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Genetic Engineering and Bio-technology Monitor

Issue No. 41 and 42 March 1993
(Double Issue)

Special article: Mushrooms - trends in production and technological development, by Professor S.T. Chang, Dept. of Biology, The Chinese University of Hong Kong, and Professor P.G. Miles, Dept. of Biological Sciences, State University of New York at Buffalo, USA.

Distributed free to a targeted audience in developing countries

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A. NEWS AND EVENTS

UNIDO News

UN Genetic Centre independent

The UN's International Centre for Genetic Engineering and Biotechnology based in New Delhi and Trieste is to become autonomous in 1993, with the potential to serve as a powerful commercial agent for the transfer of biotechnology to the developing world.

The UN estimates that one third of the world's food potential is currently lost through inadequate control of insects, diseases and weeds, increasing to around 40 per cent for Africa. Biotechnology could help to reduce this loss substantially.

The centre will become independent of both the UN and the Governments individually associated with its activities, but the national organizations in 40 countries being set up in affiliation to the body will continue to serve as focal points for the exploitation of genetic engineering.

The institution was established in 1983 under the auspices of the United Nations Industrial Development Organization (UNIDO) and is involved in many research projects ranging from the control of diseases such as hepatitis, malaria and human *Papilloma* virus to agricultural research into pest- and stress-resistant crops.

A key role of the centre has been to train scientists from developing countries in basic genetic engineering and biotechnological research techniques.

UNIDO officials met in October 1992 to finalize arrangements for the centre's independence. Its $72 million budget for the 1992-1996 work programme has already been appr d.

The officials also considered a proposal for a task force of experts and marketing service to be set up to improve collaboration between academia and industry and speed up commercialization of biotechnology discoveries. (Sour e: *European Chemical News*, 28 September 1992)

MUSHNET

Development of an international network for bioconversion of waste materials to food and useful products by edible fungi

The bioconversion of waste materials to food and useful products by fungi is an environmentally sound biotechnology for sustainable development which has already had an impact at national and regional levels, and there are predictions that this impact will continue to increase. The impacts of this biotechnology have favourable socio-economic and employment effects and can be without serious legal, ethical, or safety consequences, when issues of biosafety are taken into account and properly addressed.

Enormous potential benefits are to be derived through the wide-scale introduction into developing countries of processes for cultivating edible mushrooms using as growth substrates the huge quantities of lignocellulosic wastes generated annually through the activities of the agricultural, forest and food-processing industries. These include a product having a high content (18-35 per cent dry weight) of protein with balanced amino acid composition that could serve to enrich the human diet in regions suffering from a shortage of high-quality protein. Edible mushrooms have high vitamin and low fat content, good flavour qualities and recognized tonic qualities. Mushroom protein can be produced with greater biological efficiency than protein from animal sources and relatively little