives of the German state governments protested that they lacked staff who were competent to judge the safety of genetic manipulations. Under the new law, licensing genetic manipulations would be a State responsibility. Most decisions will remain with the states, but in a change to the bill that has now passed the committee stage, the Federal Government in Bonn will approve the licensing of any release of genetically modified organisms, and the marketing of products containing them.

In another change, the law now requires that installations where genetic engineering is to be used must be granted a permit by state authorities. This was to have been done under the law on chemical emissions, with only specific genetic manipulations subject to approval. But in a further change, the law will now require public discussion before any modified organisms are released or any facilities are licensed for commercial production using genetic engineering. (Source: New Scientist, 10 March 1990)

Cetus wins approval for anti-cancer drug

The Federal Health Authority has granted marketing approval for Cetus Corp's Proleukin interleukin-2, as a treatment for advanced renal cell carcinoma (kidney cancer). With a population of approximately 61 million, the FRG is the largest single market in Western Europe and it is estimated that over 10,500 West Germans are treated for kidney cancer each year.

The FRG is the sixth member country of the European Community (EC) to grant approval, following last May's recommendation by the Committee for Proprietary Medicinal Products (CPMP), the central EC regulatory body.

Cetus is the only company yet to gain approval for IL-2, which boosts the effectiveness of the human immune system. IL-2 is also being developed by rivals such as Hoffmann-La Roche and Shionogi. Britain's Glaxo terminated its IL-2 development programme. Details from: Cetus Corp., 1400 Fifty-Third Street, Emeryville, California 94608, USA. (Source: Biotechnology Bulletin, Vol. 8, No. 12, January 1990)

India

Recombinant DNA regulation

Safety guidelines for recombinant DNA research released by the Department of Biotechnology seek to regulate genetic engineering research in India more by self control than by legal measures. Companies in countries such as the FRG where laws are strict may even find India's relaxed approach sufficiently attractive to shift some of their genetic engineering research to India.

The guidelines are the work of an 18-member recombinant DNA advisory committee led by S. Varadarajan, an industrial chemist and former chief of the Council of Scientific and Industrial Research. Interestingly, issues relating to genetic engineering of human embryos, use of embryos and foetuses in research and human germ-line gene therapy are excluded from the scope of the guidelines.

Under the new rules, recombinant DNA work is classified into three categories depending on the perceived risk, and taking into account local factors such as immunity to diseases, laboratory environment and tropical conditions. Approval by the competent authority is needed only for such experiments as cloning of genes for toxins and for vaccine production, gene therapy and field release of altered organisms. Most recombinant DNA experiments need only notification and not approval.

The guidelines are to be implemented by a three-tier mechanism, but the onus of ensuring safety rests mostly with an in-house biosafety committee within the research institute itself.

Whether or not the institutions abide by the guidelines will be monitored by a Review Committee for Genetic Manipulation on the basis of surprise visits and bi-annual reports from the biosafety committees. Any violation, deliberate or due to negligence, will lead to cancellation of research grants - a threat of no consequence to private companies, Indian or foreign, which do not depend on government funds.

Legal action will be taken only in case of violations in regard to field release of engineered organisms or products. Such releases must have the approval of a genetic engineering approval committee to be set up under the Department of Environment. It will be a statutory body with "judicial powers to inspect, investigate and take punitive action" under the Environmental Protection Act, the same act that deals with air and water polluters. The act has not been successful in controlling industrial pollution because it contains many loopholes and imposes few sanctions. (Source: Nature, Vol. 343, 22 February 1990)

Local oil for birth control

Indian acientists have isolated a substance from neem tree oil which they claim can be refined into a new contraceptive for women.

The team of scientists from the Defence Institute of Physiology and Allied Sciences (DIPAS) together with the Indian Agricultural Research Institute (IARI) has named the substance "Nim 76".

DIPAS scientists maintain that the oil can immobilize and kill sperm, and can even prevent a fertilized egg from being implanted in the uterus.

Even if used between 48-72 hours after conception "Nim 76" can prevent the development of a fertilized egg, trials have shown. The oil acts by interfering with oestrogen, which plays a crucial role in the implantation of the egg in the uterus.

Tests on rabbits, rats and monkeys have confirmed that a substance in neem oil has contraceptive properties. The experiments will continue until "Nim 76" can be made in the laboratory or manufactured commercially.

Contraception from plants and herbs is used by tribal societies in South America. In Ecuador, for example, a plant called piripiri has also proved effective. (Source: Development Forum, January/February 1990)

Israel

Surprises from salt water

Today, thirsty plants are not only drinking, but thriving on seawater at an experimental farm near the Israeli town of Ashkelon on the Mediterranean Sea.

The seawater-irrigated plants, which have been proven nutritious as well as edible for sheep and camels, are the first of many which Dr. Dov Pasternak, the head of the project, hopes to grow on water from the sea.

Dr. Pasternak, head of the Boyko Institute for Agriculture and Applied Biology of the Ben Gurion University, oversees studies of 150 species of plants irrigated by seawater. So far, he and his team of five scientists have screened 20 species for salt tolerance.

"We are concentrating on the raising of plants for fodder", he explains, carrying out nutritional studies of animals to see if these plants are suitable for them. One salt bush from Baja, California, for example, successfully grown in salt marshes, has been found to be palatable to both sheep and camels.

The team is also giving its attention to grains, oil and medicinal plants. Ornamental plants are already growing on saline water in gardens near the ultra-salty Dead Sea and the port city of Eilat on the Red Sea.

Dr. Pasternak says that the Universities of Arizona and Delaware in the US are carrying out similar experiments; the University of Delaware is concentrating on grain and fodder, while scientists at Arizona are interested in oil plants.

The research into seawater for irrigation is directly related to the successful efforts of Dr. Samuel Mendlinger, also from the Boyko Institute, to produce a special strain of sweet, high quality autumn melon grown on brackish water using drip and sprinkler irrigation.

"Stress induces sweetness", explains Dr. Pasternak, obviously referring to fruits and vegetables, but, he adds, like people, each plant possesses a personality and has individual needs. Some young plants are sensitive and must be irrigated with fresh-water at an early stage; others get sensitive to salt as they mature.

Other fruits and vegetables being successfully irrigated by saline water from underground acquifers, commonly found in many desert areas, are asparagus, broccoli, sorghum, olives, pears and pomegranates.

Dr. Pasternak believes that the growing of field crops from salty water is the key to the future of desert agriculture and he points out that cotton has so taken to salt water that its yield has been increased by 20 per cent.

A major effort is also being invested in the development of salt tolerant medicinal plants, like the evening primrose, and the buffalo gourd for starch production. The cashew, jujube, papaya, jack fruit tree and some cactus species are among lesser-known fruits which are the concern of a long-term project being carried out at the Boyko Institute aimed at the selection and development of a wide range of subtropical high quality fruits. (Source: Development Forum, January/February 1990)

Italy

AIDS update

The Department of Informatics of the University of Milan, with the support of the Italian National Research Council (CNR), is initiating an informatic system for research on AIDS. Through a work station based at the University of Milan, it will be possible to access data bank, bibliography, statistics and research descriptions concerning AIDS, which will be constantly updated.

Professor Fernando Aiuti, Immunology Institute, University of Rome, has tested the Italian drug Fluimcil on AIDS serum positive patients affected by opportunistic bronchitis. The experiment is inspired by the test being conducted at Stanford University with NAC (N-Acetylcisteina) corresponding to Fluimcil. Professor Aiuti said that so far the treatment did not show significant modifications or improvement on AIDS or related syndromes; nevertheless, testing of Fluimcil will continue, introducing variation in the therapy length and dosage.

The new Minister of Health, Francesco De Lorenzo, has announced a national plan against the disease. The Ministry of Health has 2,100 billion lire (about $1.5 billion) to spend through 1991. Twenty-four billion lire

(about $17 million) will be used for research and 20 billion lire (about $14 million) for a new information campaign through newspapers, TV, and schools. The trend of the new information campaign will be to sponsor and recommend using the condom as suggested by the World Health Organization. The new campaign will carry more information and fewer admonitions, but will not support the project of free distribution of condoms and syringes nor the proposal by some Parliament members for government-controlled heroin distribution to limit the increase of the disease among drug addicts.

The Defense Committee of the Italian Senate approved a law that exempts AIDS serum positive individuals from military service. A bipartisan Parliament group has presented a draft law requesting to extend to AIDS patients the rules, legislation, and social security norms approved about 70 years ago for tuberculosis (TB) patients, who were discriminated against at the turn of the century. The draft law provides also for the transfer of the unused TB funds to assist AIDS patients.

In Italy, out of 10 persons with AIDS, eight are men and two are women, while the average in other countries is nine men and one woman. The number of homosexuals developing AIDS in Italy is slowly decreasing, while the number of drug addicts developing the disease is climbing. (Source: European Science News, January 1990)

Japan

Biomaterials information network

The Science and Technology Agency, Japan, has reported the results of its Study on Science and Technology Co-operation with Underdeveloped Countries, which explores the possibility of establishing an Asian information network for biomaterials.

Underdeveloped Asian countries are rich in material resources such as micro-organisms and animal and plant cells, and many of these countries are conducting active research on them. Such biomaterials are indispensible fc Japan's life sciences. The agency recognized that this is the most hopeful area for co-operation between Japan and countries such as the Republic of Korea, Thailand, Indonesia, Singapore, and China; it proposed establishing a network facilitating regular information exchange and discussion. Initially, this network will work bilaterally; a multilateral arrangement will come later. (Source: Bio/Technology, Vol. 8, January 1990)

Human genome project

The Japanese Government has dashed hopes that it will respond to American pressure and make an early contributrion to the international effort to sequence the human genome. Yoshire Miki, Director of Policy Research at the Government's Science and Technology Agency (STA), said at the end of 1989 that the Japanese Government is not yet able to intervene in the project.

The statement was an admission of the debate taking place in Japan following calls for the country to play a formal role in a project which many see as the crucial scientific endeavour of the 1990s. The Science Council of Japan, an advisory body of senior scientists, has already called for the country to participate. James Watson, the director of the Institute for Genetic Research at the US National Institute for Health, has warned that unless Japan makes a formal commitment it will not be able to share results gathered from the project.

The Japanese Government is still divided over which department, if any, should co-ordinate a national effort. The fight is between the Science and Technology Agency (STA), which has responsibility for co-ordinating research, the Ministry of International Trade and Industry, and the Ministry of Education.

Japan spends roughly the same proportion of its gross national product on science and technology as other leading nations. Unlike the US or Europe, however, private industry pays for the lion's share of research and development, some four fifths of the total. In 1989 this amounted to some 8.5 trillion yen (£37 billion), but little of this money went on basic research, which is largely the responsibility of the Government.

The white paper says Japan's goal should be to spend 1 per cent of its gross national product on basic research.

Plans to support basic science were scrutinized by the Japanese Finance Ministry, which has set a deficit-free budget in 1990. This means little extra money above the rate of inflation for all but a favoured few projects, such as the H2 rocket and a new prototype magnetic levitation train. (Source: New Scientist, 6 January 1990)

Current status in R&D of biotechnology and bioindustry

By S. Fukui
Chairman, Bioindustry Development Centre (BIDEC), Professor emeritus, Kyoto University

The traditional basis of Japanese biotechnology and bioindustry is laid on a long history of producing a variety of fermented foods and beverages. The knowledge and experience accumulated through this tradition have endowed Japanese industries with skilful modern techniques of applied microbiology and enzymology.

Industrial applications of immobilized biocatalysts in bioreactor systems have been for the first time achieved in Japan for the production of optically active amino acids and organic acids, then antibiotics etc. Both basic and applied studies on immobilized biocatalysts and their applications on industrial scales have been extensively carried out. Biosensors are also very actively investigated and an appreciable number of biosensors are commercially successful.

Pure basic studies in various fields of biosciences are strongly promoted. Splendid researches are being carried out on the molecular base of immuno-modulators and their receptors, that of neurotransmitters and their receptors, mechanisms of transmembrane signal transduction, physiologically important peptides, such as human natriuretic hormone, and structure-function relationships of enzymes and other biologically active proteins. However, application-oriented R & D is still much stronger than pure fundamental studies in biosciences.

Japanese firms have by themselves or under the umbrella of the governmental supports made great efforts for adopting the new biotechnological processes using rDNA and cell fusion techniques. Beside the projects to produce numbers of biologically important polypeptides and proteins as

American and European industries are carrying out, applications of these novel techniques are being done for the production of traditionally strong industries, such as the production of amino acids and others.

Increasing interest is being paid to plant biotechnology. Several secondary metabolites produced by tissue cultures and new types of plants and flowers are commercial successes. Biotechnology for stockbreeding, fishery and forestry and for solving environmental pollution is also promoted by the Government in collaboration with industrial sectors and academia.

The Bioindustry Development Centre (BIDEC) has been established as the co-operating body of industry-academia-government. BIDEC promotes the co-operation of these three sectors. Also BIDEC plays an indispensable role for international co-operation between Japan and overseas countries in the fields of biotechnology and bioindustry.

BIDEC

The Bioindustry Development Centre (BIDEC) is a non-profit organization whose function is to promote biotechnology and bioindustry. BIDEC was established through the support and co-operation among industry, academia and government, and is the only organization of this kind in Japan. BIDEC functions as a means of communication among researchers, technologists and managers interested in the promotion of biotechnology.

Members of BIDEC include about 320 major bio-related companies from many industrial areas, 50 public research institutes and over 1,600 individuals from universities, companies and research institutes. The Executive Director is Mr. Fujio Ishikawa.

Address: BIDEC
Dowa Bldg., 10-5, Shimbashi,
5-chome, Minato-ku, Tokyo 105, Japan
Tel.81-3-433-3545, FAX 81-3-459-1440

Expected annual sales of biotech-related products for 1989

(Units: 100 million Yen)

Pharmaceuticals	870
Diagnostics	136
Enzymes/reagents	118
Food products	227
Equipment/facilities	445
Seedlings/plants	17
Feeds/agrichemicals	59
Cosmetics	86
Others	28
Total	1,986

(BIDEC 1989)

(Data taken from Nikkei Biotechnology, 8 May 1989)

Company budgets for life science R & D

(1987, billion Yen)

Foods	62
Textiles	7
Chemicals	78
Pharmaceuticals	303
Others	1
Total	451

(BIDEC 1989)

(Source: Biotechnica Journal No. 1)

Taiwan, Province of China

Biotechnology in Taiwan

The Republic of China is undertaking comprehensive plans for the development of biotechnology. The National Science Council co-ordinates this effort and is the major source of research grants. Extensive research activities are carried out in the Chinese Academy of Science, various medical centres, and university laboratories.

In order to promote technology transfers, the Government has established the Development Centre for Biotechnology to carry applied R&D up to the pilot stage, as well as to engage in small-scale production. The Government encourages the application of new biotechnology techniques in State-owned companies, and provides investment incentives to stimulate the creation of new high-technology companies. The National Hepatitis Programme is an early example of this government-directed approach. The principal biotechnology-related industrial sectors in Taiwan are agriculture and food processing.

The National Science Council (NSC) has primary responsibility for the co-ordination and implementation of biotechnology programmes, including basic research, technology transfer, and industrial development. Basic research covers such areas as genetic engineering, hybridoma technology, tissue culture techniques, enzymology, fermentation, and bioconversion.

At present such research focused on pharmaceuticals, agriculture, speciality chemicals and environment protection. In biotechnology efforts encompass vaccines, diagnostic reagents, hormones, antibiotics and amino acids produced by fermentation for bioconversion, enzymes, microbial reagents for pollution control, biopesticides, plasma fractionation products, and monoclonal antibody products.

The Development Centre for Biotechnology (DCB) is a non-profit organization sponsored by the Government of the Republic of China on Taiwan. Its goals are to establish a biotechnology R & D capability and promote bioindustrial development in Taiwan. Its functions include technology evaluation, market analysis, the introduction of new technologies, process development, technical services, technology transfer, and the training of technical personnel.

The DCB has developed technologies for biopesticides, monoclonal antibodies for diagnostic kits, transgenic plants, insect-cell culture, vaccines, industrial enzyme catalyzed processes and antibiotics production. Further details from:

Mr. Tai Sen Soong
Director
Development Centre for Biotechnology (DCB)
81, Chang Hsing St., Taipei
Taiwan, R.O.C.

Telephone (02)7325123
Fax 886-2-7325181
Telex 14176 DCBROC
(Source: Biotechnica Journal No. 1)

Tanzania

The cockroach: a reason for living

Two micro-organisms which live in productive harmony in the hind-gut of cockroaches are exciting microbiologists at the University of Dar-es-Salaam in Tanzania. Commenting on the creatures, Dr. Huub Gijzen of the microbiology unit says they are "a complete machine for the conversion of plant matter (biomass) into fuel".

The organism Nyctotherus ovalis, a type of ciliate or protozoan minute acellular organism - and the methane-producing bacteria which live within it, are being cultivated in fermenters to convert organic matter into fuel. Thousands of bacteria are found within a single ciliate cell.

Researchers were alerted to the potential of the bacteria inhabiting cockroaches because it had been observed that these omnivorous creatures could eat and digest almost any organic material, including cellulose, which makes up most of the mass of plant material and is in abundant supply. Research results are 30 to 100 times those reported for conventional methane digesters. (Source: Development Forum, January/February 1990)

United Kingdom

Releases face dual controls

Under the UK Environmental Protection Bill, published last December, the Department of the Environment would take on significant new powers over the release of genetically modified organisms (GMOs). Currently, operators are required to notify the Health and Safety Executive of plans to release GMOs into the environment, and proposals are subject to the approval of the HSE's advisory committee on genetic manipulation. This group of experts, which has overseen all GMO releases in the UK to date, may be eliminated and replaced with a new advisory body answering to both the HSE and the DoE.

Under the new bill, operators would be required to notify both the DoE and the HSE, and in some cases a positive consent would be required. They would also assume a formal duty of care to protect the environment, as well as human health. HSE inspectors, who have substantial experience in the field, would be authorized to act on behalf of the DoE. The Government plans to rely on existing legislation to mitigate threats to worker and public safety, and to control new bioengineered products, such as pesticides.

In effect, the industry would now serve two masters, and the idea of dual regulation has met with strident resistance from several quarters. The BioIndustries Association, the Confederation of British Industry and the Health and Safety Commission have all voiced opposition to a split in authority.

Although the DoE has promised to keep the public informed about GMO releases and to maintain a level of commercial confidentiality acceptable to industry, the issue of public information is not raised in the bill as it stands. (Source: Chemistry and Industry, 15 January 1990)

Open University investigates risks of biotechnology and their regulation

In a two-year project, funded by the Economic and Social Science Research Council and beginning last autumn, the Open University's Faculty of Technology is studying the risks associated with biotechnology - and their regulation. The aim is to expand on the risk assessment outlined by the Royal Commission on Environmental Pollution in its twelfth report, designed to select the "best practicable environmental option" (BPEO) when planning the deliberate release of a genetically engineered organism (GEO). Details from: Les Levidow, research fellow, Faculty of Technology, SYSTEMS, The Open University, Walton Hall, Milton Keynes MK7 6AA. (Source: Biotechnology Bulletin, Vol. 9, No. 1, February 1990)

Deliberate release regulations - scope of proposals widened

Scientists proposing to release genetically engineered organisms into the environment soon will be obliged not only to safeguard human health but also to protect the environment from harm. Present arrangements under the Health and Safety at Work Act are designed to minimize hazards to workers and the general public. Now, there will be a complimentary requirement to use "the best available techniques not entailing excessive cost" to avoid damage to ecosystems. Although the Advisory Committee on Genetic Manipulation will continue to advise government departments on gene technology, a new regulatory body will deal specifically with deliberate releases of engineered organisms.

These are the key provisions proposed by the UK Government in a wide-ranging Environmental Protection Bill. The proposals, which will be debated in Parliament over the coming months and should become law before the end of this year, follow closely recent recommendations by the Royal Commission on Environmental Pollution. They have been drafted to ensure safety without hampering science or industry with unneccessary regulation.

Under the proposals, researchers intending to import, acquire, keep, or release a genetically engineered organism will have to supply a safety assessment and obtain consent accordingly. HSE inspectors, now armed with the broader mandate of environmental protection, will enforce the regulations. As at present, their powers will extend to entering laboratories, and removing and destroying organisms deemed to pose a hazard. Tough new penalties, including a maximum five years' imprisonment, are proposed for scientists who fail to comply with the new rules.

After considerable debate in the biotechnology community, the Government has concluded that the new controls should not apply to techniques that involve only naturally occurring processes of reproduction - including selective breeding techniques and in vitro fertilization - or techniques that merely assist such processes. Therefore they will not embrace conventional or animal breeding. They do cover the release of

organisms made by "any technique for the modification of any genes or other genetic material by the recombination, insertion or deletion of, or of any component parts of, that material from its previously occurring state". A potential catch-all provision also includes other gene modification techniques to produce organisms "which should ... be treated as having been genetically modified".

The UK Genetics Forum, a lobby group that is trying to open up debate about the dangers of genetic manipulation, has welcomed the proposed extension of legislation to cover environmental protection. But the group continues to call for a Public Biotechnology Commission "with representatives from public-interest and environmental groups". (Source: Biotechnology, Vol. 8, February 1990)

Biotechnology in the LINK initiative

The Science and Engineering Research Council (SERC) has announced six further programmes under the LINK initiative which provides financial support for university-industry co-operation projects. This brings the total number of approved programmes to 15.

The LINK initiative now covers biotechnology with four separate programmes:

	£	
- Eukaryotic genetic engineering	(4.4 million)	
- Biotransformations	(4.0 million)	
- Protein engineering	(8.0 million)	(new)
- Biochemical engineering	(15.0 million)	(new)

The protein engineering programme aims to develop the systematic ability to design proteins rationally with new or improved properties, and to advance the understanding of structural properties and the rules governing structure and function and biological activity. Main topics within this programme include tertiary structure determination, protein structure/function relationship, and mutagenesis and expression of proteins.

The biochemical engineering programme is concerned with the exploitation of biotechnology through the development and op .ation of industrial-scale equipment and processes. This £15 million programme will consist of a range of collaborative projects between equipment manufacturers, bioprocess companies and higher education institutions. Primary topics include innovative downstream processing, fermentation, process control and asepsis, containment and the environment.

The LINK initiative aims over all to encourage strategic research of medium-term industrial significance, increased industrial investment in such R & D and, by strengthening links between industry and the science base, improve transfer of new technology into industry. LINK supports collaborative pre-competitive research projects involving industry and the scientific community. Up to 50 per cent of the cost of these projects is available from government sources. (Source: Biotechnica Journal No. 1, 1990)

Wellcome grant for new research centre

The latest grant from the Wellcome Trust, a UK charitable foundation, includes £4 million for Imperial College, London, to set up a new research centre in parasitic diseases. The grant is one of the largest single awards ever made by the trust.

The centre will be based around a core of scientists from Imperial's biology and biochemistry departments, directed by Professor Roy Anderson. Anderson expects the centre to employ 21 new staff at Imperial, and four researchers working in Africa, Asia and South America. The emphasis on close links with countries most heavily afflicted with parasites, he says, will be an important part of the centre's effort to combat the diseases.

Wellcome has also agreed to provide funds for the European arm of the Human Genome Organization (HUGO) over the next three years. (Source: Nature, Vol. 344, 1 March 1990)

Firms link up to exploit fungi

A major collaborative initiative to exploit lichen fungi in the production of enzymes and pharmaceuticals has been established in the UK. The Department of Trade and Industry is funding collaboration between the four groups involved: CAB Mycological Institute (CMI); the Department of Botany at Nottingham University; Biocatalysts, a subsidary of Shell; and Xenova.

Lichens are symbiotic relationships between algae and fungi. They have traditionally been used for colours and fragrances but the consortium believes fungal strains exist that may produce pharmaceuticals, such as antibiotics, flavourings, fragrances and colours.

The work will be split between the academic parties, CMI and Nottingham University, which will collect, separate and identify samples of lichen, and the biotechnology companies which are screening for possible products. Biocatalysts is aiming to find enzymes for diagnostics and biotransformations, whilst Xenova is looking for pharmaceuticals.

The use of lichen fungi to produce enzymes that produce chiral intermediates is thought to be particulariy promising. The process for finding novel compounds involves screening for reactivity for a predetermined target, using spectrophotometric or gas chromatographic assays. (Source: European Chemical News, 1/8 January 1990)

Textile industry to explore microfungal filaments in wound dressings

A major, fundamental research project on a novel means of making wound dressings has just been launched by the British Textile Technology Group (BTTG). Involving the use of microfungal filaments, it is one of two new projects at BTTG designed to apply advanced biotechnological techniques in the textile industry.

The two-year programme on wound dressings will investigate and optimize the use of microfungal mycelia, whose wound healing properties have been identified as a major area for future commercial development.

There is a rapidly expanding market for new wound dressing materials and the aim is to produce wound dressing substrates which use intact microfungal filaments as a direct source of chitin/chitosan for active wound healing. Chitin and its derivative chitosan, obtained from the shells of crustaceans, have long been recognized as having wound healing properties, but the characteristics of microfungal chitin/chitosan for this purpose are largely unknown. (Source: Biotechnology Bulletin, Vol. 8, No. 12, January 1990)

Drug markers

A Shell Group biotechnology subsidiary, Biocode, based in York, UK, has developed an analytical method which it claims can be used to combat the problem of counterfeit pharmaceuticals. The company has developed a range of protein markers, which can be introduced to genuine products and an immunoassay technique, which can easily identify these markers at levels which would otherwise require expensive instrumentation.

The technique can be applied to any high value product, which could even include foods, by presenting the marker in the form of an accepted additive.

The trace levels of the markers are identified by monoclonal antibodies, which are specific to a particular antigen - in this case the marker, at levels as low as 10 ppb. The marker can be infinitely varied, and could be changed regularly, to date a particular batch of chemical product. (Source: European Chemical News, 1/8 January 1990)

United States of America

State biotechnology legislation survey

The US Industrial Biotechnology Association's nationwide survey of state biotechnology activity, released last December, found that three additional laws had been enacted since its 4 August 1989 report. As 1989 closed, a total of 22 state biotechnology laws had been enacted. The report also found that a total of 69 biotechnology initiatives were pending in 30 states - up from 66 in August and 51 in May. Most fell into the areas of state-funded programmes, DNA fingerprinting and environmental release. (Source: Biotechnology Bulletin, Vol. 8, No. 12, January 1990)

Open approach to federal co-ordination urged

A high-level federal review committee is suggesting changes in the way the US Government oversees biotechnology. In a draft report, the Committee on Regulation of the Administrative Conference of the United States (ACUS) recommends that Congress and the President's Office of Science and Technology Policy (OSTP) review the effectiveness of current regulatory statutes. The committee also sharply criticizes the federal Biotechnology Science Co-ordinating Committee (BSCC), which was created by OSTP in 1985.

The basis for the recommendations is a report, "Biotechnology and the Design of Regulation", prepared for ACUS by Sidney Shapiro, John Rounds, Professor of Law of the University of Kansas (Lawrence). The report carefully traces the combative deliberations that led the Environmental Protection Agency (EPA) to withdraw from BSCC activities during part of last year. The dispute within BSCC centred on proposed EPA rules for applying the Toxic Substances Control Act to the release of genetically engineered micro-organisms. Although the EPA draft rules have been aired publicly, they still have not been formally promulgated.

Shapiro recommends expanding the membership and scope of BSCC, and renaming it. Specific policy decisions would be left to OMB or other White House agencies.

So far, ACUS endorses many of Shapiro's suggestions, agreeing that, while no new legislation is needed, the President and Congress should "determine whether current law and regulations provide adequate authority to protect public and private interests". (Extracted from Bio/Technology, Vol. 8, January 1990)

RAC invites public comment on its future guidelines, mandate

Open meetings throughout the USA this summer and autumn will invite public comment on the future mandate of RAC, specifically on the following questions, as well as others:

- Should the definition of recombinatant DNA be modified to encompass the newer techniques of molecular genetics?
- Do these newer techniques pose any new risk, not seen with the established techniques?
- Should the RAC extend its purview to encompass the newer technologies used in today's experiments?
- Should the RAC consider transferring more of its review responsibilities to local Institutional Biosafety Committees (IBCs) - for example, adding plant pathologists to the IBCs to facilitate consideration of experiments which require environmental release?
- Under its current review system, RAC uses a process-orientated approach to identify experiments which should be evaluated, and a product-based approach to determine level of risk, and hence the containment. Is this system adequate, or should changes be considered to make the process more risk-based?

Five public meetings are planned - two each in the West and East, and one in the Midwest - plus a final one in the Washington, D.C. area just prior to the RAC's autumn meeting, scheduled for 15 October.

At its meeting on 5 February 1990 the Committee explored these questions, which must be answered if the definition of recombinant DNA is revised to shrink, broaden or otherwise change the RAC's mandate. (Source: McGraw Hill's Biotechnology Newswatch, 19 February 1990)

Bioremediation policy planned

An EPA consultant has designed criteria to choose bioremediation products for cleaning oil spills. The consultant, the National Environmental Technology Applications Corp. (NETAC, Pittsburgh), will also evaluate applications for field trials in Alaska. The criteria dictate that prospective products cannot contain genetically engineered materials; known or suspected carcinogens/pathogens; or chemicals listed under the land ban section of the Resource Conservation and Recovery Act. Proposed products must already have been used on oil. In addition, all field and laboratory data must be submitted if they support evidence of enhanced biodegradation, and toxicity data must also be furnished. Applicants must present a statement of corporate qualifications and tell how their product could be used on a large scale. The one that does best in field trials will be approved by EPA to clean future spills. (Source: Chemical Week, 7 February 1990)

Healthy future for biotech

A survey of 480 US biotechnology companies by Ernst & Young has shown that industry sales are projected to grow tenfold in five years.

Overall, the survey of chief executives says that biotechnology firms posted a 6 per cent gain in total assets with product sales averaging $8.2 million in 1988/1989.

But the whole picture is not quite as rosy, with the industry overall still losing money and only a quarter of all companies posting net profits.

Most market segments are predicted to rise to between 10 and 20 times current levels by the end of the decade, but high growth is forecast for therapeutics companies, which, led by recombinant drugs anticipate 81-fold growth by the year 2000.

Given the increasing acceptance by federal regulations of open-air testing of genetically engineered organisms, the biotech industry's agricultural sector is seen posting strong gains in the next 10 years as the number of products on the market will probably increase from 18 to 53.

Ernst & Young says "large companies with substantial R & D budgets and the staying power to compete in a young industry are still proving to be more profitable than smaller firms". (Source: Manufacturing Chemist, January 1990)

Biotechnology industry encouraged by Genentech deal

Hoffmann-La Roche has made a pioneering agreement to buy 60 per cent of the American biotech company Genentech and inject $500 million into the company, giving it its much-needed financial freedom to develop new products.

The deal is structured as a merger rather than a takeover and Genentech will continue as an independent company, but with two Roche members on the board.

Although the price paid by Roche is considered high, the deal brings to the Swiss company a strong pipeline of promising new drugs, at a time when it had been suffering from the expiry of its US patent on Valium and a lack of exciting drugs of its own.

Like most biotechnology companies, Genentech is strong on R & D and the identification of new products. But because such drugs take a long time to get to the market and make money, investors have been getting jumpy and most biotechnology shares have fallen sharply in the last few years.

The Swiss offer gives not only considerable financial help to Genentech but will also provide the worldwide marketing power needed for the emerging products. (Source: Manufacturing Chemist, March 1990)

Gamma interferon

Genentech is seeking US approval to market recombinant gamma interferon to treat patients with chronic granulomatous disease (GCD) and has filed a product licence application with the US Food and Drug Administration.

GCD is a rare inherited disorder in which the body's white blood cells are unable to kill invading bacteria or fungal agents. To date the existing therapy involves frequent antibiotic doses. Genentech envisages gamma interferon can be used along with antimicrobial therapy to treat active infections as well as for the prevention of infections.

Genentech is also looking at the drug's ability to stimulate the immune system as a potential treatment in other indications. Phase III trials continue to evaluate its safety and efficacy when treating patients with infections relating to traumatic injuries, and as an adjuvant therapy to treat patients with melanoma and small cell cancer of the lung. (Source: European Chemical News, 1/8 January 1990)

Union of Soviet Socialist Republics

Soviet biotechnology

Soviet biotechnology could offer Western firms unexpected opportunities for co-operation, according to a recent report* from a DTI-sponsored group of industrialists and academics who visited some Soviet institutes. The exploitation of such links will probably be a long way off however, since the obstacles are formidable.

"It is practically impossible to build a new biotechnology plant in the Soviet Union today", according to the report. Public opinion has turned against biotechnology in the USSR in the wake of some major ecological disasters. The blame mainly lies with the production of single cell protein (SCP), used to make up protein deficiencies in cattle feed, according to the report. The public outcry following the incidents of biotechnology pollution in the vicinity of the SCP factories has been such that part of the programme has been shelved and the word microbiology has been dropped from the Ministry of Medical and Microbiological Industry, the report recounts.

The Soviet Union's biotechnology effort is now to be redirected mainly towards medical uses. Soviet scientists have achieved amazing feats in this area, especially in the light of sometimes inadequate equipment. Even in this field, though, safety practices are well below anything that would be required in the West, according to the report. It would almost certainly be a problem to get Western agencies to approve products which have been tested in the USSR.

Rod Greenshields from GB Biotechnology, who led the UK delegation, says that the European Community should take Eastern Europe and the USSR into account when it starts drawing up rules on biotechnology. He does, however, contend that Western companies may produce in the USSR for the Soviet market, even though safety standards are low. The USSR, according to Greenshields, just cannot afford Western standards.

Not all institutes lag behind their Western counterparts. The Shemyakin Institute of Bio-organic Chemistry in Moscow is an outstanding laboratory by any standards. The institute has just finished a $45 million pilot plant, with an abundance of Western equipment, which can be compared to the best available "at the other side of the Atlantic", according to one of the British industrialists.

The Moscow Institute of Molecular Genetics (IMG) is another highly advanced establishment. The IMG has come up with

* Biotechnology in the USSR: GB Biotechnology, Swansea

lymphokine-based therapeutics against hepatitis B, herpes viruses, multiple sclerosis, hairy cell leukaemia, renal carcinoma and malignant melanoma. Only a few of these treatments are available in the West, the report points out.

The USSR's biotechnology institutes are to co-operate in the sequencing of the human genome. The programme is to concentrate on identifying those parts of human genetic make-up which may cause disease and birth defects. (Source: Chemistry and Industry, 5 February 1990)

C. RESEARCH

Research on human genes

Gene may be key immune-system controller

Scientists have discovered a gene they think is essential to the development of human immune defences. The gene, called rag-1 (for recombination activating gene), may be the master genetic switch that triggers the body to release a diverse range of protective antibodies. The immune system generates these antibodies by shuffling and recombining segments of a relatively small number of genes. Its discovery suggest that rag-1 may provide the blueprint for all or part of recombinase, the enzyme that carries out this genetic shuffling. Alternatively, they say, it may switch on other genes vital to the recombination process. In either case, rag-1 is thought to act on the bone marrow cells that produce B cells and T cells, vital components of the immune system. The discovery was made by David G. Schatz, Majorie A. Oettinger, and David Baltimore of Whitehead Institute for Biomedical Research at Massachusetts Institute of Technology. Other scientists hailed the work as a landmark in immunology, although practical applications in medicine are not expected immediately. One day the discovery might lead to better ways of bolstering the immune system when it is under attack by, say, human immunodeficiency virus. (Reprinted with permission from Chemical and Engineering News, 1 January 1990, p. 17. Copyright (1990) American Chemical Society)

Interleukin-1 inhibitor characterized

In what is apparently the first example of a natural protein that blocks the action of another protein by competitively binding to its receptor, a protein has been found that blocks the activity of interleukin-1 (IL-1). IL-1 is a cytokine that activates elements of the immune system and plays a role in inflammatory diseases such as rheumatoid arthritis. The IL-1 inhibitor substance was first observed in 1985 by William P. Arend and colleagues of the University of Colorado Health Sciences Center. Now, Charles H. Hannum, Stephen P. Eisenberg and others in Robert C. Thompson's group at Synergen Inc., Boulder, Colorado, have purified the inhibitor and have shown that it binds to the IL-1 receptor without activating it. They also determined the inhibitor's structure (which is similar to that of IL-1 itself) and expressed its complementary DNA in Escherichia coli; study of the inhibitor could help elucidate the mechanism by which IL-1 triggers cellular responses. The inhibitor also could be useful as a therapeutic agent for rheumatoid arthritis and other IL-1-mediated diseases. (Reprinted with permission from Chemical and Engineering News, 29 January 1990, p. 22. Copyright (1990) American Chemical Society)

Biogen aims for protein inhibitor

Scientists at Biogen have reported the identification, cloning and expression of a novel human receptor protein, which the company believes may offer a new approach to the treatment of autoimmune and inflammatory diseases.

The receptor protein, vascular cell adhesion molecule 1 (VCAM-1) is a central mediator of lymphocyte (white blood cell) recruitment into inflamed tissue. Biogen believes that if a VCAM-1 inhibitor can be found, a method of controlling the immune response will be achieved that can be utilized against autoimmune diseases, such as arthritis.

VCAM-1 expression is induced in response to cytokines, such as interleukin-1 and tumour necrosis factor, themselves released in response to infection and tissue injury. VCAM-1 is expressed on the surface of the cell layer lining the blood vessels, at the inflammation site.

Lymphocytes moving through the blood vessel are found to adhere to the VCAM-1 rich endothelial cell layer. Following this adhesion, the lymphocytes migrate into the underlying tissue, triggering a chain of pro-inflammatory events which cause tissue damage. Biogen aims to develop an inhibitor for VCAM-1 which it describes as "an excellent target for therapeutic intervention".

Possible disease targets include psoriasis, atherosclerosis, transplant rejection and rheumatoid arthritis. (Source: European Chemical News, 15 January 1990)

Groups attached site-specifically to DNA

A newly-developed technique can be used to direct, in a site-specific manner, the covalent attachment of fluorophores, spin labels, drugs and other ligands to DNA prepared by chemical synthesis. To date, covalent introduction of such groups into DNA has largely involved either prior synthesis of modified nucleosides containing the desired group for subsequent incorporation into DNA or the use of reactions that restrict attachment to 5'- or 3'-termini. Graduate student Jacqueline A. Fidanza and associate professor Larry W. McLaughlin of Boston College's department of chemistry report that site-specific substitution by sulphur of a non-bridging oxygen in the phosphodiester linkage between nucleotides results in a phosphorothioate diester that serves as an attachment point for other groups. (DNA containing phosphorothioate esters is known to be essentially native in structure, with physical properties that are often indistinguishable from those for unmodified DNA.) The technique could simplify studies of protein binding, resonance energy transfer, structural analysis, and nucleic acid dynamics, and it could facilitate attachment of peptides, antibiotics, antineoplastics, and antivirals to DNA. (Reprinted with permission from Chemical and Engineering News, 18 December 1989, p. 16. Copyright (1989) American Chemical Society)

Geneticists home in on heart and cancer gene

An international team of researchers has located a genetic marker for an inherited disease of the heart.

The team, which consisted of scientists from the medical schools at Harvard University,

St. George's Hospital in London, the Royal Victoria Hospital in Montreal, and Washington University in St. Louis, studied familial hypertropic cardiomyopathy, a thickening of one wall of the heart that can be fatal. They followed the incidence of the rare disease through 78 members of a Canadian family over several generations.

Although the scientists have not yet located the gene responsible for the disease, they have tracked it down to the long arm of chromosome 14 and located a genetic marker that is inherited with the gene. People who have the marker can reliably be expected to suffer from the heart disorder.

The leader of the medical team, Christine Seidman of Harvard, says that finding the gene will help clinicians to understand the general condition of hypertrophy, which is associated with other heart ailments. She hopes that their discovery will lead to an understanding of other heart disease.

The discovery follows the announcement of the discovery of a gene for Wilm's tumour at the annual meeting of the American Society of Human Genetics, held in Baltimore, Maryland, in November 1989. Wilm's tumour is a form of cancer that attacks the kidneys of children. Katherine Call of the Massachusetts Institute of Technology led a group that isolated the gene on chromosome 11.

The gene produces a protein that is similar to others that regulate oncogenes, which are involved in the development of cancer. A pair of genes that is missing or faulty fails to produce the protein, which apparently quells other genes that stimulate uncontrolled growth and cancer. (Source: New Scientist, 2 December 1989)

Viral route to antibodies found

US researchers have developed a method of producing monoclonal antibodies (Mabs), which could allow biotechnology companies to produce a vast array of products on demand.

Scientists at the Research Institute of Scripps Clinic in La Jolla, California, have reported a technique for inserting antibody genes from mouse spleen cells into bacteria-infecting viruses. Functional antibodies are secreted from bacteria such as Escherichia coli when infected with these viruses.

The current method of producing Mabs is the hybridoma technique. This uses B-cells, which produce antibodies fused to an immortal partner. However, the hybridoma technique is difficult to adapt for human cells which do not fuse easily. This problem will not arise using bacteria-infecting viruses called bacteriophages as the vector for the genes.

Antibodies are made of light and heavy chains, which are encoded by separate genes. The varying sequence of these genes determines the nature of the antibody.

The researchers were able to clone many different heavy and light chain genes from the mouse cells and combine them at random in the bacteriophage. These phages can be used to infect bacteria which then contain the genes necessary to produce antibodies. So far, the researchers have produced antibody protein fragments known as Fabs. Fabs contain the antigen-binding regions of the antibody and are used in diagnostics work. The system can be easily modified to produce Mabs, says William Huse of the Scripps team.

In contrast, hybridomas are made after looking for one specific antibody. In this technique, an animal, typically a mouse, is immunized with an antigen for which the antibody is needed. Immunized lymphocytes are removed and fused with myeloma (cancer) cells. The result is a line of immortal cells which produce the antibody. (Source: European Chemical News, 26 February 1990)

Antibodies developed to treat allergies

Monoclonal antibodies against a particular site on immunoglobulin E (IgE) molecules have been developed by Tanox Biosystems, Houston, Texas. The firm expects to start clinical trials in two years to test the ability of the antibodies to prevent allergic reactions to pollen, foods, drugs and insect stings. Reactions of allergens with IgE attached to basophils in blood and mast cells in connective tissue cause these cells to release mediators of allergic reactions, such as histamine. The Tanox antibodies bind to freely circulating IgE and to IgE attached to the B cells that produce it. Binding of monoclonal antibodies to IgE attached to B cells triggers an immune attack that kills these IgE-producing cells, thus resulting in depletion of IgE in the patient's immune system. (Reprinted with permission from Chemical and Engineering News, 12 February 1990, p. 23. Copyright (1990) American Chemical Society)

Improved route to "antisense DNA"

Scientists are excited about the potential of oligodeoxyribonucleoside phosphorothioates as "antisense" molecules against the AIDS virus. These molecules have been difficult to prepare in the large quantities necessary for clinical studies because of the difficulties of using elemental sulphur (S_8) as a sulphurizing agent in automated DNA synthesizers. Now, nucleic acid chemist Serge L. Beaucage and colleagues Radhakrishnan P. Iyer, William Egan, and Judith B. Regan at FDA's Center for Biologics Evaluation and Research in Bethesda, Maryland, have found that 3H-1,2-benzodithiole-3-one 1,1-dioxide is a faster and more efficient sulphurizing agent than elemental sulphur. Unlike elemental sulphur, whose insolubility can cause instrument problems, the reagent is soluble in a wide variety of organic solvents. It can create a phosphorothioate linkage within 30 seconds and in near-quantitative yields without modifying the nucleosidic bases. The use of this reagent in conjunction with the "phosphoramidite" synthetic approach could make it easier to produce large amounts of phosphorothioate oligomers. (Reprinted with permission from Chemical and Engineering News, 12 February 1990, p. 23. Copyright (1990) American Chemical Society)

Tracking carcinogen exposure

A new antibody-based technique may help researchers track occupational and environmental exposures to carcinogens. The technique, which uses monoclonal and polyclonal antibodies to measure DNA-carcinogen adducts in white blood cells, was described by Regina Santella, assistant professor of environmental science at Columbia University.

Because the covalent binding of a carcinogen to DNA is often the first step in carcinogenesis, the assay may eventually provide a way to estimate the risk of developing cancer as a result of exposure to a particular carcinogen. Such a reaction between

DNA and a carcinogen, Santella says, can result in mutations, gene rearrangements and amplifications of gene expression, any one of which may lead to cancer.

Santella's group at Columbia has developed antibodies to a number of carcinogen-DNA adducts and characterized them in terms of sensitivity and specificity. The best antibodies can detect one carcinogen adduct in one million normal DNA nucleotides, she explains.

For example, antibodies have been developed against the major DNA adduct of benzo[a]pyrene, a polycyclic aromatic hydrocarbon (PAH) that is a common environmental pollutant found in cigarette smoke and combustion products. The antibodies also detect adducts of DNA and PAHs closely related to benzo[a]pyrene. Using the assay, the researchers have measured PAH-DNA adducts in workers in a number of different industries. Results for Polish coke oven workers and people who live near the antiquated facilities suggest, for example, that both are at risk from PAH exposure.

Santella's research, as well as that of other groups who are involved in the field, has "demonstrated that measurement of carcinogen adducts in humans is now a viable method to determine exposure to a number of environmental and occupational carcinogens", she says. In the future, the assays may be useful in determining the efficacy of methods to control workplace exposure to occupational carcinogens or whether intervention to change lifestyle-related risk factors, such as smoking, results in changes in adduct formation. (Source: Chemistry and Industry, 19 February 1990)

Platelet factor 4 slows tumour growth

Scientists at Repligen Corp. think they have discovered a natural protein which could be used to treat tumours. In normal adults, new blood vessels are formed only to help heal wounds or during pregnancy. But when tumours take root, they spread and grow by stimulating the formation of new blood vessels. In animal tests, platelet factor 4 has retarded the growth of such blood vessels and Repligen has pinpointed the active area of the protein. Recombinant DNA techniques are now being used to make large quantities of the potential drug, called Endostatin B. Among the diseases the company intends to target with the protein are Kaposi's sarcoma (often a feature of AIDS cases), eye diseases and diabetic retinopathy. Details from: Repligen Corp., One Kendall Square, Building 700, Cambridge, Massachusetts 02139, USA or on +1(617)225-6000. Fax: +1(617)494-1786. (Source: Biotechnology Bulletin, Vol. 9, No. 1, February 1990)

Cell transplant relieves Parkinson's disease in rats

Researchers in California have developed a technique that partially restores normal brain function in rats with the equivalent of Parkinson's disease in humans. The technique is an alternative to transplanting foetal tissue to the brain. At present, this is hampered by a ban on funding imposed by the US Government.

Fred Gage and his colleagues at the University of California in San Diego injected modified cells from rat skin into the brains of rats that were suffering from a type of neurological damage that resembles Parkinson's disease.

The researchers first modified the cells by introducing a genetically engineered virus that contained the gene for the enzyme tyrosine hydroxylase. The enzyme catalyzes the conversion of tyrosine into L-dopa, and is produced in small amounts by the cells. Next, Gage and his colleagues injected the modified cells into the brains of the rats. They found that brain function improved by 40 per cent.

In the brain, the injected cells produce L-dopa which is converted to dopamine and other neurotransmitters. This allows some normal brain functions to be restored. Gage and his colleagues stress, however, that the transplant method is not yet ready to be applied to humans.

An advantage of the method is that it holds out the possibility of injecting skin cells from the same animal or individual as the recipient. This would greatly reduce the chance that the transplanted material would be rejected.

Gage says that transplants of foetal cells are a more effective method of alleviating the symptoms of Parkinson's disease because they produce quite naturally the neurotransmitters that are deficient. Nevertheless, Gage is optimistic about the technique of transplanting skin cells, despite its limitations. (Source: New Scientist, 6 January 1990)

Research on animal genes

Virus-like agent blamed for mad cow disease

About 600 head of cattle a month in the United Kingdom are coming down with a mysterious new disease. The affliction, which seems to have spread to the cattle from sheep, is costing British cattle breeders £50 million a year. Bovine spongiform encephalopathy (BSE) - "mad cow disease" - seems to be caused by a little understood, virus-like agent that causes a brain disease called scrapie in sheep. The United States and the European Community have banned some imports of British cattle and beef while awaiting the results of a research effort in the United Kingdom aimed at finding out whether the disease can spread from cow to cow or, more worryingly, to humans.

In late 1986 a dairy farmer in Kent, in southeast England, noticed several cows with symptoms in his herd. Tissue samples from slaughtered animals went to the Central Veterinary Laboratory of the Ministry of Agriculture, Fisheries and Food (MAFF) in nearby Sussex. Gerald Wells, head of the neuropathology unit, took one look through his microscope at samples of brain tissue and thought he recognized the appearance of scrapie.

Scrapie is related to the human brain diseases kuru and Creutzfeldt-Jakob disease. Both are caused by pathogens whose nature is controversial. Sometimes called "slow viruses" or merely "unconventional agents", they make the brain appear spongy and full of holes. Wells saw this pattern in the cattle brains and dubbed the syndrome BSE. He was confident enough of his diagnosis to tell a colleague he "suspected we had scrapie in cattle".

But if BSE was scrapie how did it get into cattle? John Wilesmith, head of epidemiology at MAFF's Veterinary Laboratory, began an epidemiological survey to find out. The few known cases were spread around the country, implying that BSE was caused by a factor in general cattle management rather than by a local condition. It was relatively easy to eliminate an array of possible causes, including vaccines, other biological agents, agricultural chemicals, and direct contact with sheep.

"The thing that we were left with", Wilesmith said "was the the feeding of meat and bone meal in rations". Although it may seem surprising, animal protein is a standard part of cattle rations - especially the "weaner" rations fed to young calves. Wilesmith questioned manufacturers and found that sheep unfit for human consumption (perhaps because they had scrapie) often ended up in cattle rations.

In 1987 MAFF banned the use of ruminant-derived protein in feed for cattle or sheep, which should ultimately put a stop to mad cow disease. Unfortunately, one characteristic of unconventional agents is the lag time - four to five years in cattle - between infection and symptoms. Hence the roughly 600 cases a month now being seen are the result of infection before the ban on ruminant protein in cattle feed.

The fact that the number of new cases is remaining steady is good news, according to most epidemiologists. If the disease were being transmitted directly from one adult cow to another, the curve indicating new cases would probably be climbing much more steeply, researchers say.

Yet questions remain. Can the disease be transmitted from an infected cow to her calf? And what is the risk to human beings? The recently announced UK science budget has earmarked £12 million to provide some answers. MAFF has purchased 300 calves born to infected cattle; observation of them should answer the first question.

The second question - the risk to humans - is more difficult to answer. Some diseases caused by unconventional agents can definitely be transmitted to human beings. Kuru, for example, which afflicted natives of New Guinea, seems to have been spread through the consumption of human brains in ritualistic cannibalism.

Whether Creutzfeldt-Jakob disease (CJD) is generally contagious is more problematic. The disease is relatively common among Libyan Jews, who eat sheep's eyes. Anatomically, the eyes are an extension of the brain, and they might contain the scrapie agent. No solid evidence yet supports such a link, however, and CJD has been reported in Japan, where there is little scrapie, and also in a lifelong vegetarian.

In any event, the risk of BSE being transmitted to humans has already been greatly reduced, according to Sir Richard Southwood. Southwood chaired a working party to advise the British Government on BSE. The group recommended that all offal from cattle be banned from human food, including brain, thymus, and spleen - the major reservoirs of the scrapie agent.

Why did BSE arise in Britain in 1986? Three factors may have been responsible. In the early 1980s Britain's sheep population was growing rapidly, and an increasing number of the animals wound up as meat and bone meal at rendering plants. At the same time, in the wake of the oil crisis renderers adopted energy-efficient techniques that were less likely to destroy the highly resistant scrapie agent. Finally, government policy encouraged farmers to produce more milk by removing calves from their mothers quickly, and the weaned calves were fed diets containing infected sheep protein.

That constellation of factors seems unique to Britain. Few experts expect outbreaks of BSE elsewhere, although the US Department of Agriculture has set aside funds for increased research on scrapie and BSE. In the mean time, the larger research effort in the United Kingdom proceeds apace, in the hope of assuaging public fears and persuading the United States and Europe to lift their bans on British cattle. (Source: Science, Vol. 247, p. 523, Jeremy Cherfas. Copyright AAAS)

Antelopes die of "mad cow" disease

Some zoo animals may have been infected with the agent which causes bovine spongiform encephalopathy (BSE), the disease which has killed over 10,000 British cattle. Five antelopes have died in British zoos from a BSE-like condition, thought to have been transmitted in commercial feed containing sheep meat infected with scrapie, a similar disease. Although this practice has been stopped, the long incubation period of spongiform encephalopathies means it may be several years before the extent of infection in zoo animals is known. James Kirkwood, senior veterinary officer at London Zoo, where an Arabian oryx and a kudu died last year, says that conservationists will have to wait to assess the impact of the outbreak on endangered species.

London Zoo officials have written to other British zoos suggesting that "careful consideration" should be given before animals at risk are exported to foreign zoos or for reintroduction programmes. London Zoo's circular says that any ungulate fed proprietary meal between 1980 and 1989 may be affected.

The first recorded case of the disease in a zoo was in 1986, the first year of the outbreak of BSE in cattle, when a nyala at Marwell Zoo, near Winchester, died. Since then, in addition to the London cases, a gemsbok has died at Marwell, and an eland at Port Lympne Zoo, in Kent. The cross-species transmission of spongiform encephalopathies is not a surprise; results published in the Veterinary Record in February showed that laboratory mice can contract BSE symptoms after eating infected cattle brain tissue.

Geoff Holmes, from the agriculture ministry's veterinary centre at Itchen Abbas, where the Marwell cases were examined, says his biggest worry is whether the disease will be passed from female cattle and antelope to their offspring, via the placenta. This does occur in scrapie-infected ewes, but research to test for this "vertical transmission" in cattle is still in progress. (Source: Nature, Vol. 344, 15 March 1990)

Research on plant genes

Corn plant advance

A US biotechnology company has achieved a breakthrough with the genetic manipulation of the corn plant, which could lead to a new generation of hybrid corn species designed to maximize yield.

BioTechnica International, based in Cambridge, Massachusetts, has developed a technique by which a gene can be introduced into the DNA of a corn plant, which can then be grown producing seeds. These in turn express the gene in the next generation of plant.

BioTechnica vice-president David Glass explains that the technique will enable the company to impart commercially valuable traits into strains of corn. Glass explains that BioTechnica intends to introduce insect resistance using the UK-firm Agricultural Genetic Company's (AGC) CpTi gene which it has licensed. (Source: European Chemical News, 5 February 1990)

Viral burglars use chemical keys to break into cells

Biologists in the US have observed how viruses spread through a plant by breaking into its communication system. The viruses use chemical "keys" to unlock the channels along which chemicals pass between cells. An understanding of the mechanism may enable scientists to develop new ways of protecting plants against viral infection, which causes huge amounts of damage and loss of crops worldwide.

"The viruses act as burglars", says William Lucas of the University of California at Davis. "They have to break into each cell undetected. If the plant cells detect an invader, they have numerous ways in which to prevent the virus from spreading." Lucas and his colleagues from Davis and Washington University, St. Louis, have developed techniques to observe such viruses in action.

To grow and develop normally, the cells in a plant must communicate with each other. They do so along plasmodesmata, fine strands of cytoplasm, which are laid down when the cells divide initially. It is along these channels that chemicals, including sugars and hormones, pass from cell to cell. The width of the channel determines the sizes of the molecules that can pass.

For many years, researchers have known that viruses can change the channels in various ways. Now Lucas and his colleagues have found that the viruses hijack the plant's system of protein expression to manufacture chemical keys, proteins that widen the plasmodesmata. The virus can then slip through undetected and replicate.

Lucas and his colleagues took RNA from the tobacco mosaic virus and inserted it into a tobacco plant. By this means, they produced plants in which the plasmodesmata remained wide open all the time. Using new techniques, they were able to watch molecules move from cell to cell and to measure how far the plasmodesmata open. Until now, studying molecular activity inside living plant cells has been impossible because the active part of the cell, the cytoplasm, occupies only a very thin layer inside the cell wall.

Lucas and his colleagues used a micro-pipette to release a tiny drop of a specially designed liposome. This carried a small amount of fluorescent marker inside the cell. The liposome fused with the plant cell, allowing its contents to be released.

The researchers used a camera that can detect very faint light and translate it into electrical signals which are then amplified a hundred million times. With this equipment, they built up a colour computer image of molecular activity inside the living plant as it took place. By attaching molecules of known size to the fluorescent marker, they could measure how wide the channels between cells open.

If scientists can discover more about the way in which these viral burglars make their chemical keys, it should be possible to change plants so that the chemical locks cannot be picked; in effect, engineering virus-proof plants. Also, the new techniques developed to study the molecular activity inside plants will enable researchers to study normal plants. (Source: New Scientist, 2 December 1989)

Molecular biology solves the riddle of Mendel's wrinkly peas

When in the 1860s, Gregor Mendel made his seminal studies of heredity in pea plants, he knew nothing about the molecular basis for his rules. Now, a team of researchers in the UK has cloned the gene responsible for one of the characteristics that Mendel described in the pea seeds: wrinkles.

Mendel observed seven pairs of characteristics in peas. They include tallness and dwarfishness, colour or colourlessness in the flower, and differences in the shape and colour of the seed. He found that the peas were either round or wrinkled, and that the round character was dominant to the wrinkled character. The factors that governed these two phenotypes were later labelled as R and r respectively.

Since then, other researchers have shown that there is a marked difference between the starch in the round (RR or Rr) peas and the wrinkled (rr) ones. In 1988, Alison Smith at the John Innes Institute in Norwich found that the structure of the starch depended on the presence or absence of one of two forms of an enzyme called the starch-branching enzyme I (SBEI).

A seed that lacks the enzyme has a higher sugar content than one that has the enzyme. This makes it accumulate more water than its counterpart, so it swells to a larger size at an early stage in its development, and shrinks as it dries out. The shrinkage gives it its wrinkled appearance. Smith found that the rr peas always lacked SBEI.

Now Madan Bhattacharyya, Cathie Martin and their colleagues at the institute have cloned the fragment of DNA that encodes SBEI from the pea that Mendel would have used, Pisum sativum, and demonstrated that it lies at the r locus.

They found that the messenger RNA transcript of the SBEI gene in rr seeds was much bigger than in RR forms. And rr seeds produced only about one tenth of the amount of transcript that RR seeds did, weight for weight.

Finally, the team found that the extra genetic material in the sequence coding for SBEI was an inserted fragment, about 800 base pairs long and with repeated base pairs at either end. According to the researchers, this fragment is very similar to certain transposable sequences of DNA in other plants such as maize. The insertion causes the wrinkled phenotype, rr, because it prevents the normal expression of the SBEI gene.

Bhattacharyya and his colleagues conclude that "since all the data Mendel provided fit the assumption that he used the r mutant and since there is no other evidence of another mutation available at this time, we believe that the gene we have cloned is the one studied by Mendel". (Source: New Scientist, 17 February 1990).

Research on bacterial genes

Mosaic bacteria move into the market

Genetic engineers who in 1989 devised a way to cross two distinct species of bacteria to create a new "mosaic" species now plan to exploit the commercial prospects of the technique. "If the practical applications of this work bear out, we think that this is a means of revolutionizing the whole of genetic engineering", said Miroslav Radman

of the Jacques Monod Institute in Paris, one of the researchers who made the mosaic species.

Radman said that a French company called Setratech hopes to use the technique to incorporate extra genes into micro-organisms, plants and animals, to create hybrid species suitable for live vaccines, and to stabilize new strains.

He and his colleagues, Christiane Rayssiguier in Paris and David Thaler at the University of Utah, experimented with two bacteria, Escherichia coli and Salmonella typhimurium. These two bacteria have a common ancestor, but have been separated for 150 million years and the DNA in their genetic sequences differs by more than one fifth. The researchers managed to create a new "mosaic" strain composed of genes from each species. They did so by interfering with the mechanism by which cells that are about to divide verify that their DNA has been copied faithfully.

A group of enzymes known as mismatch repair proteins are the key to this process. The researchers reasoned that these enzymes might act as a barrier to the recombination of genetic material from different species.

To test their prediction, they studied bacteria which have mutations that made them unable to carry out this "repair" routine. They found that mutations in the mutL, mutS or mutH genes did indeed dramatically increase the rate at which the two species of bacteria could exchange DNA, leading to the "mosaic" bacteria.

Radman says that he has now found a technique to inhibit the enzymes in this system during the crucial period in the cell cycle of the two bacteria when DNA is recombining. This opens the way, he says, for many practical applications of this new approach to genetic engineering, in plant, animal and human cells.

As a method of introducing new genes into cells, the procedure offers several advantages. It is possible to obtain a large number of recombinant cells, and a great variety of mutants, in a few hours. The method is protected by a licence, and Setratech is now interested in forming partnerships with other researchers in the field. It is negotiating joint ventures with industrial partners that it declines to name at the moment.

"The first practical applications are expected in two years' time, in fields such as yeast for fermentation, and agriculture and food", said Gilles Amsallem of Setratech. The company's research laboratory is in Paris, but it also uses the premises and staff of the Jacques Monod Institute. Such collaboration between industry and academia is rare in France, where basic research does not often lead swiftly to the market.

Radman is continuing research into the "evolutionary" consequences of his work, and hopes to study the genetic mechanisms that separate two species. He is searching for the "biological constant" that determines the moment when two species diverge and can no longer reproduce with one another. (Source: New Scientist, 3 February 1990)

Magnetic bacteria

Soil bacteria from a field in Bavaria, FRG, may be able to navigate along lines of electromagnetic force, researchers from Munich have discovered. The bacteria could also influence whether the soil becomes magnetic.

The mineral that gives soil magnetic properties is known as magnetite. Soil scientists previously assumed it had an inorganic origin. The Munich team suggests, however, that deposits of magnetite could be fossils of these bacteria.

Water-borne bacteria, similar to the ones the team discovered, convert iron into magnetite in their cells. The magnetite helps the bacteria to "swim" along lines of force in the Earth's magnetic field. Scientists believe the soil bacteria may be similarly "magnotatic", detecting and responding to magnetic forces. Studies show that, like the water-borne variety, these soil bacteria also contain crystals of magnetite. (Source: New Scientist, 20 January 1990)

Altered bacteria produce Mabs

Researchers at the Scripps Clinic in La Jolla, California, say they have devised a new technique, using genetically altered bacteria instead of mice to expand by a thousand-fold the variety of monocolonal antibodies.

The method, they say, promises new antibodies that could spur industrial chemical reactions that are currently difficult to produce. Meanwhile, a private San Diego biotechnology start-up, Stratagene Corporation, says it is founding a company, Stratacyte Corporation, to license the new technology in collaboration with Scripps.

The new technique involves a sort of genetic manipulation that lets researchers use genetically altered bacteria to produce randomly, in a first step, tens of millions to hundreds of millions of clones, each of which produces a stream of identical antibodies. In a second step, the researchers can rapidly screen these millions of clones and pick the ones producing the antibodies best suited for a particular function. The new technique is the first major departure from a 1975 technique currently used.

Under the 1975 method, researchers must sort through hundreds of hybrid mouse cells to find the one that is producing the antibodies that, say, home in on a cancer cell protein. They then scale up the hybrid to produce the antibodies in large quantities. Under the new technique, researchers can directly test a chemical against the millions of antibodies to see which ones trigger a reaction without knowing ahead of time what the reaction will be. This allows the chemists to discover antibodies that trigger new kinds of chemical reactions. (Extracted from Chemical Marketing Reporter, 11 December 1989)

Fermentation shows one-step conversion of carbon monoxide to butanol

Researchers from Michigan Biotechnology Institute (MBI) and Michigan State University (MSU) have shown in a novel fermentation that Butyribacterium methylotrophicum converts carbon monoxide, a major component of synthesis gas, directly into butanol.

This discovery represents first evidence of a direct biological pathway from carbon monoxide, a one-carbon gaseous substrate, to a four-carbon alcohol, and indicates the potential for a one-step

butanol production based on synthesis gas. Synthesis gas is a widely used chemical feedstock, is composed chiefly of carbon monoxide and hydrogen, and is obtained through the gasification of coal, petroleum or biomass.

Butanol is a large-volume industrial chemical and potential fuel additive. For the chemical industry and others that use butanol as a raw starting material, this fermentation could offer some distinct advantages. The abundance of coal reserves in the US - an estimated 936 billion net tons in 1988 offers a readily available, low-cost synthesis gas source in the future.

This one-step conversion process can operate at ambient pressure and temperature and produce butanol in the presence of sulphur contaminants. The commercial catalytic processes for producing alcohols from synthesis gas are sulphur-sensitive.

The fermentation is being optimized for improved reaction rate and butanol concentration in two ways. First, methods are being developed to inhibit the formation of less desirable products, such as organic acids. Second, the cell concentration is being increased using cell recycle.

In these preliminary studies, butanol concentrations of 0.5 g/l have been achieved. An order of magnitude increase in yield and concentration could make the recovery process economically attractive.

Researchers collaborating on this Department of Energy-sponsored project include Dr. Rathin Datta, Vice-President for Research, MBI; Dr. Mark Worden, Assistant Professor, Department of Chemical Engineering, MSU; Dr. Mahendra Jain, Senior Scientist, MBI; and Andrew J. Grethlein, doctoral candidate in the Department of Chemical Engineering, MSU.

The project was sponsored by the Pittsburgh Energy Technology Center of DOE. The discovery was first presented at the Eleventh Symposium on Biotechnology for Fuels and Chemicals, held in Colorado Springs, Colorado in May 1989. (Source: Bioconnection, Winter, 1989)

Bacteria degrade cellulose and fix nitrogen

A large number of newly discovered bacteria are unique in that they can degrade cellulose in plant materials while at the same time fixing nitrogen from the air, according to J. Michael Gould, a biochemist at USDA's Northern Regional Research Center, Peoria, Illinois. With their ability to fix nitrogen (thereby producing ammonia), the bacteria have the potential to "increase the protein content of normally deficient crop by-products such as wheat and rice straw", Gould says, making such material more useful as animal feeds. Gould and USDA colleague Lee B. Dexter isolated the bacteria from 17 different sources, ranging from Illinois acorns to Texas ants to Wisconsin bog soil. Of the 194 organisms discovered to date, 30 appear to be new strains or species of the genus Bacillus, while the others fit into no existing classification, Gould says. They apparently have been overlooked in the past because they can both fix nitrogen and degrade cellulose, and most assays look for organisms that can do one or the other. (Reprinted with permission from Chemical and Engineering News, 8 January 1990, pp. 36-37. Copyright (1990) American Chemical Society)

Research on viral genes

Lymphocytes which destroy hepatocytes discovered

The research groups of Michio Imawari at the University of Tokyo Medical School and Takashi Umieda at Asahi Kasei's Research Institute for Medical Technologies (Shizuoka) have discovered a class of lymphocytes that destroys hepatocytes infected with non-A, non-B hepatitis virus. The researchers presented details of their work at a recent Japanese Hepatology Society meeting. They isolated lymphocytes from 480 patients who had become infected with the virus after receiving blood transfusions. The scientists then identified a T-cell population that was able to kill infected hepatocytes from both the same patients from which the cells had been isolated as well as those from a different patient population. (Source: Bio/Technology, Vol. 7, December 1989)

Modified virus confers immunity in chickens

A modified avian leukosis virus (ALV) has been used to create transgenic chickens that are resistant to infection with ALV, according to Lyman Crittenden a researcher with the USDA's Regional Poultry Research Laboratory, East Lansing, Michigan. Crittenden and USDA co-worker Donald Salter created a strain of ALV that delivers part of the viral genome to chicken cells without inducing disease. Newly-laid eggs are injected with the modified virus, which apparently delivers viral DNA to the chicken embryo DNA. Chicken cells with viral DNA integrated into their DNA produce viral proteins that coat the cells and protect them from penetration by the virus. The offspring of such chickens should inherit the trait, Crittenden says. "Studies in cell culture suggest that this approach can be extended to other retroviruses and to herpes viruses in several species of animals", he notes. (Reprinted with permission from Chemical and Engineering News, 8 January 1990, p. 36. Copyright (1990) American Chemical Society)

Viral protein knocks the guts out of caterpillars

Some viruses infect insects by using a protein that dissolves the protective layer in the insect's gut. The protein could be used to make many insect viruses more potent, so that they could function as pesticides. It may even make a pesticide by itself.

This is the finding of Robert Granados, the director of the plant protection programme at the Boyce Thompson Institute at Cornell University in Ithaca, New York. He calls the protein "viral enhancement factor" (VEF). He says it is "the first protein with this mode of action ever found in an insect virus, and the only one of its kind found in insect-killing viruses".

Granados discovered VEF in a common baculovirus, a virus that attacks insects. The virus, known as Trichoplusia ni granulosis virus, or TnGV, infects the cabbage looper (Trichoplusia ni). This is a caterpillar that eats more than a dozen types of vegetable, including cabbage and broccoli.

TnGV has a core of DNA that is surrounded by a thick capsule of protein which protects the DNA from the environment. When an insect, such as the cabbage looper caterpillar, eats the virus while feeding on plant tissue, the protein coat dissolves in its midgut, which is alkaline. This frees the virus particles.

The cabbage looper caterpillar's midgut is lined by the peritrophic membrane, a leathery layer that permits digestive enzymes to flow into the gut, and the nutrients to flow out into the cells around the gut. It also prevents bacteria and viruses from reaching these cells. The membrane is made of substances such as chitin, the tough material of insect exoskeletons. The holes are just large enough to let food molecules pass, but too small to allow the passage of virus particles or bacteria.

Granados fed the virus to cabbage caterpillars. "The insect's stomach membranes literally fell apart", he says. "The structure of the lining was damaged, and its chemical composition was altered as well". Once the peritrophic membrane was destroyed, the virus was able to reach the cells of the midgut, infect them, and kill the caterpillar.

Granados discovered that it was the VEF alone that dissolved the membrane. The presence of the protein dramatically affected how infectious the virus was. When Granados fed the caterpillars with InGV from which the protein had been removed, only about 10 per cent of the insects died. But when he fed them the virus containing the protein, every insect died. Granados says that VEF makes the virus between "25 and 100-fold" more infectious when fed to cabbage caterpillars.

Granados foresees an important role for baculoviruses in the biological control of pests. Biologists know of more than 500 such viruses that attack agricultural and forest pests. He says that baculoviruses infect only insects, and are harmless to humans and animals. (Source: New Scientist, 23/30 December 1989)

AIDS theory questions drug R&D

A new theory which challenges the conventional view of how the AIDS virus works could have major implications for the development of drugs and vaccines. The theory strengthens the argument for the use of soluble CD4 as a decoy receptor; at the same time it casts doubts on the use of GP120 in vaccines.

The current generation of drugs, including zidovudine, attack virus replication, which can only take place once the virus has invaded cells. Scientists at the UK's Medical Research Council (MRC) now believe the HIV virus is able to destroy the immune system simply by masking the CD4 protein on the surface of healthy immune cells. CD4 plays the key role in the immune system's ability to detect and fight infection.

If the theory holds true, future drug research will need to be targeted at preventing the AIDS virus from binding to CD4, rather than attacking it once it has invaded. Angus Dalgleish, head of retrovirus research at the MRC, suggests the best therapy may lie in combining soluble CD4 with zidovudine or a protease inhibitor.

The current belief that the coat protein of the AIDS virus, coded GP120, could be used in a potential vaccine may also have to be discarded: the new theory implies that GP120 actually triggers AIDS.

The new theory may explain: why the immune system loses its potency well before significant numbers of healthy cells have been destroyed; why other viruses that can kill cells equipped with CD4 do not cause AIDS; and why only certain common infections are often the first to develop in AIDS patients, rather than new bacterial infections. (Source: European Chemical News, 5 February 1990)

New anti-HIV-1 agents most potent ever

A team of researchers in Belgium and the US has found a series of compounds that it calls "the most specific and potent inhibitors of HIV-1 replication studied so far". HIV-1, or human immunodeficiency virus type 1, is the main cause of acquired immune deficiency syndrome (AIDS).

The Belgian/American research team consists of Rudi Pauwels, Jan Desmyter, Erik De Clercq, and their colleagues at the Rega Institute for Medical Research at Katholieke Universiteit Leuven in Belgium; and Koen Andries, Paul A.J. Janssen, and others at two units of the Janssen Research Foundation in Beerse, Belgium, and Spring House, Pennsylvania.

The new antiviral agents are members of a class of compounds called tetrahydro-imidazo[4,5,1-jk] [1,4]-benzodiazepin-2(1H)-one and -thi-one (TIBO) derivatives. Remarkably, they inhibit the replication of HIV-1 but not of HIV-2 (a cause of AIDS in Western Africa) or of any other DNA or RNA viruses.

Certain TIBO derivatives have been found to inhibit HIV-1 replication in cell culture at nanomolar concentrations 20,000 to more than 30,000 times lower than those levels that impair the viability of uninfected human lymphocytes. By contrast, zidovudine (AZT), the only licensed anti-HIV drug in the US, inhibits HIV-1 replication at a level only about 6,000 times below its cytotoxic concentration. For newer, experimental anti-HIV agents such as 2',3'-dideoxycytidine (DDC) and 2',3'-dideoxyinosine (DDI), the margin of safety is even smaller.

One highly potent TIBO derivative, R82150, was well tolerated when given to dogs and six healthy, male volunteers. However, more derivatives are being synthesized as the research team searches for the one most suitable for clinical studies in HIV-1-infected patients.

The synthesis of R82150 and its cousins was complex, time-consuming, and provided only small amounts of these compounds. Scaling up the synthesis of a suitable clinical candidate may be difficult.

The scientists discovered the new anti-HIV compounds after screening 600 molecules - all prototypes of different chemical series - that showed no effect in standard pharmacological assays and that caused little or no toxicity in rodents. (Abstracted with permission from Chemical and Engineering News, 5 February 1990, pp. 5-6. R. Dagani . Copyright (1990) American Chemical Society)

SmithKline and Upjohn both find HIV "diffuser"

SmithKline Beecham and Upjohn have, within days of each other, both reported the discovery of several chemicals that "diffuse" the HIV virus in a test tube. The compounds could, in theory, act as prototypes for a new class of drugs that prevent HIV from replicating itself in uninfected cells.

Many drug companies have been looking for a chemical that blocks the action of the enzyme protease, thought to be crucial to the virus's reproduction.

The first report, from SmithKline, stated that researchers had found two chemicals that blocked HIV replication in a test tube.

Upjohn's results repored that a chemical called U-81749 had reduced the amount of viral particles in a test tube containing HIV cells by 70 per cent compared with a test tube of cells not exposed to the chemical.

The general opinion is that a drug based on such findings is a long way away, but the area is extremely competitive with Merck & Co., Abbott Laboratories and Monsanto all reported to be involved in similar work. (Source: Manufacturing Chemist, March 1990)

AIDS researchers outline progress towards cure

Recently published research into the life cycle of the human immunodeficiency virus (HIV) shows that scientists are beginning to pinpoint genetic targets for potential chemotherapeutic drugs or a vaccine for the disease AIDS.

Scientists at the University of California have refined a technique of DNA replication that enables a better understanding of the AIDS virus life cycle. The researchers have modified the polymerase chain reaction (PCR) technique, a sensitive way of detecting and amplifying genetic material, to allow more comparative studies on the tissue of AIDS patients.

Irvin Chen explains that the PCR technique enzymatically reproduces a sample of DNA so that it can be detected by physical means. Using the modified process the scientists have found considerably more HIV-1 in the brain tissue of AIDS sufferers than would otherwise be expected or indicated by its presence in the blood. Chen explains that this suggests the virus is a direct cause of the neurological dementia.

The research team has also been able to detect and analyse the structure of the virus. The genetic material of HIV-1 is found either "free" or integrated within a host cell chromosome. Chen and his colleagues have found, again in the AIDS dementia case, that most of the HIV is free and unintegrated.

Chen explains that by comparison with other retroviruses in cats and chickens, cytolytic (cell killing) effects correlate with an excess of unintegrated genetic material. Chen believes the results show free virus DNA in the brain is responsible for the particular case of AIDS dementia. (Source: European Chemical News, 22 January 1990)

Proteus models AIDS virus to find potential vaccine

Proteus Biotechnology, a UK company based in Marple, Cheshire, has designed a protein which it has shown could be a potential AIDS vaccine.

Proteus' scientists have used a computer generated model of the virus to genetically engineer a molecule which mimics the surface of the AIDS virus as it appears to the body's immune system, causing it to stimulate the production of antibodies. The development overcomes the need to introduce an inactive form of the virus to the body, as would be done in conventional vaccination methods but which would be exceedingly dangerous for the case of AIDS.

The artificial peptide vaccine is based on discontinuous determinants, i.e. the sites by which the immune system recognizes a virus. Proteus used its BioEngine computer design system incorporating its own Prometheus software to obtain the three-dimensional fingerprint of the AIDS virus. The company claims to be first in developing a potential vaccine which bears little chemical similarity to the virus formula, but instead is similar to its shape.

The company has tested the molecule in sheep under a collaborative agreement with Peptide Technology of Australia. The vaccine successfully led to the formation of antibodies. These antibodies showed a higher specificity to the AIDS virus than any other agent tested previously.

Proteus has also produced a molecular copy of the virus which it used in tests as a target for the antibodies produced earlier in response to the vaccine. This has enabled experimental results to indicate such promise towards a vaccine for HIV.

Proteus managing director, John Pool explained that the vaccine stimulated antibodies specific to a single part of the AIDS virus envelope. The stimulation should be applicable to most variants of the virus as the surface area is least susceptible to mutation.

The Peptide Technology researchers believe the unusual strength of the interaction between the antibody and the virus may indicate that a curative therapy can be envisaged. (Source: European Chemical News, 29 January 1990)

Synthetic antisense strands in viral RNA research

Some researchers are investigating ways to directly block the action of HIV RNA rather than attacking the protein products of the genes. A synthetical "antisense" strand would attach to the viral RNA, preventing it from ordering the production of viral proteins. Antisense technology is also being studied for treating cancer. It remains to be seen if antisense technology is effective and whether start-up companies entering the field will be able to survive. The materials needed to make just one gram of antisense RNA cost some $1,000. The final cost to the patient would be much higher. Oligonucleotides and ribozymes are both being investigated for antisense therapy. Ribozymes offer the greatest specificity, and will probably not produce any cytotoxic effects, since they are naturally occuring molecules. Getting the ribozymes into infected cells will be a matter for much research. (Extracted from Medical World, 25 December 1989)

Research instrumentation

Scanning tunnelling microscope

A scanning tunnelling microscope might some day allow direct determination of the nucleotide sequence of DNA, according to researchers at the University of New Mexico (Albuquerque). Images of strands of a synthetic DNA have already been produced. The pseudo-DNA was made only with deoxyadenylate. The images show the two chemical rings attached to the poly(dA) strands. Further refinements are needed before the technique could be used with real DNA. (Extracted from Science News, 25 November 1989)

Bioseparation technologies

Technology Catalysts (Falls Church, VA) has reviewed the field of bioseparation technology and will make its report available at the end of February. Liquid chromatography and membrane

filtration are the most common techniques. New technology discussed in the report includes polymeric microfiltration membranes that are more hydrophilic; thin-film composite ceramic membranes that are stronger and more chemically inert; new chromatography column support media with greater porosity and column stability; and techniques that mix separation methods. The firm says separations market growth of 15-20 per cent per year over the past decade will continue, bringing the value of the business to $2.5 billion in 1995. Technology Catalysts notes that at least 50 per cent of manufacturing costs arise from downstream processing, and that may in fact prevent introduction of some bioproducts. (Source: Chemical Week, 14 February 1990)

General

Immortal cells

Using bits of brain from human embryos to treat Parkinson's disease poses moral as well as practical problems. Scientists at two British universities are working on a way to do the job less controversially by growing brain tissue in laboratory cell cultures instead. The same technique may be used to grow enough liver or pancreatic cells to use in organ transplants. This would let one organ serve for many operations.

Dr. Julian Burke at Sussex and Dr. Caroline Macdonald at Strathclyde are working on new ways to use "immortal" cell cultures. Normally every cell in the human body has a fixed lifespan. It divides a certain number of times, then stops dividing and lives on for a set period. Both the number of cell divisions and the lifespan after the last division vary greatly between types of cells.

Occasionally, however, one or two mouse or human cells in a laboratory culture throw off their genetic controls and divide and grow indefinitely. The immortals take over the culture plate as the other cells die off. They go on growing and dividing for as long as anyone cares to keep them alive.

Unfortunately it is impossible to produce a supply of specialized cells, such as nerve cells, simply by immortalizing them. As they grow and divide, the cells revert to an undifferentiated state and lose the special characteristics which make them nerve cells, and thus useful for transplants. A better understanding of the ways in which genes control cells, and the ways in which genes themselves are controlled, might help to get round this problem.

The idea is to take a small number of differentiated cells (nerve cells, for example) that no longer divide and grow, and immortalize them so that they grow and divide once more. When enough cells have been grown in this way, the trick is to throw a genetic switch to make the cells revert to their mortal, differentiated state (thus the work suggests that "undifferentiated" cells are in fact tacitly differentiated all along). Then, if all goes well, they will be ready to be collected and used in an implant to treat, say, Parkinson's disease.

The process involves some sophisticated genetic engineering. Some years ago it was discovered that cells can be immortalized by infecting them with a monkey virus, SV40. Dr. Burke, Dr. Macdonald and others have found a single gene from the virus that will do the job when inserted into the cell in culture. The product made by the implanted gene, called a T-antigen, switches off the genes responsible for the cell's aging and death. If the new gene stops making the T-antigen the cell becomes mortal again.

Dr. Burke and Dr. Macdonald are now dissecting the T-antigen to see which bits of it are needed to make cells immortal, and how they work. They are also developing two ways to return the cells' mortality when enough of them have been produced. One way is to engineer the T-antigen gene so that it stops making the antigen when an antibiotic is added to the cell culture. Standard techniques exist for switching off the expression of genes in this way, so this looks promising. The other approach is to engineer the T-antigen gene so it is only switched on in the presence of an antibiotic. The technique might also be used to produce cultures of specialized human cells for screening drugs to be used on the corresponding cells in a body. For example, drugs being developed to treat rheumatoid arthritis could be tested on macrophages, the cells responsible for joint damage. (Source: The Economist, 6 January 1990)

Gene therapy inches closer

The prospect of curing some diseases by gene therapy is coming closer, with the publication this month of three reports of possible ways of treating cancer, immune deficiency and Duchenne muscular dystrophy. Doctors in the US have already begun their first tests of genetically manipulated cells in patients with cancer: comparable treatments for immune deficiency or Duchenne muscular dystrophy are much further off.

A team led by Steven Rosenberg of the National Cancer Institute in Bethesda, Maryland, is studying ways of harnessing the body's own defences against cancer. The researchers want to introduce therapeutic genes into body cells that selectively kill tumour cells. The genes would be ones that make natural chemicals involved in combating cancer.

Lymphocytes play an important role in fighting infection and eliminating cancer cells from the body. Studies have shown that lymphocytes isolated from a patient's tumour are often specifically programmed to kill that patient's cancer cells.

Researchers can grow these lymphocytes in the laboratory with the help of substances, such as interleukin 2, that are produced by cells of the immune system. The cells, returned to the body, circulate in the blood and end up at the tumour. This behaviour explains the name "tumour-infiltrating lymphocytes" or TILs.

Rosenberg's group believes that this property makes these cells an attractive vehicle for delivering therapeutic agents to the tumour. As a prelude to introducing genes whose products would be therapeutically useful in cancer, the researchers say they have successfully introduced a harmless gene from bacteria into TILs without affecting the behaviour of the cells.

Such genes might include those for various cytokines - substances produced by cells of the immune system - such as tumour necrosis factor, interleukins and interferons. Cytokines can help the body to kill tumour cells.

At present, the researchers have permission to test the TILs carrying the gene for neomycin resistance on 10 patients suffering from melanoma. Doctors will take blood samples and tumour biopsies at intervals up to two months after the injection of

TILs. These studies should show where the genetically manipulated TILs go to in the body, and how long they survive.

In many diseases, medical scientists will find it much more difficult to find ways of putting the additional genetic material where it is needed. Disorders of the blood cells may prove more amenable to such therapy, because immature blood cells are easily accessible and transplanted.

For this reason, researchers in the US have been studying ways of treating certain severe forms of immune deficiency. Several types of severe combined immune deficiency in humans are thought to be caused by defects in single genes. Some of these are already identified and could be suitable candidates for this type of therapy in the future.

Applying gene therapy to the treatment of Duchenne muscular dystrophy is particularly tricky. Children with this disease lack a protein called dystrophin, which results in muscle weakness. They usually die of heart failure or lung disease, so delivering dystrophin to the skeletal muscles - even if that were possible - would not help much. Another difficulty is that the gene that codes for dystrophin is too large to fit into the retroviruses that scientists use to insert genes into cells. (Source: New Scientist, 20 January 1990)

Poison oak has the power to split DNA

The chemicals in poison oak and poison ivy can irritate and inflame skin. Now researchers in California have found that they can also split DNA. The discovery is interesting because many compounds that attack DNA in living cells can also cause mutations or even cancer.

The swelling and itching caused by poison oak and poison ivy are allergic reactions. Chemicals in the plants react with proteins in the skin to form antigens. The immune system then attacks these antigens in people who are sensitive to the chemicals.

Eloy Rodriguez and Christian Wasser of the University of California at Irvine have yet to study the effect of poison oak in living cells. But their preliminary experiments with the plant in the laboratory show that the active compounds, which are known as urushiols, can split DNA.

Rodriguez speculates that contact allergies may happen when the body is trying to get rid of a chemical that might be even more damaging than the allergy if it allowed it through. The body, therefore, accepts an allergic reaction in order to prevent a future cancer.

Next Rodriguez hopes to investigate in more detail the molecular mechanisms of the allergic reaction and the DNA splitting. He plans to test the compounds on animals and cultured human skin, to assess if they can damage DNA in living cells. For this work, he has secured a grant from the National Institute of Allergy and Infectious Diseases. (Source: New Scientist, 17 February 1990)

Malaria stalemate

Cures and vaccines for malaria have been elusive, and the optimism of public health officials in the mid-1980s, when much was being discovered about the structure and behavior of the malaria parasites, has all but vanished. Today 100 million people, mostly but not exclusively in the tropics, have malaria, and the parasites are becoming resistant to quinine-based drugs that for years helped to keep the disease in check. In three articles, Eliot Marshall and Jeremy Cherfas describe the combined approach that has been taken towards controlling malaria - one that has included development of vaccines, genetically engineered mosquitoes, and pharmaceuticals and use of insecticides and physical traps for catching mosquitoes - and explain how this approach has none the less failed to significantly improve the global malaria situation. As future efforts are planned, one of the continuing dilemmas will be to determine how best to spend the limited available funds (less than the total US AIDS budget), whether for quick fixes like training health care workers to deal with symptoms or for research that might yield longer-term solutions. (Source: This Week in Science, 26 January 1990)

D. APPLICATIONS

Medical and pharmaceutical applications

New HPV identification test

The Finnish company Orion Pharmaceutica is launching a rapid and accurate test kit for the identification of human papilloma viruses (Human Papilloma Virus - HPV). The company has patented the technology, sandwich hybridization. Identification with AffiProbe, as the test is called, is simple to carry out and requires no specialized skills.

Papilloma virus infections are among the most common sexually transmitted diseases, expressing themselves in various forms. Infections caused by the HPV types 6 and 11 can be detected in genital warts and are at the moment considered as low risk types, being relatively easy to identify. But infections types 16 and 18 are mostly subclinical, and therefore more difficult to detect using the conventional routine methods. The AffiProbe test, on the other hand, is both reliable and sensitive to different HPV virus types. Details from: Orion Pharmaceutica, Biotechnology Group, Valimotie 7, SF-00380 Helsinki, Finland or on +35 8 0 434 6061. Fax: +35 8 0 565 3164. (Source: Biotechnology Bulletin, Vol. 9, No. 1, February 1990)

Test detects gum disease bacteria

A simple, 15-minute test has been developed by dentistry and microbiology professor Walter J. Loesche and colleagues at the University of Michigan's School of Dentistry to indicate whether dentists have eradicated anaerobic bacteria responsible for most cases of advanced gum disease. At present, the only assurance is follow-up examinations every three months. The dentist applies tooth scrapings to a strip of paper impregnated with N-α-benzoyl-DL-arginine-β-naphthylamide and wets it. The anaerobes make unique peptidases that hydrolyze this compound, liberating β-naphthylamine. The amine diffuses to an underlying paper strip impregnated with a diazonium salt, Fast Black K. A coupling reaction produces a blue to black spot. The university has licensed its pending patent for the test to Oral-B, a division of Gillette Co., which expects to market it later this year following FDA approval. (Reprinted with permission from Chemical and Engineering News, 12 February 1990, p. 23. Copyright (1990) American Chemical Society)

Toxins used to develop drugs

Nerve toxins from South American poisonous tree frogs are being used in research to help develop new drugs to treat pain and spasms. The brilliantly

coloured frogs produce extremely potent toxins. The toxin from a single one-inch long Phyllobates terribilis can kill 50 humans. It is used by South American hunters on poison darts. C.W. Myers of the American Museum of Natural History and J. Daly of the National Institute of Health are attempting to find and study as many of the frogs as possible before they become extinct due to habitat destruction. Over 200 toxins from 50 frog species are now known. The alkaloid toxins are secreted when the frog feels threatened. One family of frogs produces a compound with analgesic properties, but which works differently to morphine. E. Albuquerque of the University of Maryland says the compounds are useful in studying nerve impulses, since they open or close cellular ion channels or affect cell receptors. In addition to nerve impulses, the compounds might affect muscles (including the heart). Naturalists are also studying the natural history of the tree frogs, which might allow the animals to be raised in captivity. (Extracted from New York Times, 23 January 1990)

Human blood substitute

A substitute for human blood that could be available in almost unlimited quantities will be tested on human volunteers in a Boston hospital early this year. An American company called Biopure has produced ultra-purified haemoglobin taken from cows' blood, which has already passed tests in several species of animals, from rats to primates.

A viable substitute for whole blood would have many advantages over donated blood. In addition to its longer shelf life, blood substitutes would not have the potential to transmit blood-borne diseases such as AIDS and hepatitis B and haemoglobin could be given to any person, regardless of their blood type. If these initial human clinical trials are a success, the haemoglobin could have a major impact everywhere from American hospitals, with their overstrained blood banks, to the third world, where blood cannot be stored easily.

Biopure's technique extracts haemoglobin from cows' blood, which is a waste product at slaughterhouses. The two most important steps in its proprietary process are purifying the haemoglobin so that contaminants do not cause toxic or immune reactions when transfused into a human patient, and treating the molecules so that the haemoglobin is stable for long periods inside the body.

In a test carried out last year, bovine haemoglobin kept sheep alive for over a month. The researchers first removed the sheep's spleens, which are reservoirs of red cells, and then drained 95 per cent of their blood. After transfusions with the Biopure haemoglobin, the sheep lived for more than a month, far longer than the substitute haemoglobin itself would have survived. The animals were able to survive long enough to produce new blood of their own.

The company faces several years of additional clinical testing before the haemoglobin can be used routinely in humans. The bovine haemoglobin is now produced as a frozen liquid, with a shelf life of six months. Biopure is also working on a different preparation which would only require refrigeration, and hopes eventually to have a freeze-dried haemoglobin that would have an indefinite shelf life at room temperature. (Extracted from New Scientist, 20 January 1990)

Whooping cough vaccine

A genetically engineered vaccine to protect children against whooping cough may be available within a few years. Researchers at Amgen, the American biotechnology company that developed the potential vaccine, hope that it may cause far fewer side-effects than the vaccine that is in current use. Fears about the safety of the existing vaccine have caused many parents to avoid having their children vaccinated.

Scientists are interested in developing a new vaccine against whooping cough because in the developed world the public perceives the existing vaccine as unsafe. This vaccine is made from whole cells of Bordetella pertussis, the organism that causes whooping cough. It contains components that may, in rare cases, cause severe side-effects such as brain damage.

Worldwide, there are 20 million cases annually, with more than 1.5 million deaths - which means that one in every 50 children born succumbs to whooping cough, even though a vaccine can prevent the disease.

The aim was, therefore, to develop a vaccine that was at least as effective as the existing one in protecting against infection but without the associated side-effects. The problem is that the component of the vaccine that induces a protective immune response, the pertussis toxin, is the same one that causes side-effects.

Researchers led by Jerry Keith of the Rocky Mountain Laboratories of the US National Institutes of Health had already cloned and sequenced the gene that carries the code for the pertussis toxin. Amgen took the analysis a step further by cloning the DNA for the five individual subunits of the toxin into bacteria called Escherichia coli.

The Amgen team then looked to see if any of the subunits could, by themselves, induce protective immunity to B. pertussis. None of them did, the researchers found. So they decided to reassociate the toxin from its component parts manufactured in E. coli. They also studied the "holotoxin", as they called the reassembled molecule, to find out which part stimulated immunity and which part had the damaging activity.

Disconcertingly, the two regions turned out to be very close together, making it very difficult to eliminate the side-effects while retaining the stimulus to the immune system. Earlier work had shown precisely where the region responsible for toxicity lay, so the Amgen team introduced mutations in that area that resulted in substitutions of single amino acids in the holotoxin.

The next move was to try to assess whether the mutants had lost the ability to cause the toxic side-effects. The researchers did this by adding the altered toxins to a certain variety of cells cultured in the laboratory. Unadulterated pertussis toxin causes these cells to clump. So did most of the mutants - except for one. This had undergone a change in a single amino acid, and was much less effective in causing the cells to cluster.

Other tests have reassured the researchers that this mutant "holotoxoid" (a toxoid is a chemically inactivated toxin) is nevertheless reassembled in such a way that it is very similar to the naturally occurring toxin. It should, therefore, be able to stimulate the immune system like the native

molecule. Chemical trials of the potential vaccine could take several years. (Source: New Scientist, 23/30 December 1989)

Novel method to remove auto-antibodies from blood

Researchers at Asahi Medical (Shizuoka) have developed a novel resin for removing auto-antibodies from the blood of patients with the neuromuscular disease myasthenia gravis. Asahi Medical has received permission from the Japanese Ministry of Public Health for clinical use of this resin, and will begin marketing a disposable separation column containing the resin soon.

Reportedly, the resin removes only anti-acetylcholine receptor antibodies, which are suspected of causing the muscular weakness and degeneration characteristic of the disease. Since a patient's own blood can now be treated and returned to his body, blood transfusions and the accompanying risks of infection can be avoided. (Source: Biotechnology, Vol. 7, December 1989)

Protein drug delivery system nears approval

Polyethylene-glycol-modified adenosine deaminase (PEG-ADA) may be on the verge of gaining US Food and Drug Administration approval. If, as the manufacturer expects, that approval comes in the next month or two, it will mark not only a new therapy for children with ADA-deficient severe combined immuno-deficiency, it will also herald what may well be the start of a more broadly applicable new drug delivery technology.

PEG-ADA would be the first product to be marketed by Enzon Inc., a South Plainfield, N.J., company set up in 1981 to develop PEG technology. It is being developed as an orphan drug for the disease associated with an inherited deficiency of ADA, in which the immune system fails to develop. The disease is usually fatal unless a child is kept in protective isolation.

The current activity involving PEG-modified drugs shows that protein-based drugs have great potential as therapeutic agents for diseases such as cancer and for genetic disorders, with the proteins being derived from genetic engineering, fermentation, or animal sources. Protein-based drugs have the benefits of site specificity and low incidence of side-effects. But there also are obstacles to use: poor uptake into the bloodstream, short blood-circulating life, and potential for eliciting an immune (allergic) reaction.

More than 24 different types of drug delivery systems are now under development for proteins. These include liposomes, bioerodible polymers, encapsulation, osmotic pumps, and others. The technology being developed at Enzon employs covalent attachment of the inert polymer PEG to the proteins. PEG appears to block access to sites on the surfaces of the proteins, thus inhibiting clearance from the circulation and attack by the immune system.

More than 40 proteins have been modified with PEG. Enzon has three in clinical trials: PEG-ADA (being developed by Enzon as an orphan drug); PEG-L-asparaginase for treatment of acute lymphoblastic leukaemia; and PEG-uricase for treatment of hyperuricaemia associated with chemotherapy. Two other PEG products - PEG-superoxide dismutase (PEG-SOD) for use in destroying excess oxygen that may damage injured tissue, and PEG-catalase, another antioxidant - have been licensed to Sterling Drug for clinical development.

PEG-L-asparaginase provides an example of the difference PEG modification can make. It has been used in treating acute lymphoblastic leukaemia since the early 1970s. But it has the serious side-effects of short lifetimes and of eliciting immune reactions. Modification with PEG increases circulating half-life from 30 hours to two weeks and significantly decreases immune reaction. Another application of PEG technology is development of a blood substitute, PEG-haemoglobin. It is still in the research stage. (Abstracted with permission from Chemical and Engineering News, 15 January 1990, pp. 38+40, J. Krieger. Copyright (1990) American Chemical Society)

Natriuretic factor tested

A strategy for deploying the heart's own blood-pressure regulator against hypertension starts clinical trials in France this quarter. The cardiac hormone, atrial natriuretic factor (ANF), relaxes constricted blood vessels, but is rapidly degraded by enzymes, in a feedback process that keeps the healthy body's blood-pressure steady. ANF also causes the body to excrete water and sodium.

Recombinant ANF, a 28-amino-acid peptide dubbed Auriculin by California Biotechnology Inc., which developed it five years ago, works like nature's own hormone, but must be injected intravenously. In acute kidney failure and congestive heart failure, Auriculin infusion can save lives. But ANF cannot be ingested or inhaled. Only oral or intranasal medication is practical for millions of otherwise healthy people who swallow diuretic pills daily to control their "essential" hypertension - i.e., of unknown cause.

To get around this obstacle, the Neurobiology and Pharmacology Unit of France's National Institute of Health and Medical Research (INSERM) aims to block enkephalinase, the enzyme thought mainly responsible for degrading ANF as fast as the heart's atrium secretes it. In mice and in Phase I clinical trials, Jean-Charles Schwartz and his team found that a potent enzyme-inhibitor, sinorphan, cuts down enkephalinase, and so prolongs the half-life of ANF. Its build-up in the bloodstream tripled; in the kidneys, quintupled, with enhanced reduction of blood-pressure and excretion of urine and sodium. Now they are about to try sinorphan as a long-term, antihypertensive in a large-scale, double-blind, randomized clinical trial.

Jointly with Bayer AG, Leverkusen, Federal Republic of Germany, CalBio is developing orally active analogs of Auriculin based on downsizing the molecule so it can pass through the gastrointestinal wall into the circulation. Such a mini-peptide could also be inhaled, via CalBio's patented Nazdel system for delivering drugs through the nasal membranes. (Source: McGraw-Hill's Biotechnology Newswatch, 19 February 1990)

Subdermal insulin?

Researchers at the Ben-Gurion University in Israel have developed a subdermal delivery system for insulin, controlled by ultrasound, which responds to insulin levels in the blood.

The device consists of an acid-sensitive polymeric matrix, insulin and an enzyme that converts glucose into glucuronic acid. Insulin

release is triggered when blood sugar levels rise, producing more glucuronic acid and causing the matrix to swell.

The system can be controlled by ultrasound, and, after meals, when greater amounts of insulin are needed, the system can be boosted by external ultrasound.

In practice, a probe near the implant will be needed to turn the ultrasound unit on and that would affect the release rate. The system has not yet been tested on humans, but animal trials have been successful. (Source: Manufacturing Chemist, January 1990)

New drugs for diseases of aging

US pharmaceutical firms are in the process of developing over 200 new medicines to treat heart diseases, osteoporosis, Alzheimer's disease and other illnesses that plague older people, according to recent surveys.

The Pharmaceutical Manufacturers Association, in co-operation with other organizations, conducted a series of surveys to identify medicines for the elderly now in human tests or waiting approval by the US Food and Drug Administration (FDA). The surveys identified 221 medicines in clinical trials by 77 companies to treat 23 diseases.

It is estimated that $3,600 million, about half the pharmaceutical industry's R&D budget in 1989, has been invested in research on diseases that primarily afflict older people. Biotechnology became important for drug development. Already 29 per cent of the anti-cancer drugs are based on biotechnology. (Source: BIOTECHNICA Journal, No. 1, 1990)

Progress in rhinovirus research

Scientists have created a protein that blocks infection by viruses that cause colds, a possible step towards drugs for preventing or treating half the forms of colds, a study says.

The research, based on a strategy that shows promise against the AIDS virus, is focused on rhinoviruses, which cause about half of common colds. As a first step toward infecting cells, many rhinoviruses attach themselves to a structure on the cell surface called the intercellular adhesion molecule-1, or ICAM-1.

Scientists created a special form of ICAM-1. They hoped it would act as a decoy, so that free-floating viruses would bind to it rather than their normal target on cell surfaces. By this process, researchers found the ICAM-1 was largely able to block rhinovirus infection of human cells. (Source: International Herald Tribune, 1 March 1990)

AIDS treatment found substantial improvement

A team of Belgian physicians announced that their preliminary study conducted on 28 AIDS patients over the course of one year was very effective in boosting the immune system and reducing many complications related to the disease, officials from the San Fernando Valley-based World Research Foundation (WRF) Information Network reported.

At a cost of 25 to 50 cents a day - significantly less than that of AZT which runs approximately $17.50 a day - the treatment utilizes several modalities used in many other pathologies of the human immune system, and in preliminary tests caused no side-effects to any of its patients.

The treatment, classified as an immunotherapy using highly diluted proportions of DNA, RNA, cyclosporin and an anti-heavy gamma chain antibody was conducted on 14 black men and 14 black women up to the age of 65. By the Centers for Disease Control (CDC) standards, 26 of those infected with HIV were in group IV and two were in group III.

In conducting the study, 11 patients in group IV were used as the control group, with the remaining 17 used in the treatment group. The study was not double-blind or randomized; however the researchers will undertake a double-blind study to further test the efficacy of the treatment. Currently, the doctors are undertaking additional studies throughout Europe that involve 70 other patients - with one in treatment and active since 1984.

The report was conducted in Zaire and evaluated by statisticians at the University of Louvaine, Belgium.

Although the doctors do not say they have a cure for AIDS - since there is no efficient biological test to affirm, by any manner or treatment, a cure for the disease - they felt it important to relate the results of their research because of the urgency of the AIDS epidemic, according to World Research Foundation.

An international non-profit organization, the World Research Foundation is dedicated to collecting the totality of health information from around the world and sharing it with the public. WRF's international headquarters are located in Sherman Oaks. (Source: Chemical Marketing Reporter, 1 January 1990)

Further research into CD4

Researchers are seeking ways to make soluble CD4 more long-lasting in the bloodstream so that it might be a useful AIDS treatment. The compound is apparently safe and effective in blocking viral entry into immune system cells, but it disappears from the bloodstream within an hour, according to D.L. Capon of Genentech. CD4 linked to immunoglobulin G antibody is now being tested for IV infusion or IV bolus injection. Combining CD4 with zidovudine may also enhance its effectiveness. Combining CD4 with immunotoxins such as ricin, Pseudomonas exotoxin and diphtheria toxin may make it possible to kill the virus released from infected cells. (Extracted from Medical World 25 December 1989)

Mouse model for AIDS drugs

Scientists at a Californian biotechnology company, SyStemix, have developed a mouse which could prove important as a model for testing potential AIDS drugs. SyStemix's researchers have demonstrated that the SCID-hu mouse, a naturally immunodeficient animal endowed with human immune system characteristics, provides a method of testing potential anti-viral drugs and comparing them with existing AIDS therapies.

The SCID-hu is derived from a mouse strain which suffers a genetic defect - Severe Combined Immuno Deficiency (SCID) - but which was surgically implanted with three types of human tissue. SCID strain mice produce no functional immune cells. They are devoid of both T cells (which regulate the immune response) and B cells (which produce antibodies). Such mice readily accept tissue grafts because they do not differentiate between "self" and "non-self". By implanting human blood cell precursors, thymus (necessary for the maturation of

T cells) and lymph nodes (required for B cells), SyStemix scientists endowed the mice with a model of the human immune system.

Systemix's scientists tested the ability of the mice to respond to the human immunodeficiency virus (HIV). The SCID-hu mice were found to be infected with the HIV following inoculation, which would not be expected for a human-specific virus such as HIV. Only the implanted tissue in the mice was HIV positive, which illustrates the key feature of the animal's use as a model.

The researchers also demonstrated the effectiveness of Wellcome's zidovudine in suppressing the HIV infection. SyStemix predicts the SCID-hu mouse will be the most useful in performing comparative studies of AIDS therapies and for testing new drugs. (Source: European Chemical News. 19 February 1990)

Possible AIDS drug developed

The UK's Glaxo is pinning hopes for an AIDS drug on a nucleoside compound licensed from IAF BioChem International of Montreal. The compound, BCH-189, may be less toxic and more effective against HIV than Wellcome's zidovudine.

Under a five-year master licensing agreement, the Glaxo group will have exclusive rights to BCH-189 outside the US and Canada. The UK company will be responsible for obtaining regulatory approval worldwide, including the funding of clinical trials.

BCH-189 is believed to attack replication of the HIV virus in a similar way to zidovudine, the only approved AIDS drug. However, BioChem says it appears to have less of the dose-limiting toxicity. It also shows promise against HIV strains resistant to zidovudine. The compound is currently in preclinical trials at the US National Cancer Institute. (Source: European Chemical News, 19 February 1990)

AIDS-related fungal infections drug

Pfizer's (New York) drug Diflucan fluconazole has won Food and Drug Administration approval for two AIDS-related fungal infections - a life-threatening form of meningitis, and candidiasis, which leads to mouth and throat sores and afflicts 80-90 per cent of patients with advanced stages of AIDS. The new drug is also appropriate for cancer patients and others with weakened immune systems. FDA notes that alternative treatments to fluconazole already exist, but "their use is limited by side-effects or other factors". One example is amphotericin B, which can impair kidney function. However, fluconazole can lead to liver damage, and, in rare cases, to liver failure and death. (Source: Chemical Week, 7 February 1990)

New AIDS treatment

The University of Pittsburgh and the Pittsburgh Cancer Institute are testing the efficacy of drawing samples of AIDS patients' white blood cells, stimulating those cells to better fight the virus, and then injecting them back into the patients. The cells are activated with interleukin-2 (IL-2). Clinical trials are in progress to study changes in the immune system after each of six doses of the killer T-cells, known as CD8 cells. The researchers will also track the route of the treated CD8 cells and determine the impact of administering additional IL-2 with the cells. (Source: Chemical Week, 7 February 1990)

New AIDS diagnostic

British Bio-technology Limited (BBL) the UK based health sciences company, has launched a rapid test kit for detecting AIDS infections.

The assay, called "SpeedScreen HIV", can distinguish HIV-2 from HIV-1 infection, which is important because HIV-2 is believed to be a less virulent form of the AIDS virus. The assay also detects antibodies to novel components of the common HIV-1 virus which may help predict the course of infection and improve patient care.

The kit permits simple, rapid testing of body fluids for antibodies to several different components of HIV-1, including p24 and nef, and for antibodies to the gp36 protein of HIV-2, all in one assay. "SpeedScreen HIV" uses genetically engineered viral antigens in particulate form such that the antigens are displayed in a concentrated form which is particularly reactive with antibodies. The versatility of this technology is being further exploited to develop other rapid specific diagnostic assays.

"SpeedScreen HIV" is based on a technology proprietary to BBL which evolved from basic research at Oxford University, the rights to which have been assigned to British Bio-technology Limited. (Extracted from Chemical Marketing Reporter, 15 January 1990)

New AIDS drug starts clinical trials

Scientists in Britain and France hope to begin parallel clinical trials within a few weeks to evaluate the efficacy and toxicity of dideoxyinosine (DDI), a potential new treatment for AIDS. At present, only one drug, zidovudine (AZT), is licensed for the treatment of AIDS.

Zidovudine has proved capable of doubling the survival time of people with AIDS. However, the severity of the side-effects force as many as 40 per cent of recipients to abandon treatment within a year. These side-effects include anaemia and nausea.

Britain's Medical Research Council and its counterpart in France, INSERM, consulted suport groups for people with AIDS to work out a unique and compassionate protocol for the trials. Most of the subjects will be people who have lost tolerance to zidovudine. The protocol will allow subjects who wish to take the drug to do so, though neither they nor their doctors will know whether they are receiving a high or low dose, so there is no bias in the evaluation.

A separate group of subjects may receive a high or low dose, or a placebo. Again, neither the recipients nor the doctors will know who receives what. The trial has been approved in about half the time it usually takes. Normally, a decade elapses between the discovery of a drug and the approval of clinical trials. In this case, it has taken only five years.

Sam Broder, of the National Cancer Institute in Bethesda, Maryland, discovered DDI in 1985 when he was investigating its potential as an anti-cancer agent. It appears to work by slowing the rate at

which the virus replicates itself in human cells and spreads through the immune system. (Source: New Scientist, 10 March 1990)

AIDS drug trial resumes

The controversial study of the AIDS drug Compound Q, which was halted in August 1989 by the US Food and Drug Administration (FDA), is to be resumed with full FDA approval. It is the first time the FDA has granted an independent IND (Investigational New Drug) licence to a community-based research group.

The new study is designed to evaluate the safety and effectiveness of GLQ223 over the longer term. GLQ223 will be administered to over 100 patients in San Francisco, Los Angeles, Miami and Florida, all of whom will have previously been treated with the Chinese version of the drug. Patients will be assigned randomly to two groups, one receiving treatment every three weeks, the other every six weeks, while being allowed to continue with other AIDS therapies.

Genelabs, who holds the patent rights for GLQ223 as a possible treatment for HIV infection, ARC and AIDS, is evaluating the drug in its own FDA-approved clinical trials. Preliminary findings of phase I trials are expected to be submitted for FDA review in mid-1990. (Extracted from Nature, Vol. 344, 15 March 1990)

Adverse tumours found with AZT rodent trials

High doses of Wellcome's AZT AIDS drug has been found to cause tumours in rodents, a discovery that may limit the company's plans for wider distribution of the drug.

The US Federal Drug Agency was expected to rush through approval of AZT for treating HIV-positive individuals, after results last August showed that it slowed the onset of AIDS, but the company has stated that it does not expect use of the drug to fall significantly as a result of the tests.

The trials involved giving rodents up to ten times the recommended human dose over a period of three years.

Doctors at the John Hopkins medical school in Baltimore have reported the apparent eradication of the AIDS virus from a patient who had received AZT and a bone marrow transplant.

The patient, who died of lymphoma cancer 39 days after the transplant, was found to have no trace of the AIDS virus in his body in a post mortem. Researchers at Baltimore are conducting tests to see if the treatment can be repeated on other AIDS sufferers. (Source: Manufacturing Chemist, January 1990)

A better drug than Retrovir?

Mitsubishi Kasei, together with Japanese, Belgian and UK universities, have jointly developed a compound that Mitsubishi says may stop the spread of AIDS.

Apparently, the compound - 1-(2-hydroxyethoxy) methyl(-6-thenylthiothymine) - is as effective as Wellcome's Retrovir (zidovudine) and has fewer side-effects.

Mitsubishi says it plans to start clinical trials in the third quarter of 1990, with sales starting in 1992.

The University of Birmingham was involved in helping develop the compound. (Source: Manufacturing Chemist, March 1990)

Kabi expands in the Federal Republic of Germany

Pfrimmer Kabi has taken over a wide range of products for the administration of enteral nutrition solutions from Pfrimmer-Viggo. Both companies are located in Erlangen, FRG. The acquisition will put Pfrimmer Kabi in a better position to increase its share of the enteral nutrition market, which is estimated to be worth DM 240 million in Western Europe.

Pfrimmer Kabi, a partly owned subsidiary of the Swedish pharmaceutical company, Kabi, markets infusion fluids, nutrient solutions, blood derivatives, and growth hormones. With the acquired products, Kabi Pfrimmer will round out its coverage of the nutrition product sector.

Enteral nutrition often involves the use of a feeding tube. This method of feeding is used primarily in patients with tumours and inflammations of the bowel or when an adequate uptake of food cannot be secured otherwise, due to severe illness.

Hitherto, Pfrimmer Kabi has marketed the enteral solutions while the necessary accessories, such as pumps and feeding tubes, were sold by Pfrimmer-Viggo. Physicians and pharmacists will now be able to obtain all the articles needed to give patients enteral nutrition solutions from the same supplier.

The shortage of nursing staff and the increased costs of health care are likely to result in greater use of enteral nutrition. In most cases, it can be administered by the patients themselves and they need not be confined to bed. The customers do not only include hospitals, but nursing homes, homes for the aged, and pharmacies as well.

For further information, contact Hans Melbinger, president of Pfrimmer Kabi, telepone number 00949-91318010, Lars Lindegren, head of Kabi-Nutrition, telephone number +468138000, or Carl-Johan Wachtmeister, chief information officer, telephone number +468138000. (Source: Company Press Release, 22 March 1990)

Livestock applications

Manufacturers in Africa manufacture rinderpest vaccine

Rinderpest, a virulent disease of ruminants, may soon be wiped out of Africa as laboratories on the continent increasingly turn out the necessary vaccine.

Under a Pan African Rinderpest Campaign (PARC), laboratories in a dozen countries have produced 50 million doses of the vaccine, the Inter-African Bureau for Animal Diseases (IBAR) disclosed.

According to IBAR, a specialized agency of the Organization of African Unity (OAU), the laboratories are located in Botswana, Cameroon, Chad, Egypt, Ethiopia, Kenya, Mali, Niger, Nigeria, Senegal, Somalia and Sudan.

A shot of the vaccine provides lifetime immunity to an animal. Production of a dose costs $0.03.

"This reflects increasing self-reliance among African nations which in the last rinderpest

epidemic of 1980-1983 often relied on imported vaccine", IBAR said.

Quality of the vaccines is ensured by testing to international standards at the OAU/PARC/FAO quality control laboratories in Debre Zeit, Ethiopia and Dakar, Senegal.

Debre Zeit alone produced 20 million rinderpest vaccine doses last year and the laboratory shipped supplies to Burkina Faso, Cameroon, Central African Republic, Chad, Oman, Tanzania and Uganda.

Jointly co-ordinated by the OAU and IBAR, PARC covers 34 countries, mainly in the sub-Sahelian zone.

The European Community has extended $68 million towards financing of the campaign.

About a century ago, rinderpest nearly exterminated Africa's livestock herds when it killed between 80 and 90 per cent of the cattle population and cloven-hoofed wildlife.

Meanwhile, Ethiopia is carrying out its largest ever anti-rinderpest drive, aiming to immunize some 23 million cattle, or 80 per cent of the national herd, this year.

"Freedom from rinderpest is our objective", said Dr. Mulugeta Habte Selassie, national co-ordinator of the undertaking launched March 1989.

Ethiopia earns about $8 million from exports on livestock products.

Although no fresh outbreak was reported from Ethiopia since 1988, neighbouring Kenya, Sudan and Uganda reported incidences of the disease early last year. (Source: IPS, 2 January 1990)

Animal health products

Cambridge BioScience Corp has announced that a vaccine for feline leukaemia it has developed with Virbac SA of France will be marketed exclusively in the US and Canada by International Minerals and Chemical Corp. The vaccine has not yet been cleared by the US Agriculture Department for marketing in the United States, although the company expects it to be introduced this year.

Feline leukaemia is an infectious, incurable disease that causes cancer, respiratory ailments and other fatal illnesses in cats. Among other animal diseases that may be diagnosed, treated or prevented with biotechnology in the USA are the following:

Cats and dogs: Canine parvovirus (diagnostic kit); Canine rotavirus (diagnostic kit); Distemper (diagnostic kit); Feline infectious peritonitis (diagnostic kit); Feline leukaemia (vaccine, diagnostic kit); Heartworm (diagnostic kit); and Rabies (vaccine).

Cattle: Bluetongue (diagnostic kit); Bovine lymphosarcoma (diagnostic kit); Bovine papillomavirus (vaccine); Bovine rhinotracheitis (vaccine); Bovine scours (monoclonal antibodies, diagnostic kit); Bovine viral diarrhoea (vaccine); Brucellosis (diagnostic kit); Leptospirosis (diagnostic kit); Mastitis (diagnostic kit); Shipping fever (interferon, interleukin-2); and Tropical tick disease (vaccine).

Horses: Equine infectious anaemia (diagnostic kit); Equine influenza (interferon); and Potomac fever (diagnostic kit).

Pigs: Paratuberculosis (diagnostic kit); Pseudorabies (vaccine); Swine scours (vaccine, diagnostic kit); and Trichinosis (diagnostic kit).

Poultry: Avian retrovirus (diagnostic kit); Coccidiosis (vaccine); and Fowl cholera (vaccine).

Other: Foot-and-mouth disease (diagnostic kit); Rift Valley fever (diagnostic kit); Rabies in wildlife (vaccine); and tapeworm in sheep (vaccine). (Source: Biotechnology Bulletin, Vol. 8, No. 12, January 1990)

AIDS vaccine for monkeys possible

Research with rhesus macaques indicates it is possible to safeguard them from AIDS with vaccines. A vaccine used at the Delta Primate Research Center in Los Angeles provided perfect protection for eight of nine of the animals. Tests on cells removed from their lymph glands revealed one of the macaques was infected with an AIDS virus. The stage of infection was benign, as no virus was found in the blood. While the vaccine did not prevent infection, it is possible the vaccine assisted the animal's immune system in dealing with the virus. (Extracted from The Economist, 4 January 1990)

Agricultural applications

Spliced plants open up the field for hybrid crops

A company in Belgium has used genetic engineering to produce hybrids of crops that cannot be cross-fertilized effectively by traditional methods. By exploiting a fragment of DNA from the tobacco plant to target specific genes in other plants, the company has made strains of many more crops that are suitable for efficient cross-fertilization. Seed companies who want crops with higher yields often cross-fertilize separate strains of a particular species to produce hybrid offspring which are bigger and healthier.

Plants whose flowers have both stamens and pistils can easily fertilize themselves with their own pollen. The seeds produced are then a mixture of those fertilized by each plant's own pollen and those fertilized by other plants.

Hybrid crops can be extremely profitable for seed companies. But to create large numbers of hybrid seeds efficiently, plants must be fertilized exclusively with pollen from another, unrelated strain.

In corn, this is made possible by the natural occurrence of so-called "male-sterile" varieties, which do not produce fertile pollen. The male-sterile characteristic is bred into one strain, which is then pollinated by another strain, to yield 100 per cent hybrid seed. But hybrids cannot be produced economically in many crop plants, because there are no usable male-sterile varieties. Male-sterile strains may also have unwanted traits that cannot be removed by breeding.

Plant Genetic Systems, based in Ghent, has isolated a fragment of DNA from the tobacco plant which can be used to create male-sterile strains of plants. The company's researchers isolated the messenger RNA transcribed from the DNA in the cells of the plants' anthers, their pollen-producing organs. By comparing the RNA from the anther with that from other cells, the scientists found genes that were active only in anther cells.

They then cut these genes with specific enzymes and isolated a fragment called the promoter, which controls whether or not the gene is turned on. This particular promoter ensures that the gene carrying it is expressed only in anthers. By attaching the promoter to other genes, the scientists could create genes that would be active only in anther cells.

To produce male-sterile plants, the team then spliced the promoter with a bacterial gene for an enzyme called ribonuclease. This enzyme blocks the function of the tapetum cells, a layer of cells in the anther. In order to incorporate these new genes into other plant cells, the researchers inserted the new genes into the DNA of the bacterium Agrobacterium tumefaciens which is routinely used to insert new genes into plant cells.

The bacterial gene was inserted into the anthers of rape plants. As a result, the plants produced no fertile pollen, they became male-sterile and could be used to create hybrids.

The same anther-specific promoter appears to occur in a wide variety of plants. The company is now introducing the promoter, along with genes to induce sterility, into cotton, lettuce and alfalfa, each representing a separate family of crops.

John Beringer, head of the microbiology unit at the University of Bristol and an expert on the deliberate release of genetically altered material, said that there are few risks in this sort of genetic manipulation. The changes to genetic material are so specific to the particular genes in anther cells that they are unlikely to have adverse effects on other genes. (Source: New Scientist, 3 February 1990)

Insect repellant in mint condition

Researchers at the Archbold Biological Station (Lake Placid, FL) have discovered a new substance secreted by a nearly extinct mint plant, that wards off insects. The discovery expands the scope of biopesticides, which have become a research-intensive but attractive market now that chemical pesticides are coming under heavy public and regulatory pressure. Most biopesticide work to date has involved the adaptation of naturally occurring insect parasites and antigens. According to Cornell University researchers making the discovery, the substance, trans-pulegol, is contained in microcapsules in the mint leaf. The substance was found to irritate most test insects, causing them to cease feeding and flee. The encapsulation preserves the potency of the substance and prevents unnecessary release, the researchers suggest. Trans-pulegol, which has now been synthesized, was found as part of a "chemical prospecting" programme at Archbold to isolate and analyse beneficial substances occurring naturally in endangered ecosystems, before those plants and animals become extinct. (Source: Chemical Week, 17 January 1990)

Food and food processing applications

Fingering salmonella

In rich and healthy countries members of the salmonella family of micro-organisms cause a few upset stomachs, periodically scare people off eggs, but not - usually - much more than that. In poor countries some 3.5 million children die each year of diarrhoea that is linked to salmonella. Most tests for salmonella-infected foods take time to complete, and may miss new and dangerous strains. A better test would be one that could reliably spot the genetic fingerprint of salmonella - a DNA probe.

Dr. Joseph Gopo of the University of Zimbabwe has developed one. He and his colleague, Dr. Lilian Marovatsanga, say that it is faster and more sensitive than existing ones. In Harare's shops and restaurants, 57 per cent of sandwiches and pies proved positive in tests. Conventional tests spotted salmonella in just 2 per cent of them. The probe also found that two thirds of chickens that died on farms were contaminated with salmonella.

Dr. Gopo developed his DNA probe while he was at the Institut Jacques Monod in Paris. First he dissected the genes of a salmonella bacterium. Out of its 400-500 pieces he found one that was specific to all of the hundreds of types of salmonella and to nothing else. This length of DNA is the key to Dr. Gopo's probe, since copies of it bind only to salmonella genes.

The idea of the test is simple. Food is dissolved together with the probe. If there is any salmonella in the solution, the probe will bind to it. Everything else is washed away, leaving behind a tagged sample. The problem is that the sample is too small to see. Back home in Harare, Dr. Gopo perfected the test by labelling the probe with biotin, an acid found in egg yolks and beef liver. So when the probe detects salmonella, biotin goes along for the ride. The sample is then exposed to avidin, a protein found in egg whites that likes to gobble up biotin. The avidin is itself labelled with an enzyme that imparts a colour to the solution as avidin eats up the biotin. The more salmonella in the food, the more biotin-labelled probes will be eaten by the avidin and will turn the solution (in this case) green.

It is a simple test that Dr. Gopo thinks he can package as a cheap and rugged kit. Dr. Gopo claims his DNA probe can handle 500 samples accurately in a few hours, as opposed to the normal few days. But success in the laboratory does not always imply success outside it. It has taken two years to find someone to think about manufacturing his kit commercially, despite efforts to patent and market it himself. Even a Zimbabwean company showed surprisingly little interest. Now a Scottish company, Stirling Diagnostics, is considering marketing Dr. Gopo's salmonella probe.

Some western scientists are sceptical of the claim that a colour-labelled test could be sufficiently finely tuned to give accurate readings. Others complain that Dr. Gopo's probe confusingly detects levels that are too low to pose a health risk. Dr. Gopo maintains that people, including Africans, find it hard to believe it is possible for Africans to do first-rate science. (Source: The Economist, 13 January 1990)

Proteins with a cool, quick test for salmonella

An American company has developed an unusual test for detecting salmonella and other food contaminants. It claims that the test is 100 times as fast and 1,000 times as accurate as its traditional counterparts.

The method, developed by DNA Plant Technology of Oakland, California, depends on an unlikely property of some bacteria: they cause water to form ice. Water often remains liquid below its freezing point, in a so-called "supercooled" state, unless solid particles are present for the water to freeze around. The most effective particles, or "nuclei", are small crystals of ice. Other templates that mimic the structure of an ice crystal, such as crystals of sodium iodide, can also bring about "ice nucleation".

So can several organisms, including five species of bacteria: Pseudomonas syringae, P. fluorescens, P. viridiflava, Erwinia herbicola and Xanthomonas campestris. These ice-nucleating, or "ice-plus" bacteria are thought to be responsible for causing the frost that sometimes damages crops in greenhouses.

These micro-organisms contain compounds called ice-nucleation proteins. But molecules of the protein in isolation do not cause nucleation. The membranes of the bacteria appear to fold the proteins in such a way as to produce a hexagonal symmetry similar to that of ice crystals.

Paul Wolber and Robert Green of DNA Plant Technology developed the food contamination test by incorporating the gene responsible for the ice-nucleation protein into a virus that specifically attacks salmonella bacteria.

The virus then injects its genetic material into the bacteria, where the genes become part of the bacteria's own DNA. The salmonella bacteria then start to reproduce the proteins of the virus.

Any salmonella present in the food sample and infected with the virus will contain the ice-nucleation protein. As the temperature drops, the technician can detect any contaminating salmonella bacteria by the ice crystals that form on the sample, encouraged by the ice-nucleating proteins. The test takes only 40 minutes - considerably faster, say the researchers, than detection tests currently used which can take up to several days.

The company is also developing similar tests to detect listeria and campylobacter. (Source: New Scientist, 27 January 1990)

Biological food testing method

A biological indicator for sterile control of products in pharmaceutical and food-processing industries has been developed by the Swedish biotechnology company Diffchamb AB at Gotheburg. Intended for monitoring sterilized and pasteurized substances, it will serve as a complement to instrument control methods now used for a number of products and heat treatment processes.

The bio-indicator is an aqueous gel sphere in which specific micro-organisms have been encapsulated. The sphere is surface-sterile and spore-tight and can pass all processes without risk of contamination. Should a heat treatment process prove to be insufficient, surviving micro-organisms would bring about a colouring of the gel sphere within 24 hours. (Source: BIOTECHNICA Journal No. 1, 1990)

Modified yeast fine for food

The British Government is to allow the commercial development of a genetically manipulated strain of bakers' yeast manufactured by the Dutch company Gist-Brocades. This is the first time any country has sanctioned the development of a food product containing a live genetically manipulated organism (GMO). Other European countries, the United States and Japan are also evaluating the yeast's safety.

No genetic material has been added to the yeast from another species, according to Klaus Osinga of Gist-Brocades. The maltose permease and maltase genes from the yeast were combined with new promoters from another strain of the same species, Saccharomyces cerevisiae. The genes and promoters were then spliced back into the yeast genome together with short pieces of "synthetic" DNA. Osinga says that this DNA contains "stop" codons, to minimize the chance of any hybrid proteins being produced. The end result is a yeast that should take up and digest maltose more efficiently and release carbon dioxide, which makes bread rise, more quickly.

In its evaluation, the Advisory Committee on Novel Foods and Processes (ACNFP) says it decided that the yeast was safe mainly because the genetic manipulation was within a single species. For the same reason, and following the advice of the Government's Food Advisory Committee, bread made using the yeast will not have to carry a label indicating genetic manipulation.

Gist-Brocades' application was also considered, and approved, by two other committees, one in the Department of the Environment and the other part of the Health and Safety Executive, which advise the Government on the environmental release of GMOs. Some escape of the yeast from bakeries is assumed to be inevitable. (Extracted from Nature, Vol. 344, 15 March 1990)

Protein from fungi

Research at the Biochemical Technology and Microbiology Institute of the Vienna Technical University concentrates on mould fungi which are capable of excreting up to twice the amount of their own proteins in the form of exoproteins. These exoproteins have similar glycosylation characteristics to proteins in mammals. In order for the mould fungi to be employed on a commercial scale, the Institute is trying to identify the genetic structures that are responsible for the high excretion rates. The research team is also studying the factors that influence the passage of the proteins through the cell walls to minimize losses. A third research goal is to employ genetic engineering techniques to obtain optimum strains for specific substrates. (Source: BIOTECHNICA Journal No. 1, 1990)

Energy and environmental applications

Spotting pollution damage by gene technology

The Swedish National Environment Protection Board has allocated SKr 15 million ($2.5 million) to a five-year research project to improve early detection of environmental problems such as acidification, heavy metals, dioxins and organic solvents.

The current theory is that organisms in the soil adapt to environmental changes and studies of their germ plasm with DNA technology could therefore indicate a process of change in the environment. A research group led by Dr. Göran Bengtsson in the Department of Ecology at the Lund Institute of Science and Technology has now been set up to look into this hypothesis.

The overall aim is to develop new sensitive methods to spot early stages of change in the environment that at present go undetected. The problem with soil testing is that changes are taking place very slowly over decades and centuries. But once the tolerance level is reached, the deterioration rate escalates rapidly to reach a

"beyond repair" stage within a short period. (Source: BIOTECHNICA Journal No. 1, 1990)

Warner-Lambert unveils "bio-plastic" starch

Warner-Lambert is claiming a "major advance" in materials science with the development of a biodegradable material made almost entirely from starch, such as derived from corn or potatoes. The "bio-plastic starch" could replace conventional plastics in a wide range of applications.

The research programme is in its very early stages, but "it does hold promise as an attractive business opportunity". The company is establishing a facility at its headquarters in Morris Plains, New Jersey, to exploit the technology further.

The new material is the result of an eight-year research programme at the company's Capsugel division, which produces empty hard gelatin capsules. Scientists attempting to develop a more efficient way to manufacture capsules discovered they were able to melt starch without it decomposing.

"Others have tried in the past, but the water has boiled off and the starch burned. By using a chamber akin to a pressure cooker we have succeeded in trapping the water inside", a spokesman said. "The material is completely different from any other so-called bio-degradable product on the market."

The material has already been used to produce a starch-based pharmaceutical capsule manufactured by injection moulding to engineering tolerances.

The company intends to market the material under the trade name Novon. First potential applications are envisaged where end-products are of short-use or a disposable nature and where high mechanical properties are not required. Longer term, the company says it expects improvements in mechanical properties from further modifications of the starch material. (Source: European Chemical News, 29 January 1990)

Shedding new light on methane production

SERI researchers have invented a unique way of enhancing anaerobic digestion, a process that uses bacteria to convert sewage and other organic wastes to useful methane gas.

Conventional anaerobic processes suffer from accumulations of organic acids, which break down slowly and may "sour" the digestor mixture. SERI researchers may have solved this problem by adding light and photosynthetic bacteria. These micro-organisms rapidly convert organic acids to hydrogen, which is then readily converted to methane by methanogenic bacteria.

Four strains of photosynthetic bacteria with special conversion ability have been identified. Each strain absorbs a different portion of the solar spectrum, so that a combination of the four can use about 85 per cent of the sun's energy in the conversion process. Laboratory tests indicate that use of these bacteria may lead to a minimum tenfold increase in methane production from organic acids. Tests have now moved into the field, where natural sunlight stimulates bacterial action through a transparent lid on a special bathtub-shaped digestor.

SERI has applied for a patent on its unique process, which has already attracted industry attention. For example, Hawaii's Unisyn Company is now evaluating the commercial feasibility of adding sunlight and photosynthetic bacteria to conventional anaerobic digestors. (Source: SERI S&T In Review, Autumn 1989)

Detoxifying pulp effluents

A new method to detoxify chemi-thermo-mechanical pulp (CTMP) effluent biologically, by using micro-organisms not requiring oxygen, has been developed in the Department of Applied Microbiology at the Chemical Center of Lund University. Tests in a pulp mill in Timra, North Sweden, have shown that the anaerobic treatment primarily reduces acetate, methanol and carbohydrates from the effluence, while wood extractives are removed by the aerobic post-treatment. The methane which forms during the reactor process is an additional advantage, as it can be used as fuel for the plant. The detoxification method has been used successfully for two years, to purify some 2,800 m^3 of toxic effluent per day. (Source: BIOTECHNICA Journal No. 1, 1990)

Biotechnology - a fast-growing technology in environmental management

A recently released Business Communications Co. (BCC) study, Environmental management through biotechnology: Micro-organisms and enzymes for waste treatment (C-110) analyses processes, technologies and markets involved in municipal waste treatment, hazardous waste treatment and waste-to-energy.

Municipal water treatment has relied on the use of micro-organisms for many decades. Indeed, without biological contactors, trickling filters or various kinds of digestors, it would be prohibitively expensive to purify municipal and commercial wastewater.

Some existing applications

Of the over 145 million tons of municipal waste generated in the USA alone each year, nearly 65 per cent (paper, yard and food wastes) are considered easily biodegradable and therefore especially amenable to biological treatment. Another 16 per cent (rubber, leather and plastic wastes) are considered "potentially biodegradable". That leaves 19 per cent (glass, metals and miscellaneous) which is not potentially treatable with advanced biological processes.

Oilfields have long relied on "landfarming" the hydrocarbon-rich contaminants produced during oil recovery. These wastes are not considered "hazardous" by the US Environmental Protection Agency (EPA), despite their often toxic characteristics. During landfarming, the wastes are buried and exposed to the natural oil-degrading micro-organisms present in the soil.

More recently, it has become possible to biodegrade or otherwise treat a variety of hazardous wastes, including oils, fuels, solvents, pesticides and even heavy metals. Microbial hazardous waste treatment can be used for **disposal** (storage of wastes, either permanently or temporarily), **treatment** (neutralization or destruction of wastes), **remediation** (destruction or removal of wastes accidentally or purposefully released into the environment) and **minimization** (techniques to reduce the generation of wastes).

Microbial action can also convert "wastes" into energy through biodegradation and fermentation. It

is now increasingly impossible to "mine" old municipal waste dumps for the methane produced by these processes. One day, municipal wastes will be converted directly into fuel, bypassing the need for potentially polluting incineration.

According to BCC, these markets added up to a biotechnology environmental management market worth $823 million in 1989, excluding R&D. At least $144 million was spent on the research and development of various aspects of biotechnology environmental management, with the bulk of this money coming from corporate sources, rather than from government.

Some applications to watch

The fastest growing sector is the **bioremediation of hazardous wastes**. This market was worth $30 million in 1988, is expected to have reached $34 million in 1989 and should grow to $50 million (in 1989 dollars) during 1990. By 1995, BCC estimates that it will be worth $153 million (1989 dollars), representing an inflation-corrected average annual growth of 25 per cent.

The largest biotechnology environmental management market is for **landfarming**, especially oilfield waste landfarming. This is a $400 million market, although little growth is expected.

Both the bioremediation and landfarming market sectors are part of the overall **hazardous waste management market**. Operating and capital costs for the biotechnology component of this sector should total $464 million in 1990 and are expected to grow at an average annual rate of 4.2 per cent through 1995, to $571 million.

The keys to biotechnology environmental management are the micro-organisms used, BCC notes. In many cases, naturally occurring micro-organisms are used. However, **proprietary microbial cultures** are a well-established and growing market worth $24 million in 1989. Between 1990 and 1995, the market for waste treatment microbial cultures should grow at nearly 13 per cent a year, from $33 million to $60 million.

Composting is another "low tech" microbial waste treatment. Both sludges and biodegradable solid wastes can be composted. Composting yard wastes is an especially attractive possibility, since it cuts air pollution and frees up municipal landfill space. The solid waste composting market was $109 million in 1989 and will grow to $150 million by 1995. This growth should significantly increase the size and sophistication of the solid waste composting infrastructure.

Other promising market subsectors include such **clean-up applications** as the use of microbial treatments to clean up leaking underground fuel storage tanks, to clean up after oil spills and treat pulp and paper industry effluents.

The R&D sector

BCC suggests that it is "perhaps misleading" to consider R&D a "market sector" in the same sense as the sale of chemicals or the marketing of services are market sectors. There is very little "pure science" R&D in the biotechnology environmental management field.

$138 million worth of biotechnology environmental management R&D was funded in 1989. Of this sum, hazardous waste management was best-funded, at $80 million. By 1995, hazardous waste management R&D could be as high as $200 million. By that time, BCC predicts that microbial coal desulphurization will once again start to be a "hot topic", with $45 million in funding. Details of the report, priced at $2,450, from: Business Communications Co. Inc., 25 Van Zant Street, Norwalk, CT 06855, USA or on +1 (203) 853-4266. Fax: +1 (203) 853-0348. (Source: Biotechnology Bulletin, Vol. 8, No. 12, January 1990)

E. PATENTS AND INTELLECTUAL PROPERTY ISSUES

Patent DNA sequences

The issue of standardizing DNA sequences recoded in patent literature is being examined in the USA and in Europe.

In May 1989 the US Patent and Trademark Office (PTO) announced the proposed rulemaking for the descriptions of nucleotide and amino acid sequence data. Standardized formats would improve the efficiency and quality of examination, and improve dissemination of sequence data in electronic form.

In Europe, the World Intellectual Property Organization (WIPO) is now considering similar moves and the Permanent Committee on Industrial Property Information (PCPI) is aiming to recommend standards for coding which could be based on the technical specifications used by the US PTO.

Further information: World Intellectual Property Organization (WIPO), 34 Chemin des Colombettes, CH-1211 Geneva 20, Switzerland. (Source: BIOTECHNICA Journal No. 1, 1990)

California Supreme Court hears oral arguments in tissue ownership case

On 6 February, the California Supreme Court was due to hear oral argument in the case of Moore versus Regents of University of California in San Francisco. At dispute: whether someone whose body cells have been used in medical biotechnology should be able to claim property rights - and sue for commercial uses of his cells. In this case, the cells at issue were derived from John Moore's spleen.

The US Industrial Biotechnology Association is arguing that the establishment of property rights to such cells would "be detrimental to medical research and to the biotechnology industry. The decision would result in enormous financial and time costs to the research community". (Source: Biotechnology Bulletin, Vol. 9, No. 1, February 1990)

US patent awarded for genetically engineered fungi

Canadian Allelix Biopharmaceuticals has announced that the United States Patent and Trademark Office has awarded an important patent to the company. This patent is significant, since it relates to the genetic manipulation of a widely used industrial fungus so it may now be used for efficient production of many new protein products. It also confirms the company's leading position, first established in the early 1980s, in the use of fungi to make protein pharmaceuticals (biopharmaceuticals).

The patent, US 4,885,249, covers a method of introducing genes into Aspergillus niger (a filamentous fungus), and also fungi containing the new genes. This means that genes not normally present in the fungus can be introduced so that it

now makes a new protein. In addition to the US patent, Allelix was recently granted patent protection in Australia and expects also to receive patents in other countries for this important technology.

A. niger is a well-establishing industrial micro-organism with a long history of successful use to produce bulk enzymes and important specialty chemicals. An advantage of filamentous fungi is their ability to produce and release large quantities of protein products during the manufacturing process. This makes filamentous fungi a good system for low-cost, high-yield production of biopharmaceuticals. The process described in the Allelix patent, first filed in 1984, demonstrates a key step in achieving this goal. Allelix Biopharmaceuticals has since developed additional proprietary technology, and has collaborated with other companies and the University of Waterloo in these developments. (Source: Company News Release, 22 March 1990)

Patent suit filed against MicroGeneSys

Cambridge Bioscience of Worcester, Mass., has filed suit against MicroGeneSys of West Haven, Conn., for patent infringement. The patent, owned by Harvard University and licensed to Cambridge Bioscience, which supported the university's research, covers the purified envelope protein of the AIDS virus. The protein is used in testing for AIDS and in the development of drugs and vaccines to treat the disease. Cambridge Bioscience has offered non-exclusive sub-licences to companies wishing to use the protein for diagnostics, therapeutics, vaccines, and research products. The complaint alleges that MicroGeneSys is selling purified patented products and conducting commercial vaccine research without such a sub-licence. Cambridge Bioscience looks to prohibit other infringing uses of the protein and obtain sub-licencing fees and royalties on MicroGeneSys' protein-based vaccine. MicroGeneSys has not commented on the suit. (Reprinted with permission from Chemical and Engineering News, 8 January 1990, p. 14. Copyright (1990) American Chemical Society)

Emerging biotechnology products focus of patent disputes

Now that more and more genetically engineered drugs are close to becoming marketed products, patent rights will play a major part in determining which of the numerous biotechnology companies control major markets.

Currently, 45 US companies have 80 products based on genetic engineering that are under development, according to the Pharmaceutical Manufacturers Association. Food and Drug Administration approval has been granted to only 10 biotechnology drugs, but about the same number of applications is pending.

The number of new major biotechnology products reaching the market is expected to rise throughout the 1990s. US sales of human therapeutic and diagnostic biotechnology products will reach almost $1.3 billion in 1990, according to Consulting Resources Corp. of Lexington, Mass., growing to about $3.7 billion by 1995 and $9 billion by the year 2000. Despite the potential for large rewards, the costs for a biotechnology company are high - as much as $100 million per product and possibly even the fate of the company. The level of competition is also very high with at least two companies, if not many more, in each of the major product areas.

Although all the major areas of biotechnology drug development are seeing patent litigation, the trend in the industry is more towards cross-licensing than litigation.

Cetus led in drug patents based on biotechnology in 1988

	Biotechnology patents		
	Pharmaceuticals	Pharmaceuticals based on genetic engineering	Major drug development areas
Amgen	3	3 a/	Anaemia, cancer, infection, hepatitis
Biogen	2	2	Cancer, AIDS, inflammation
Burroughs-Wellcome	3	0	Heart attacks, cancer
Cetus	12 a/	6 a/	Cancer, AIDS, infection, diagnostics
Du Pont	3	1	Diagnostics
Genentech	11 a/	9 a/	Diabetes, cancer, AIDS, heart attack, human growth
Genetics Institute	5	4 a/	Anaemia, haemophilia, cancer, infection, heart attack
Hoffmann-LaRoche	5 a/	0	Human growth, cancer
Eli Lilly	11 a/	4 a/	Cancer, diabetes, diagnostics, heart attack, human growth
Ortho Pharmaceutical	6	4 a/	Anaemia, transplants

a/ Among top 10 recipients of biotechnology patents in the US in 1988.

Source: Pharmaceutical Manufacturers Association. (Abstracted with permission from Chemical and Engineering News, 5 February 1990, p. 17, A. M. Thayer. Copyright (1990) American Chemical Society)

F. BIO-INFORMATICS

Bioprocessing safety: worker and community safety and health considerations
(Warren C. Hyer, Jr.)

This book presents basic concepts in the safe and responsible integration of the bioprocessing facility into the local community. Eighteen peer-reviewed, general papers for a non-technical audience address safety issues related to large-scale bioprocessing: legal, insurance, health protection, risk analysis, worker productivity, plant design (especially containment), government regulation, protective clothing, spill control, medical surveillance, waste disposal and community awareness points of view. Sections include:

- Overview of safety in the bioprocessing industry
- Design criteria for safety
- Safety plan - personnel
- Community awareness and emergency responses
- Regulatory aspects of bioprocessing - international, national and local.

The term bioprocessing is treated broadly to include traditional bioprocessing (such as biological aspects of cheese and beer production); the production of bulk chemicals (e.g. citric acid); the production of antibiotics, vaccines, and microbial pesticides; and newer developments, such as large-scale bioprocessing using genetically modified micro-organisms and mammalian cell culture techniques.

The target audience of this book are decision makers who have had no formal training in biosafety issues. The book has 175 pages (1990) and is available for $39.00. For copies please write to ASTM, 1916 Race Street, Philadelphia, PA 19103, USA (Tel.: (215) 299-5400. TWX: 70-670-1037) or ASTM European Office, 68a Wilbury Way, Hitchin, Herts SG4 OTP, England (Tel.: (0642) 31525. TWX: 825684 ATP G). (Source: ASTM News Release)

Biotechnology and its impact on international trade

The International Federation of Institutes for Advanced Study (IFIAS) is planning the second symposium of the International Diffusion of Biotechnology Programme, directed by Dr. Calestous Juma of the African Centre of Technology Studies (ACTS), to be held in June 1990, in Maastricht, The Netherlands.

Entitled "Biotechnology and International Trade: 1992 and Beyond", the symposium will deal with the overall impact of biotechnology on economic relations between developed and developing countries. One area of interest: the consequences of environmental legislation and the relocation of some companies to less regulated environments. Details from: Ms Rohini Acharya, IFIAS-Maastricht, Witmakerstraat 10, 6211 JB Maastricht, The Netherlands or on (043) 250465. FAX: (043) 218820. (Source: Biotechnology Bulletin, Vol. 9, No. 1, February 1990)

European biotechnology information study

The European Chemical Industry Federation (CEFIC) and a consortium of publishers (Elsevier, Derwent and Springer) are carrying out a study entitled Strategies for a European Biotechnology Information Structure.

The objective of the study is to find out the needs of the user community and to propose working models, taking into account the scientific and commercial requirements of European biotechnology. Details from: Dr. Jack Franklin, ASFRA, Voorhaven 33, 1135 BL Edam, The Netherlands. (Source: Biotechnology Bulletin, Vol. 9, No. 1, February 1990)

New biotechnology directory data base

BioCommerce Data's international directory data base on the biotechnology industry is now available on two on-line systems, Dialog and Data-Star, as part of the file BioCommerce Abstracts and Directory. Details from: Biocommerce Data Ltd., 95 High Street, Slough, Berkshire SL1 1DH, UK. (Source: Biotechnology Bulletin, Vol. 8, No. 12, January 1990)

The genetic engineer and biotechnologist

From 1990 onwards, International Industrial Biotechnology will be published under a new format, under the title The Genetic Engineer and Biotechnologist. Details from: GB Biotechnology, 4 Beaconsfield Court, Sketty, Swansea SA2 9JU, UK. (Source: Biotechnology Bulletin, Vol. 8, No. 12, January 1990)

Australia and New Zealand Biotechnology Directory

The second edition of the Australian and New Zealand Biotechnology Directory is nearing its final stages prior to printing. All companies and organizations listed in the Directory have had an opportunity to update their entries from the first edition and there are many new articles describing various aspects of biotechnology included in the Directory. The government contact section has been enlarged and improved and the publishers are hoping to have an improved index section in this second edition.

At this stage, it looks as though the Directory will be available for sale in late March. The first edition of the Directory proved very successful and this improved second edition should be an item accessible to every biotechnologist. Australian Industrial Publishers Pty. Ltd. are participating once again in this publication with the ABA. (Source: ABA Bulletin, Vol. 5, No. 1, February 1990)

Canadian Biotechnology Directory 1990

The Canadian publisher of New Biotech has announced the first edition of a new Canadian Biotechnology Directory which should be available now. The regular price is $Can 85.00 plus shipping charges. You may obtain a copy by sending your order to: New Biotech, Directory 1990 Offer, P.O. Box 7131, Station J, Ottawa, Ontario, Canada, K2A 4C5. Editors of the Directory are Peter Winter and Dr. Hans Giese. (Source: ABA Bulletin, Vol. 5, No. 1, February 1990)

Ernst & Young Annual Biotech Survey

Ernst & Young recently released Biotech 90: Into the Next Decade. This survey, produced annually, shows that 74 per cent of the US industry now has products for sale and that this is led by the public biotechnology companies where product sales exceed $1.3 billion. Once again the author is G. Steven Burrill. This study surveys 480 US biotechnology companies and interviews many industry professionals, academics and government advisers. The survey is published Mary Ann Liebert Inc. and is available from Ernst & Young at around $90.00 (Source: ABA Bulletin, Vol. 5, No. 1, February 1990)

ATCC catalogue
Human and mouse DNA probes and libraries

The American Type Culture Collection has announced the availability of the third edition of the ATCC/NIH Repository of Human and Mouse DNA Probes and Libraries. This is a 136-page reference catalogue. The catalogue lists materials deposited at the ATCC as part of the genetic repository supported by the NIH, National Institute of Child Health and Human Development (NICHHD) and the Division of Research Resources. The catalogue also lists related materials from the ATCC's own molecular biology collection and Patent Culture Depository. Direct inquiries to: ATCC/Mkting NR 43, 12301 Parklawn Drive, Rockville, MD 20852, USA. (Source: ABA Bulletin, Vol. 5, No. 1, February 1990)

UK Biotechnology Handbook

Judging by the number of new entries in the second edition of the UK Biotechnology Handbook, published in January of this year, the British biotechnology industry has expanded by over 10 per cent during 1989. Many of the new listings are small start-up firms but there are signs of consolidation too with a number of takeovers reflected. In addition to companies, the UK Biotechnology Handbook '90 covers universities and other academic sites, the financial community, government bodies and service organizations such as publishers and consultants. It contains over 550 full-page descriptions, each including a detailed profile of research and business interests plus senior contact names with job titles. Fully indexed under more than 50 areas of activity and divided into five easy-to-use sections, all the information has been extensively revised and updated within the last three months of 1989.

The 1990 edition of this reference work includes new information on current and expected turnover and staff numbers, providing further evidence of healthy growth. Overall the British biotechnology industry seems to be thriving but covers a wide spectrum of participants from specialist research-based companies through to equipment distributors, all of whom are well supported by sources of finance and fundamental research.

The climate is changing rapidly however with widening opportunities for marketing to Europe and new regulations on the use of genetically manipulated organisms providing new opportunities and challenges. Key issues which will influence the strategic development of biotechnology in the United Kingdom are discussed in nine review articles in this book, making it much more than just an annual directory. There are papers covering venture capital, patenting, European research funding and legislative plans, the markets for bioprocess equipment, cell line information services, career opportunities, the new rules on environmental release and UK Government projects.

Priced at £85/$US150.00 (+ $US30.00 airmail postage outside Europe), the UK Biotechnology Handbook '90 is published by BioCommerce Data in collaboration with the BioIndustry Association (BIA) (formerly the Association of the Advancement of British Biotechnology AABB) and a 10 per cent discount is available to BIA members. To place an order, contact BioCommerce Data Ltd. at Prudential Buildings, 95 High Street, Slough, Berkshire, SL1 1DH, UK. Tel.: (0753) 511777. Fax: (0753) 512239. (Source: Company News Release, February 1990)

Anglo-Soviet biomedical journal debuts

Copies of the first issue of Biomedical Science are now available. The publication, which will be published monthly in English and will present key biomedical research results, is a collaborative effort of the Soviet Academy of Sciences, the Royal Society of Chemistry's Turpin Transactions, and Pion, a UK-based publishing company. Although the journal will focus largely on work undertaken in the Soviet Union, it also will accept contributions from the international scientific community. The first Anglo-Soviet publication of its kind, Biomedical Science is edited jointly by Bernard T. Donovan of Turpin Transactions and Rem V. Petrov, Vice-President of the Soviet Academy of Sciences. (Reprinted with permission from Chemical and Engineering News, 12 February 1990, p. 23. Copyright (1990) American Chemical Society)

New computer link for Japan

The DNA Data Bank of Japan (DDBJ) at the National Institute of Genetics in Mishima will open a high-capacity computer link that will allow exchange of much larger volumes of data with DNA data banks in Europe and the United States. But Japan's contribution to international efforts to handle the growing flood of DNA data remains small.

At a time when GenBank in the United States and the EMBL Data Library each employ teams of tens of researchers to run their data banks, Japan still struggles along with only two full-time researchers and a couple of part-timers at DDBJ. Not surprisingly, DDBJ at present processes only about 3 per cent of all the DNA sequences published world wide; the remaining 97 per cent are dealt with at EMBL and GenBank.

DDBJ constantly exchanges data with EMBL and GenBank and the volume of traffic has grown to over 1 million bits per day. This volume is expected to grow at least five times when the data banks move to a new relational data base system in the near future. Hence the need for the high-capacity computer link.

The new computer line, which will be connected on 28 March and can carry 64 kilobits per second, is between DDBJ and the University of Tokyo.

DDBJ will gain access to scientific networks in the United States and Europe and thence to the GenBank and EMBL data bases through Tokyo University. The new link will also allow DDBJ to form a distributed data base with DNA data banks at several locations in Japan.

The three data banks have agreed that from now on DDBJ will process all DNA sequences produced in Japan. This will increase DDBJ's data share to about 10 per cent. But the bank is in desperate need of more manpower to handle the increased workload. The rigid employment policies of the Ministry of Education, Science and Culture (MESC), to which DDBJ is affiliated, make it very difficult for the bank to employ new staff. DDBJ has won permission to create a new position for an assistant professor but more temporary staff are also needed for annotating DNA sequences as they are input.

The new leased computer line will also be a considerable drain on DDBJ's very limited budget.

The lack of IBM-compatible computers in Japan also adds to DDBJ's headaches. Japan is the only developed nation where IBM-compatible personal computers are not the standard; rather, the market

is dominated by NEC computers. GenBank recently developed the new software "authorin" which allows scientists to input DNA sequences directly to data banks, thereby easing the workload for the data banks. But the software is of virtually no use in Japan until it is rewritten into NEC-compatible form, something he hopes to do this summer. In any case, few Japanese biologists are computer-literate and it is likely to be a long time before large amounts of data are submitted in this way.

Japan also lags behind GenBank and the EMBL data library in the use of CD-ROM to distribute DNA data to scientists. EMBL began using CD-ROM last September and GenBank began this month. But DDBJ continues to use magnetic tapes, which are cumbersome and hold fewer data, because there is little demand for such a service from Japanese scientists and the tapes are easier to copy.

Japanese researchers promoting the human genome project are considering Mishima as a possible site for a new bio-information centre to handle data arising from the project. But although it is "quite possible" that the centre will be located at the National Institute of Genetics, it will probably be separate from DDBJ. (Source: Nature, Vol. 344, 8 March 1990)

Feeding Tomorrow's World

Will the benefits of the "green revolution" of the 1960s and progress in food production meet the needs of the world population at the end of this century? Will the "biotechnological revolution" offer a solution to world food problems? How can aid to agricultural development and self-sufficiency be attained, particularly in developing countries?

In Feeding Tomorrow's World, Albert Sasson tries to answer these and many other pressing questions through a pluridisciplinary approach to human nutrition and food production. The book, addressed to a wide readership, provides a remarkable synthesis of the scientific, economic, socio-economic and environmental aspects of nutrition throughout the world.

Subjects treated are:

Human nutrition

Nutritional needs;
Protein deficiency and malnutrition;
Nutrition and infection;
Children's diet;
Changes in diet and attitudes towards food;
Diet and health.

Production and trade in agricultural foodstuffs

Problems of evaluation and diagnosis;
Changes in food production;
Factors affecting food-production patterns;
Effects of climatic variation on production;
Regional and national situations;
Modalities of production, acquisition and use of agricultural commodities in the developing countries;
International trade in agricultural commodities.

Achievements and potential;
International co-operation and prospects

Hunger and poverty;
Requirements for rural development;
The "green revolution";
Agriculture, agro-forestry and livestock husbandry: international, agricultural research centres, regional and international co-operation, transfer of results;
Conservation and utilization of plant genetic resources;
International assistance and co-operation;
Prospects.

Feeding Tomorrow's World (Sextant, 3). 1990, 805 pp. ISBN 92-3-102083-8. FF 225.00; $US 53.00; C$56.50; £34. Co-published with the Technical Centre for Agricultural and Rural Co-operation (CTA), "De Rietkampen", Galvanistraat 9, 6716 AE Ede, Netherlands. Worldwide sales rights: UNESCO, 7 place de Fontenoy, 75700 Paris, France.

An international approach to biotechnology safety

The new biotechnology promises to have a profound impact upon the human condition and it may contribute to filling some of the most fundamental needs of humanity, from health care to supplies of food and energy to pollution control. Potential applications of the new biotechnology include the production of new drugs, food and chemicals, the more efficient production of existing products, new diagnostic techniques, the degradation of toxic wastes and major improvements in agricultural products.

Along with its promise, the new biotechnology has raised concerns about possible risks to humans, animals and the environment. It might be asked whether genetically engineered organisms could be harmful to humans or other living organisms; whether, if some of these organisms establish themselves in the environment, they could proliferate and become pests; and whether some of the powerful new chemicals that can now be manufactured by the new biotechnology could prove harmful to factory workers.

This publication was originally presented as a paper to a meeting of the informal working group, held at Vienna from 27 to 29 January 1986 and was written by Geoffrey M. Karny.

The publication covers risks and regulations of laboratory research; risks and regulation of large-scale operations; environmental applications; and an international approach to safety issues of genetic engineering.

The impact of genetic engineering will be international in scope. Accordingly, it is not surprising that the United Nations and its affiliated organizations have made a major commitment to become parties to the development and uses of biotechnology. A desire for the developing countries to share in the benefits of biotechnology sparked efforts by the United Nations Industrial Development Organization (UNIDO) to create an international centre to promote the development and peaceful application of genetic engineering and biotechnology, especially for developing countries. The centre, known as the International Centre for Genetic Engineering and Biotechnology (ICGEB) is supported by 41 countries and operates at Trieste, Italy, and New Delhi, India, under the auspices of UNIDO. Concern over possible safety and environmental risks raised by biotechnology has prompted the World Health Organization (WHO) and the United Nations Environment Programme (UNEP) to identify and study the various safety issues

involved. WHO has long been concerned about the risks to human health presented by micro-organisms and has prepared a laboratory biosafety manual. 1/ The WHO Regional Office for Europe has prepared a report on the health impacts of biotechnology. 2/ UNEP has been studying the topics of biowaste disposal and environmental uses of genetically engineered organisms. These activities have led to an affiliation between UNIDO, WHO and UNEP in the form of an informal working group to exchange information and co-ordinate activities pertaining to safety issues raised by the new biotechnology.

One of the many topics that ICGEB will need to address will be the safety issues raised by the new biotechnology. Moreover, as an international centre of excellence, the Centre will naturally be looked upon as a leader and an international model for dealing with biotechnology, including issues of safety. 3/ Therefore, it is appropriate to identify those issues and to consider what role international bodies such as WHO, UNEP, UNIDO and ICGEB can play in addressing them. The purpose of this publication is therefore:

(a) To examine current views on the possible risks presented by the new biotechnology;

(b) To identify any safety issues or concerns arising from such risks;

(c) To examine current international regulatory and supervisory mechanisms for dealing with the risks and safety concerns;

(d) To determine common approaches and identify any potential gaps, overlaps or other deficiencies in these mechanisms;

(e) To discuss the international significance of these matters;

(f) To propose roles for ICGEB, WHO, UNEP and UNIDO.

In addressing these issues, the author has drawn upon other published reports and interviews with selected experts as well as personal experience. An attempt has been made to draw on all available written materials pertaining to risk but only on selected materials pertaining to regulation. It would be unnecessary and virtually impossible to survey the laws of many different countries with regard to such broad areas as worker health and environmental protection. Thus, only a few bodies of law were selected for an in-depth study. They were the laws of Japan, the United Kingdom, the United States of America, and the European Community. The three major industrial countries have well-developed, comprehensive laws from which common regulatory principles may be ascertained. Thus, such a study is directly relevant to the interests of less developed countries, which can select from and build upon these principles. Yet, even this approach has limitations.

1/ Laboratory Biosafety Manual (Geneva, World Health Organization, 1983).

2/ Health Impact of Biotechnology: Report on a WHO Working Group, Dublin, 9-12 November 1982 (Copenhagen, World Health Organization, 1984).

3/ At present, the safety guidelines of the United States National Institutes of Health are being observed at the Centre. The Centre is also monitoring the debate concerning physical/biological containment as well as the release of genetically engineered organisms into the environment.

The publication is available from bookstores and distributors throughout the world or write to: United Nations Sales Section, New York, USA or Geneva, Switzerland. ISBN No.: 92-1-106235-7, price $26.

The European Federation of Biotechnology's Working Party on Education and the UK Interest Group in Biotechnology has published the proceedings of a meeting organized by the UK Interest Group on Education in Biotechnology and Dutch representatives of the European Federation of Biotechnology Working Party on Education held at the Delft University of Technology, the Netherlands on 2 December 1989 on Manpower and Training Needs for Biotechnology in Europe in the 1990s. Organized by C. F. A. Bryce, D. J. Bennett, J. G. Kuenen and K. Ch. A. M. Luyben, the meeting discussed a number of problems facing the manpower needs of the European biotechnology industry.

Part of the current changes in biotechnology result from the widespread changes in the political climate. The European infrastructure in science is poorly developed at present compared with the USA and Japan largely because there are 12 separate national science policies among EC member States, notwithstanding EFTA and COMECON countries. As the European Single Market continues to develop, borders will disappear and be replaced by transnational networks.

The number of employees in new biotechnology companies has increased from two- to tenfold according to country in the period 1982-1988. There has been an accelerating shift in emphasis from research and development to application and production which is likely to continue.

The application of biotechnology is likely to take place in three successive waves:

1. Diagnostic, pharamceutical and animal health products;

2. Agriculture, animal husbandry, speciality chemicals and environmental control;

3. Cheaper products, commodity chemicals, mineral leaching and electronics.

Successful application depends on what is possible, what is realizable and what is wanted, while consumer acceptance is crucial to biotechnology's continuing development.

Acute recruitment problems presently exist in areas such as protein biochemistry, downstream processing, product purification, microbial physiology and bioinformatics while there appears to be a sufficiency of genetic engineers. In general there is a shortfall in technicians.

The three main areas of concern at present are:

1. The very significant decrease in the number of graduates proceeding to post-graduate and post-doctoral training;

2. The major movement for training from southern European countries to the north due to the lack of facilities in the former;

3. The variation between European countries in the training period for the PhD degree which inhibits mobility.

Biotechnology is multidisciplinary and, while larger companies tend to favour specialist training and smaller ones more generalist, all personnel must be able to communicate to work effectively in such a context and be trained accordingly.

The framework of the European Federation of Biotechnology Working Party on Education, UK Interest Group on Education in Biotechnology, professional organizations and biotechnology industry throughout Europe has now been established and is working to improve manpower supply and training for European biotechnology.

Biotechnology pervades a great many of the areas of interest of the European Commission. One of the Commission's aims is to improve the contribution of advanced technology training to the social and economic development of the Community through Europe-wide programmes such as COMETT II.

Among the recommendations put forward was a call for a feasibility study leading to a Europe-wide, in-depth, comprehensive assessment of manpower and training requirements and provisions for biotechnology to be initiated as soon as possible. It should include all sectors of biotechnology, levels and types of training and roles of personnel in the biotechnology industry. As part of the study an inventory of training and exchange opportunities throughout Europe with the same coverage should be contructed and effectively disseminated. Funding should be provided jointly by the European Commission and by the biotechnology industry, for example via the COMETT II programme. The strategic appraisal and inventory should be implemented by utilizing the existing framework and collaborative network of the European Federation of Biotechnology Working Party on Eudcation, UK Interest Group on Education in Bioetchnology, professional associations and industry which is necessary for such a programme.

Copies of the report "Manpower and Training Needs for Biotechnology in Europe in the 1990s" (ISBN 1-872190-01-4) may be obtained from the Biochemical Society Book Depot, P.O. Box 32, Commerce Way, Colchester, CO2 8HP, UK. Price £10. (Source: The Biochemical Society, 7 Warwick Court, High Holborn, London WC1R 5DP Tel. +44 1- or 01-242 1076)

G. MEETINGS

June 1990

4-6 June Washington D.C., USA	World-wide regulation of new human pharmaceuticals, veterinary and plant agricultural products. Further information from: Technology Management Group, 25 Science Park, New Haven, Connecticut 06511, USA.
5-6 June London, UK	Autoimmunity - new targets and therapeutic approaches. Further information from: Ms. R. Duke, IBC Technical Services Ltd., Bath House (3rd floor), 56 Holburn Viaduct, London EC1A 2EX, UK.
6-8 June New York, USA	Aquaculture feeds and veterinary products: World-wide business opportunities for feed, pharmaceutical and chemical companies. Further information from: Technology Management Group, 25 Science Park, New Haven, Connecticut 06511, USA.
7-10 June Chicago, USA	1990 ASM conference on biotechnology. Further information from: American Society of Microbiology, 1325 Massachusetts Avenue, N.W., Washington, D.C. 20005, USA.
19 June to 16 July Caracas, Venezuela	ICGEB practical course on diagnosis of parasitic diseases. Further information from: Dr. G. Tzotzos, ICGEB, Padriciano 99, I-34012 Trieste, Italy.
22-23 June Berlin	International symposium on the usage of polymerase chain reaction in genetic and infectious diseases. Further information from: Dr. A. Rolfs, Department of Neurology, Klinikum Steglitz, Hindenburgdamm 30, 1000 Berlin 45.
26-28 June Trieste, Italy	Colloquium on lignin, its structure, biodegradation and practical utilization. Further information from: Dr. G. Tzotzos, ICGEB, Padriciano 99, I-34012 Trieste, Italy.
27-29 June University of Manchester, UK	XIth international congress of pharmacology. Further information from: Dr. E. Szabadi, Department of Psychiatry, University of Manchester, Stopford Building, Oxford Road, Manchester M13 9PT, UK.
29 June to 7 July Huddinge, Sweden	CBT Summer School - Eucaryotic Gene Expression. Further information from: Dr. S. Pettersson, Centre for Biotechnology, Karolinska Institute, NOVUM, S-141 52 Huddinge, Sweden

July 1990

1-6 July Kiruna, Sweden	8th international conference on methods in protein sequence analysis. Further information from: Dr. H. Jornvall, Department of Chemistry I, Karolinska Institute, S-104 01 Stockholm, Sweden.
2-6 July London, UK	Proteins: Isolation, characterization and analysis. Further information from: Mr. L. A. Hart, Royal Society of Chemistry, Burlington House, Piccadilly, London W1V 0BN, UK.

8–13 July Copenhagen, Denmark	European Federation of Biotechnology – 5th congress. Further information from: EFB Congress Secretariat, Spadille Congress Service, Sommervej 3, DK 3100, Hornbaek, Denmark.
8–13 July University of Bristol, UK	Practical course on fluorescent techniques for imaging and measurement of ion concentrations in living cells. Further information from: Dr. D. J. Hill, Department for Continuing Education, University of Bristol, Bristol BS8 1HR, UK.
9–11 July George Mason University, Fairfax, Virginia, USA	International meeting on bio-informatics, integration of organismic and molecular data bases and use of expert systems in biology. Further information from: Prof. H. Morowitz, 207 East Building, George Mason University, Fairfax, VA 22030, USA.
25–27 July Pennsylvania State University, USA	9th summer symposium in molecular biology – molecular pathways of cell growth control. Further information from: Symposium Programme Co-ordinator, 9th Summer Symposium in Molecular Biology, 329 South Frear Laboratory, The Pennsylvania State University, University Park, PA 16802, USA.

August 1990

5–9 August University of California, San Diego, USA	Conference on hepatitis B viruses. Further information from: The Conference Manager, University of California, San Diego, D-013, Molecular Biology of Hepatitis B Viruses, La Jolla, CA 92093-0513, USA.
5 August to 1 September Woods Hole, USA	Advanced lecture and laboratory course on methods in computational neuro-science. Further information from: Admissions Co-ordinator, Marine Biological Laboratory, Woods Hole, MA 02543, USA.
15–19 August Cold Spring Harbor, New York, USA	Molecular biology of SV40, polyoma and adenoviruses. Further information from: The Meetings Office, Cold Spring Harbor Laboratory, Bungtown Road, Cold Spring Harbor, NY 11724, USA.
19–22 August Toulon, France	2nd meeting of the international group on high pressure biology. Further information from: The Secretariat, CERB – BP 610, F 83800 Toulon Naval, France.
19–22 August University of York, York, UK	Three-day course on capillary electrophoresis. Further information from: Dr. C. Calvert, Symposium Manager, Department of Chemistry, University of York, York YO1 5DD, UK.
21–26 August Cold Spring Harbor, New York, USA	Molecular genetics of bacteria and phages. Further information from: The Meetings Office, Cold Spring Harbor Laboratory, Bungtown Road, Cold Spring Harbor, NY 11724, USA.
22–24 August University of York, York, UK	International symposium and commercial equipment exhibition on capillary electrophoresis. Further information from: Dr. C. Calvert, Symposium Manager, Department of Chemistry, University of York, York YO1 5DD, UK.
24 August to 1 September Spetsai, Greece	FEBS International Summer School on Immunology – the immune system: Genes, receptors and regulation. Further informa- tion from: Dr. S. Avrameas, Unite d'Immunocytochimie, Institut Pasteur, 28, rue du Dr. Roux, 75724 Paris, Cedex 15, France.
24–26 August Berlin	IUMS – Symposium on development in diagnosis and control of infectious diseases. Further information from: Congress Secretariat, Institute for Clinical and Experimental Virology, Free University of Berlin, Hindenburgdamm 27, D-1000 Berlin 45.
26–31 August Berlin	VIIIth international congress of virology. For further information please see previous item.
26 August to 6 September Il Ciocco, Tuscany, Italy	NATO Advanced Study Institute (ASI) on the molecular pathology of alcoholism. Further information from: Dr. N. Palmer, Department of Biochemistry, Charing Cross and Westminster Medical School, Fulham Palace Road, London W6 8RF, UK.
28–31 August Paris, France	Biology of vascular cells. VIth international symposium. Further information from: IVS, Hôpital Lariboisière, Secrétariat, Biology of Vascular Cells, 8, rue Guy Patin, 75010 Paris, France.
29 August to 2 September Cold Spring Harbor, New York, USA	Mouse molecular genetics. Further information from: The Meetings Co-ordinator, Cold Spring Harbor Laboratory, Bungtown Road, Cold Spring Harbor, NY 11724, USA.

September 1990

2-6 September Ile de Bendor (near Bandol), France	EMBO Workshop on spliceosome assembly and tissue specific RNA splicing. Further information from: Dr. E. Brody, Centre de Génétique Moleculaire, CNRS, Gif-sur-Yvette, 91190 France.
2-7 September Berlin	FEBS Laboratory Course on Gene Transfer. Further information from: Dr. A. Graessmann, Institut fuer Molekularbiologie und Biochemie, Freie Universitaet Berlin, Arnimallee 22, D-1000 Berlin 33.
3-6 September University of East Anglia, UK	9th John Innes Symposium on molecular and cellular basis of pattern formation. Further information from: Sympsoium Secretary, John Innes Institute, Colney Lane, Norwich, Norfolk NR4 7UH, UK.
3-7 September Volterra, Italy	Gordon Research Conferences - "Frontiers of Science": Molecular and ionic clusters. Further information from: Gordon Research Center, University of Rhode Island, Kingston, RI 02881-0801, USA.
7-9 September University College, Aberystwyth, UK	5th Harden discussion meeting on biochemistry and physiology of inorganic phosphate. Further information from: Dr. S. Shirari-Beechey (Harden Discussion Meetings), Department of Biochemistry, University College of Wales, Penglais, Aberystwyth, Dyfed SY23 3DD, UK.
9-14 September Wye College, near Ashford, Kent, UK	35th Harden conference on cell-cell interactions in the nervous system. Further information from: Mr. R. Dale, Meetings Officer (Harden Conferences), The Biochemical Society, 7 Warwick Court, High Holborn, London WC1R 5DP, UK.
10-14 September Berlin	VIth International symposium on molecular recognition and inclusion. Further information from: General Secretariat, Congress Organization Company, Office in Berlin, P.O. Box 460440, D-1000 Berlin 46.
11-13 September Reading University, UK	Second international conference on separations for biotechnology. Further information from: Prof. D.L. Pyle, Biotechnology Group, Department of Food Science and Technology, Reading University, Reading RG6 2AP, UK.
13-14 September Paris, France	European Science Foundation - Network on Developmental Biology: Local and long-range signals in development. Further information from: ESF Network on Developmental Biology, Netherlands Institute for Development Biology, Uppsalalaan 8, 3584 CT Utrecht, The Netherlands.
12-16 September Cold Spring Harbor, New York, USA	Modern approaches to new vaccines, including prevention of AIDS. Further information from: The Meetings Office, Cold Spring Harbor Laboratory, Bungtown Road, Cold Spring Harbor, NY 11724, USA.
16-27 September Canterbury, UK	Advances in biotechnology; animal cell culture. Further information from: The British Council Courses Department, 65 Davies Street, London W1Y 2AA, UK.
17-20 September Sheraton St. Louis Hotel, St. Louis, USA	Agriculture - the decade ahead. Further information from: Freiberg Publishing Co. (AgTechnology '90), P.O. Box 7, Cedar Falls, IA 50613, USA.
17-20 September EMBL, Heidelberg, FRG	10th EMBO Symposium on the Molecular Biology of Vertebrate Development. Further information from: Dr. J. Tooze, EMBO, P.O. Box 1022.40, D-6900 Heidelberg, FRG.
18-20 September Hannover, FRG	Biotechnica '90. Further information from: Mr. Rainer Schwarz, Deutsche Messe AG, Messegelaende, D-3000 Hannover 82, FRG.
23-27 September Berlin	International symposium on the cholinergic synapse. Further information from: Mr. F. Hucho, Freie Universitaet Berlin, Institut fuer Biochemie, Thielallee 63, D-1000 Berlin 33.
24-27 September Leeds, UK	Biotech UK. Further information from: Biotech UK Information, c/o Prof. J. Bullock, University of Manchester, Manchester M13 9PL, UK.
24-27 September Cold Spring Harbor, New York, USA	Evolution: From molecules to culture. Further information from: The Meetings Office, Cold Spring Harbor Laboratory, Bungtown Road, Cold Spring Harbor, NY 11742, USA.
24-26 September Hotel Eden du Lac, Montreux, Switzerland	An intensive three-day course on selective delivery of therapeutic polypeptides and proteins. Further information from: Ms. F. Morgan, IBC Technical Services Ltd., Bath House, 56 Holborn Viaduct, London EC1A 2EX, UK.

26-28 September Glasgow, Scotland, UK	Bioflavour '90. Further information from: Ms. P. Moon, Elsevier Science Publishers, Mayfield House, 256 Banbury Road, Oxford OX2 7DH, UK.
26-27 September Royal Society of Medicine, London, UK	Gene expression under the microscope - recent advances in in situ hybridization. Further information from: Ms. F. Morgan, IBC Technical Services Ltd., Bath House, 56 Holborn Viaduct, London EC1A 2EX, UK.
26-29 September San Remo, Italy	International symposium on advances in neuro-oncology. Further information from: Fondazione Giovanni Lorenzini, Via Monte Napoleone 23, 20121 Milan, Italy.
27-28 September St. John's College, Cambridge, UK	International Conference on Bioseparations. New technologies in upstream and downstream processing. Further information from: Ms. R. Duke, IBC Technical Services Ltd., Bath House (3rd floor), 56 Holborn Viaduct, London EC1A 2EX, UK.
28 September The City University, London, UK	Parasite neurobiology. Further information from: Prof. D. Halton, Department of Biology, The Queen's University of Belfast, Belfast BT9 5AG, UK.
28 September Royal Society of Medicine, London, UK	Image analysis in microscopy - the unbiased picture. Further information from: Ms. F. Morgan, IBC Technical Services Ltd., Bath House, 56 Holborn Viaduct, London EC1A 2EX, UK.
30 September to 4 October Le Bischenberg, Obernai, France	Philippe Laudat Conferences - Biochemistry and pharmacology of the myometrium. Further information from: INSERM Symposia Department, 101 rue de Tolbiac, 75654 Paris Cedex 13, France.

<u>October 1990</u>

1-8 October Amalfi, Italy	Study workshop on development biology. Further information from: European Science Foundation, Network on Developmental Biology, Netherlands Institute for Development Biology, Uppsalalaan 8, 3584 CT Utrecht, The Netherlands.
3-6 October Crystal Gateway Marriott, Arlington, Virginia, USA	Fourth annual North American and 1990 international cystic fibrosis (CF) conference. Further information from: The Cystic Fibrosis Foundation, 6931 Arlington Road, Bethesda, MD 20814, USA.
3-7 October Cold Spring Harbor, New York, USA	Molecular neuro-biology of aplysia. Further information from: The Meetings Office, Cold Spring Harbor Laboratory, Bungtown Road, Cold Spring Harbor, NY 11724, USA.
6-12 October Tucson, Arizona, USA	3rd Congress of the International Society for Plant Molecular Biology: Molecular aspects of plant growth and development. Further information from: Woo Wester Conference Consultants, 2934 1/2 Beverly Glen Circle, Suite 383, Los Angeles, CA 90077, USA.
7-11 October Le Bischenberg Obernai, France	Philippe Laudat Conferences: Basic and clinical aspects of plasminogen activation. Further information from: INSERM Symposia Department, 101, rue de Tolbiac, 75654 Paris Cedex 13, France.
8-9 October Marburg, FRG	2nd IMT Symposium - Structure and function of eukaryotic transcription factors. Further information from: IMT Symposium, Institut fuer Molekularbiologie und Tumorforschung (IMT), Emil-Mannkopff Strasse 2, D-3550 Marburg, FRG.
8-10 October Capri, Italy	Third IIGB Meeting: Workshop on the molecular biology of major histocompatibility complex genes. Further information from: Dr. John Guardiola, International Institute of Genetics and Biophysics CNR, Via Marconi 10, 80125 Naples, Italy.
10-12 October Amsterdam, The Netherlands	European Science Foundation. Network on Developmental Biology: Advanced research workshop on retinoids in development and cancer. Further information from: ESF Network on Developmental Biology, Netherlands Institute for Development Biology, Uppsalalaan 8, 3584 CT Utrecht, The Netherlands.
10-12 October Milan, Italy	Course on molecular biology of hormone action in endocrinology and pharmacology. Further information from: The Organizing Secretariat, Fondazione Giovanni Lorenzini, Via Monte Napoleone 23, 20121 Milan, Italy.
14-18 October Le Bischenberg, Obernai, France	Philippe Laudat Conferences. Cell death: Mechanisms and functions in development, aging and disease. Further information from: INSERM Symposia Department, 101, rue de Tolbiac, 75654 Paris Cedex 13, France.
29-31 October Congress Palace, Florence, Italy	Plasminogen activators: From cloning to therapy. Further information from: The Scientific Secretaries, Department of Clinical Physiopathology, University of Florence, Viale Morgagni 85, 50134 Florence, Italy.

November 1990

4-11 November Trieste, Italy	ICGEB theoretical course: Molecular virology. Further information from: Dr. G. Tzotzos, ICGEB, Padriciano 99, I-34012 Trieste, Italy.
5-7 November Beijing, China	ICGEB colloquium (in conjunction with WHO/TDR): Diagnostic approaches to schistosomiasis. Further information from: Dr. G. Tzotzos, ICGEB, Padriciano 99, I-34012 Trieste, Italy.
5-30 November New Delhi, India	ICGEB practical course: Molecular basis of protozoan parasitism. Further information from: Dr. G. Tzotzos, ICGEB, Padriciano 99, I-34012 Trieste, Italy.
11-15 November Le Bischenberg, Obernai, France	Philippe Laudat Conferences: Immune response to proteins with recombinant epitopes - perspectives for vaccines. Further information from: INSERM Symposia Department, 101, rue de Tolbiac, 75654 Paris Cedex 13, France.
27-29 November Washington D.C., USA	Biotech USA - 7th annual industry conference and exhibition. Further information from: Gina Amatruda, CMC/Biotech USA, 200 Connecticut Avenue, Norwalk, CT 06858-4900, USA.

December 1990

11-14 December University of Warwick, Coventry, UK	Techniques and applications of molecular biology: A course for medical practitioners. Further information from: Dr. Rachel Strachan, Department of Biological Sciences, University of Warwick, Coventry, CV4 7AL, UK.

1991

20-22 February London, UK	First international symposium on immuno-therapy of rheumatic diseases. Further information from: Prof. G.S. Panayi, Rheumatology Unit, Division of Medicine, 4th Floor Hunts House, UMDS, Guy's Hospital, St. Thomas Street, London SE1 9RT, UK.
April	Wageningen Agricultural University offers an International M.Sc. programme in biotechnology. Duration: 1.5-2 years. Entrance: relevant first degree B.Sc. and entrance examination. Start: April 1991. Further information from: International Education Office, P.O. Box 453, 6700 AL Wageningen, The Netherlands.
16-18 July London, UK	2-D PAGE 1991 - an international meeting on two-dimensional polyacrylamide gel electrophoresis. Further information from: Conference Secretariat, 2-D PAGE 1991, Department of Cardiothoracic Surgery, National Heart and Lung Institute, Dovehouse Street, London SW3 6LY, UK.

H. SPECIAL ARTICLE

BIOSAFETY REGULATIONS IN DEVELOPING COUNTRIES*

by

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SUMMARY

Given the importance of biotechnology for developing countries, and particularly for their agriculture, there is a need to consider the issue of biosafety regulations. The regulation of biotechnology has evolved in general terms, in the developed world, from an initially quite restrictive and cautious attitude, to a more confident position as experience with these technologies accumulate and the confidence of the scientists in them increase. Because of this fluent situation it is advisable for developing countries to introduce such regulations only when enough experience exists in other countries or when a specific need arises. Biosafety regulations should be developed within a broader development policy context, paying proper attention to the infrastructure needed for an effective enforcement of them, as well as the need for adequate human resources and a positive public understanding of the issues involved in the development of biotechnology capacities. The most important issue is the maintenance of a proper balance between the safeguards for health and the environment and the fostering of the development and use of the biotechnologies. The leading role in these efforts should therefore be taken by the scientists involved and the organizations responsible for science and technology policies. International co-ordination and co-operation are

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crucial for biosafety regulations in developing countries, especially for smaller countries, because of the need for up-to-date information on world-wide experience in this field.

INTRODUCTION

Biotechnology has been characterized by conflict ever since its inception: early work was followed almost immediately by intense scientific and public debate over the need for regulation. This is understandable, as biotechnology is a powerful new means of manipulating life and has profound moral, ethical and safety implications. It generates fear because of its potential misuse and the unkown threats it may pose to public health and the environment.

This fear has to be overcome if biotechnology is to develop and be used productively. The creation of a climate of public trust is therefore one of the critical tasks to be undertaken so as to realize the great promises which biotechnology offers to industry, agriculture, health and other sectors. It is in this context that biosafety regulations have to be discussed.

The debate on biotechnology is not yet a hot issue in developing countries. However, there have been some incidents related to safety which highlight the dangers and importance of having a clear orientation about the rationale and limitations that need to be confronted in the development of guidelines for the regulation of this field in these countries.

In an attempt to contribute to this discussion this paper will begin by briefly discussing the importance of biotechnology in the less developed countries and some of the special dimensions that regulations have in their case. Secondly, we will analyse the situation of the regulation of biotechnologies in the developed world, with an emphasis on the United States of America because of the pioneering role of this country. Thirdly, the meaning of, and reasons for, safety regulations in developing countries will be discussed and the difficulties and limitations of developing and implementing them in these countries will be identified. Finally, some of the organizational and operational issues of the introduction of biosafety regulations will be presented. The discussion will have a strong agricultural and Latin America and the Caribbean orientation. Because of the authors' experience, institutional association and knowledge of the region, however, most of what is said also holds true for other fields and developing world regions.

Biotechnology in the developing world: opportunities and limitations

The importance and potential of biotechnology for the developing world countries is a direct consequence of the critical role the agricultural sector plays in these countries. In most of them this sector usually concentrates the largest share of the country's human and physical resources, which makes an increase of agricultural productivity an essential element for any development strategy.

It is in this context that we have to see the potential of biotechnology. First, are the issues related to the increasing concerns about the environmental impact and the sustainability of agricultural production. Traditional production strategies have in general been over-reliant on chemical and energy inputs to increase and maintain productivity. However, it is increasingly evident that it is not possible any longer to rely on high input strategies to meet future demands for increasing productivity. Future advances and breakthroughs in biological nitrogen fixation and pest and disease control, for example, made possible by biotechnology, will offer a whole new set of alternatives for reducing the ecological impact of high productivity agricultural production technologies.

Second, by permitting a much more flexible targeting of crops to specific environments, production situations and processing and marketing needs, biotechnology may also allow the bringing into production of new environments which previously were underutilized.

Third, there is the opening of a whole host of new possible uses of agricultural products in industry, which greatly impacts the extent and nature of intersectoral linkages essential for development. This is especially important in tropical regions, characterized by high levels of biomass production which is usually wasted or grossly under-exploited in the traditional production systems. Innovations in areas related to lignocellulose materials, unicellular proteins, natural products, large-scale cell cultures, fermentation technologies, etc., in many cases offer the basis for completely new industries and could greatly impact employment and overall sectoral productivity.

A fourth area of importance is related to genetic resources. Biotechnology offers the possibility of a much more efficient use of the available genetic base. Most of the developing world, and particularly the tropics, is characterized by its great genetic diversity of which to date only a very small proportion is properly exploited. Biotechnology offers a much more efficient approach for the utilization of this diversity as a factor of production.

The above discussion highlights some of the reasons why biotechnology is important to developing countries and why these countries cannot afford to stay out of the rush towards its exploitation. However, in fully incorporating it, they have to consider a number of special limiting factors. Developing countries have very little research and development capabilities and, in the short and medium term, will not have the resources to generate their own technologies. At the same time, there are critical investment capital shortages. Both aspects determine that it is very unlikely that a local biotechnology industry will evolve from domestic resources. In most cases, its development is going to be highly dependent on foreign technology and investment. This highlights a critical political dimension of the regulation of biotechnology, that of the dependence on external resources in an area which may have a critical impact in the country's development. When discussing regulation in the developed world, the questions of how it will affect the competitiveness of domestic firms and industries is frequently considered. In the less developed countries it is the access to the technology and not competitiveness *per se* which is at stake. Regulation has to recognize this and strike a fine balance between safety protection and assuring access to the technologies and the needed capital.

Regulating biotechnology: trends in the developed world

The regulation of biotechnology responds basically to three types of risk. The production of new or modified pathogenic organisms and substances

in research laboratories and their use in factories or in agriculture could clearly present individual and public health risks which are relatively easy to assess because of the information and experience available in this field. The release of genetically engineered organisms or products not pathogenic for humans could pose a health risk for other living beings and it could affect the ecological equilibrium or status of the ecosystem in an unforeseen way. For example, some new organisms could proliferate excessively, negatively affecting other organisms or the flow of nutrients in the system, thereby transforming themselves into pests. These risks are more difficult to assess because of the lack of information especially on the effects of the interventions in the general ecosystem. Finally, there are the risks derived of the genetic manipulation of human beings, with wide-ranging ethical and political implications.

Health and environmental regulations depend on the scale of activities undertaken. So for example research, which is done on a small scale, needs different regulations than industrial or agricultural use of recombinant DNA products.

Within the group of techniques and technologies generally included in the concept of biotechnology, the recombinant DNA technologies are the ones which triggered the regulation because of their power and potential widespread applications. But, increasingly, other technologies such as cell fusion, nuclear transplants, etc., are included in the regulation of the environmental release of their products.

Issues in biosafety regulations

The first initiatives to regulate biotechnology were taken by the scientific community after the first recombinant DNA experiments, when they proposed a series of procedures and review instances for these experiments at the famous Asilomar Conference, to be enforced by the scientists themselves and by the federal funding agencies in the United States. The objectives of these regulations were to ensure the proper containment of the risky organisms and products so as to avoid individual and public health risks. These initiatives were spurred by an awareness of the potential dangers involved and also by the fear these risks created in the broader community. This rapid spillover of the discussion into the political arena produced city council regulations in several towns in the United States even before federal regulations were enacted. The regulations that came out of this process are, strictly speaking, an outgrowth of the procedures traditionally used in laboratories to handle pathogenic micro-organisms.

With rapid advances in research and the consequent development of marketable products, the need to address public health and environmental risks in biotechnology has become urgent. Many of these products are living organisms and their intended use had first to resolve the question of their effects outside the laboratory or factory. This issue was taken up by some pressure groups in the United States, who through legal means challenged experiments planned in open fields, successfully delaying them for up to four years in one milestone case (the test of the effects of genetically engineered frost protection of crops, called ice-minus bacteria).

Discussion on the release of biotechnological products into the environment has been on two levels. On the scientific level, two arguments have been proposed. One, usually defended by microbiologists and plant and animal breeders, states that the biotechnologies are basically extensions of traditional ways of breeding plants and animals, used for many centuries with no deleterious effects on health and the environment. Therefore, no special regulations are needed. The other position, generally proposed by ecologists, recognizes that there are environmental risks involved, but that these are probably small. Nevertheless, there is a need to assess these risks scientifically as a requisite for the release of the products into the environment. Both positions are supportive of the further development of biotechnologies.

On a political level, other broader issues are implicit in the discussion on the safety and environmental risks of the biotechnologies. The first challenges to the release into the environment of recombinant DNA products were motivated not only by genuine concern with the risks involved, but also by a general opposition based on moral reasons (Thompson, 1987). This position, symbolized by Jeremy Rifkin in the United States, but quite widespread in Europe too, has joined forces with economic interest groups in various countries that seek to defend specific markets and products against the threats of the new products and their social and economic consequences. The regulatory approval process for these new products is used for these purposes. One example of this is the case of the bovine growth hormone (BHG) in the United States, opposed by farmer lobbies, whose approval has been delayed by the responsible federal agency.

Trends in biosafety regulations

Even without an extended and detailed analysis of the situation of the regulation of biotechnology in developed countries, which would be outside the scope of this paper, several world-wide trends can be identified in this regard. In the first instance, after some 15 years of experience, there is an increased confidence regarding the safety of the use of genetic engineering techniques in the laboratory by the scientific community. As a consequence, the initially strict safety regulations on research, basically an outgrowth of the self-regulating effort of the involved scientists, have been increasingly relaxed and will in future be handled within the same parameters as the work with hazardous organisms and substances in the laboratory (Karny, 1986). That is, genetic engineering will lose its special safety status as a research tool and at most will be a special case of the more general rules on pathogenic organisms and on good laboratory practices.

Similarly, the large-scale use of genetically engineered products and organisms in factories will be generally handled in the framework of hygienic and other regulations of the workplace, so as to ensure worker health (Karny, 1986).

In the case of environmental release, no such consensus of confidence exists to date. This is reflected in the continuous discussion and enactment of new regulations for the release of genetic engineering products in many countries, both at national and local levels (Greenberg, 1989; Tiedje et al., 1989; National Academy of Sciences, 1987; OECD). The strong commercial interests behind this issue will press for clear, progressively simpler and cheaper regulations, supported by the increased confidence of both scientists and the general public, as experience accumulates (Greenberg, 1989). The accidents, which

sooner or later will occur, will be taken as acceptable risks in view of the widespread and obvious benefits of biotechnologies.

The increasing importance of biotechnology, economically speaking, as a means for developing new products and increasing the productivity and quality of existing ones, will provide a strong incentive to utilize regulatory issues for the protection of competitive positions, both for individuals and groups of firms or countries. Safety and quality regulations have been used traditionally as weapons in trade wars between countries. Considerable effort has been invested internationally to control and regulate this use. Animal and plant disease regulations and standards are one example. But it has to be recognized that underlying many of these disputes are genuine differences in the perception and acceptance of risk for health and the environment, between different cultures and countries. This will be an important issue in the medium term for multilateral bargaining organizations as General Agreement on Tariffs and Trade (GATT), in view of the global tendencies towards an increasing integration of regional and world markets and of the corresponding development of new economic and political poles.

Biosafety regulation in developing countries

Given the nature of the potential contribution of biotechnology to economic and social development in the less advanced countries, the need and importance of effective and realistic regulatory schemes goes well beyond the moral imperative to safeguard individual and public health and the environment. First, the strengthening and further development of biotechnology in particular, and of science and technology in general, requires the support and trust of the general public. The existence of clear and comprehensive regulations to safeguard the general interest will be perceived as a sign that scientists are sincerely concerned for the public at large and are not the self-serving and socially insensitive community they are often accused of being. Only when this happens will there be the continued support and flow of domestic resources which is a necessary condition for sustained national technological development. Secondly, local safety regulations are needed so as to establish clear rules for international companies and research institutions. This, together with a framework for the legal protection of innovations in biotechnologies, is going to be one of the critical requisites for investment and location of production and research facilities in developing countries by these companies, an alternative which could be the most important means of gaining access to these technologies. Finally, there is the international trade dimension. Safety and sanitary regulations have been used to restrict access to given markets in the past and surely will eventually be used in this case also. The existence of them in developing countries can be an important bargaining element in negotiations for access to specific markets.

In spite of their importance and the fact that in many of the more advanced countries of Latin America, such as Argentina, Brazil, Chile, Colombia, Cuba, Mexico, Costa Rica and Venezuela, internationally accepted research in front-line areas using sophisticated state-of-the-art biotechnologies, is under way and in some of them small, locally owned, high-technology firms are successfully operating, yet biosafety regulatory schemes are still very weak.

No comprehensive information on the existence of biotechnology safety regulations in developing countries exists that we are aware of. In Latin America and the Caribbean, Mexico and Brazil introduced safety regulations for research in recombinant DNA quite early (Karny, 1986). The regulations of the Mexican general law regulating research in the human health area, promulgated in 1987, includes a chapter on recombinant DNA research (Estados Unidos Mexicanos, 1987). The Pan American Health Organization (PAHO) has internal guidelines for handling the support this organization gives to research involving recombinant DNA (PAHO, 1987); guidelines for the regulation of research on the level of organizations and countries were prepared jointly by this organization and the Inter-American Institute for Co-operation in Agriculture (IICA) in 1988 (IICA, 1988). No regulations exist for the release of recombinant DNA organisms into the environment in Latin America and the Caribbean that we are aware of.

At least one incident concerning biotechnology safety has occurred in the region. A United States research institute, sponsored by an international organization, carried out an experiment in a South American country involving the release of a genetically engineered micro-organism, without seeking any approval. This caused an outcry in the local scientific community which was echoed in the local press. The worst scenario had occurred for the developing countries - their use as guinea pigs for procedures not permitted in developed countries. Public opinion in Latin America has been sensitive to this type of problem because of cases of dumping of toxic wastes from developed countries, export of radioactive contaminated food from industrialized countries and local marketing of drugs and devices prohibited elsewhere.

Given the limited scientific and technological capabilities in general, and the state of biotechnology in particular, it is understandable that its regulation is not a political issue in these countries. In the scientific community, the lack of a tradition of private or public liability for damages is perhaps behind the very casual approach of scientists and research institutions to safeguards in their work, which would explain the surprising lack of safety regulations in most of these institutions in Latin America. Apparently, this is not a problem unique to developing countries, as shown by the same concern raised recently in Canada (see Canadian Agricultural Research Council, 1988). If there is an issue at all, it is the unequal standards and policies of developed countries vis-à-vis developing ones.

National strategies for biosafety regulations

Several alternative national strategies for biosafety regulation are conceivable in developing countries. At one extreme would be the adoption of very stringent regulations to safeguard public health and the environment from the potential abuses of international companies or governments, the downside of which would be negative consequences for the development of local capabilities. At the other extreme, there could be benign neglect of this issue or enactment of very lax regulations, as a means of attracting research and production facilities fleeing the strict regulatory climate in many advanced countries, which increases costs and delays the commercialization of products. This strategy, if it is feasible politically and would achieve the sought-after results, which is doubtful, would have to be a coherent part of a broader national development strategy based on the transfer of international technology.

The most sensible approach to this issue, in our view, is a wait-and-see strategy. The regulation of biotechnology in industrialized

countries is a relatively recent event and experience has shown that early rules did err in many aspects, not the least in the initial assessment of the potential dangers involved, leading to excessively tight regulations. It is therefore advisable to monitor this experience closely and to act only when a more stable situation exists or when there is a concrete need to act. For example, in several developing countries requests have been formulated to regulatory authorities in public health institutions and to authorities of research organizations for the controlled release of genetically engineered organisms. These authorities should proceed quickly to establish guidelines and rules for these experiments, perhaps even on an ad hoc basis, based on current world-wide experience. This approach has been recommended also for a developed country such as Canada (Beak Consultants Limited, 1987). To be able to do this, it is of fundamental importance to have quick access to information on similar cases and on the experience of other countries, which international technical co-operation organizations are in the best position to provide.

The international character of many biotechnology risks calls for a multilateral mechanism to regulate some of the relevant aspects (Canadian Agricultural Research Council, 1988; Karny, 1986). From the point of view of developing countries it is important to guarantee equal treatment by industrialized countries and multinational companies and to enact international regulations that do not hinder local efforts to develop a national or regional capability in the biotechnologies. As a general principle, just as on the national level, the international regulatory policy should not be captured by special national or regional interests (Thompson, 1987).

Requirements and limitations for the implementation of biosafety regulations in developing countries

No matter which strategy is chosen to formulate biosafety regulations in developing countries, there are a number of requirements and common difficulties that have to be confronted.

These general conditions and difficulties must be placed in the context of the effects of the current economic crisis currently experienced by most developing countries. The direct economic effect of the crisis on scientific and educational organizations combines with a general weakening of the state in its function as director of national economic and social development. This trend, supported by widespread ideas that the public sector has to significantly reduce its powers of intervention in many economic and social matters, has produced an anti-regulatory attitude in many countries, which could affect attempts to regulate biotechnology.

The global policy context

Regulations cannot be considered in isolation. They are a policy instrument and as such should be seen in the broader context of the development of biotechnology and in turn science and technology policies. To be effective they have to be conceived as playing an active role in the creation of the proper environment for the full exploitation of science and technology's potential contribution to economic growth and social development.

It is this interrelation that may be the greatest limitation for the implantation of effective regulatory systems in developing countries. In most cases, this hierarchical policy system (socio-economic, development-science and technology-biotechnology) does not exist or, if it does, is incomplete and not operative. Efforts to create regulatory schemes in such a context lack the needed "guidance mechanism" and run the risk of becoming formalities or what is worse, mere "control" instruments.

The infrastructure for regulation

Similar to the need for a broader policy set-up, biosafety regulation operates within the general legal and organizational infrastructure for the regulation of health aspects of food, pharmaceuticals, pesticides and the workplace. Most developing countries have such an infrastructure. In Latin America and the Caribbean, all countries have norms and regulations for the manufacturing and marketing of foods and pharmaceuticals, whose enforcement is frequently the responsibility of the health ministries or in some cases of specialized institutions. Agrochemicals are generally regulated by agricultural ministries, and many countries require the registration of seeds to be marketed locally. In the case of the regulation of working conditions, ministries and institutions responsible for labour relations are charged with their control and enforcement. Perhaps the weakest tradition is in the area of environmental controls, where only some countries in the region have institutions charged with protecting the environment.

In general, it can be stated that in Latin America and the Caribbean the tradition of regulating health and environmental aspects is weak, as demonstrated by the insufficient resources dedicated to it. This relates directly to an important condition needed for biosafety regulations, that is, the existence of organized public opinion and pressure groups interested in this issue, to produce the required political momentum for action when it is needed. In many countries of Latin America and the Caribbean, and in general in developing countries, there is no tradition of public or private accountability. Authoritarian cultures and histories explain this fact, which is one important hurdle to overcome for the introduction of biosafety regulations in these countries.

The need for human resources

The involvement and participation of the national scientific community related to biotechnology is crucial for an effective regulatory scheme. It is a source of indispensable technical expertise and can provide the basic conceptual and organizational support to any effort in this field. The same may be said of the involvement of the local biotechnology industry and of the firms in related fields with actual or potential interests in biotechnologies, as well as of technical personnel in public organizations charged with enforcing health and environmental regulations in the country. This human resources dimension may eventually prove to be the most critical aspect to the implementation of an effective biotechnology policy and regulatory scheme.

Most developing countries in Latin America, Africa and Asia are constrained by huge external debts, reflecting profound structural failures in their development strategies. The economic crisis, induced by the debt problem in these countries, has severely affected the education and science and technology sectors, and in general a very important setback in terms of resources invested in these activities and other indicators of scientific and technological capabilities has been experienced. Perhaps the most dangerous development for the long-term perspectives of these countries is the net

loss of scientists they are suffering, due to emigration, but also because of change to other, more lucrative, careers.

Positive public understanding

Also needed is participation of the general public, including the media (Canadian Agricultural Research Council, 1988). Media understanding of the issues involved in the development of a national or regional capability in biotechnologies - concretely, the journalists responsible for science, health, agriculture and industrial development - is crucial for the creation of supportive public opinion and the avoidance of an atmosphere of fear which could produce extreme regulatory reactions.

SOME ORGANIZATIONAL AND OPERATIONAL ISSUES

Any initiative to introduce biosafety regulations in a country has to deal with several practical organizational and operational aspects.

Leading organization in biosafety strategy

The most important concern, from the perspective proposed in this paper - biosafety as part of a broader policy for the development of local capabilities - is the maintenance of a proper balance between the safeguards for health and the environment and the fostering of the development and use of biotechnologies. This balance will require that the initiative for the development of biosafety regulations comes from the persons and institutions most knowledgeable about it; that is, the scientists involved and the organizations responsible for the fostering and development of science and technology. In many Latin American and Caribbean countries, there are already specific committees for the development of biotechnologies; these should be the organizations charged with the development and introduction of biosafety regulations.

Jurisdictional aspects

Another question is the definition of what institution will enforce the regulations. This field overlaps most of the existing mandate of regulatory organizations, which could generate confusion and bureaucratic frictions and conflicts. The existing regulatory organizations, on the other hand, lack the specialized personnel for the proper monitoring and assessment of the different technologies and products involved. This situation calls for effective co-ordinating mechanisms to bring together the different agencies involved in the issue under the scientific leadership of the organization charged with the development of biotechnology in the country. Such a mechanism has been proposed recently for Mexico (Arroyo and Waissbluth, 1988).

The proposed co-ordinating mechanism has to create, as an important step in the fostering of a local biotechnology capability, a "single desk" approach to current requirements established for biosafety regulations (Canadian Agricultural Research Council, 1988). The existence of different regulatory organizations has the potential of creating a regulatory tangle which would be very negative for any local efforts, especially to develop and market commercial biotechnology products.

International co-ordination

The general weakness of developing countries in the biotechnologies and in health and environmental regulations makes an international or regional approach to biosafety regulations very attractive. On the other hand, many of the risks involved are international by definition, since they are ecological or epidemiological in nature, and as such do not respect national borders.

This has been recognized by many international technical assistance organizations, which have taken initiatives in this sense. The formal or informal co-ordination efforts between these organizations lessen duplication of efforts, and are therefore of utmost importance.

International co-operation

Many developing countries are simply too small for the development of a significant effort for the use and adaptation of biotechnologies. Their only alternative is co-operative ventures with similar countries or more developed ones. If this is true for the use and research in biotechnologies, it is also true for biosafety regulation efforts, which should be taken up by the existing subregional or regional co-operative institutions.

CONCLUDING REMARKS

Regulations of biotechnology and biosafety have evolved as the new technologies have matured and more experience and information has become available. The tendency has been towards a greater confidence in the new technologies and more relaxed regulatory systems.

The relevant issues on biotechnology and biosafety have different dimensions in developed and developing countries. The lack of overall policies, of trained personnel, and of public awareness in the developing countries are part of the reason for this, but most important is the existence of different overall development priorities. In developing countries, the priority is to acquire as quickly as possible the required capabilities in biotechnologies so as to solve pressing social and economic problems.

Clear regulatory mechanisms are of great importance since they are going to have a critical impact on the local development of the field. They will have to strike a fine balance between the need to protect public interests and the desire to attract local and foreign investment that will develop a local capability in biotechnology.

In setting up effective regulatory schemes, a series of limitations, such as the lack of regulatory traditions, of scientific capabilities and of resources, as well as a number of organizational and operational issues, such as the existence of a leading organization in biosafety initiatives, the need for an inter-agency co-ordinating mechanism, and for effective international co-ordination and co-operation have to be considered.

This paper has discussed these issues in a general way and from an agricultural development and a Latin American and the Caribbean countries perspective. Specific aspects will, however, have different expression and implications in different countries, depending on their economic structures and their level of scientific and technological development.

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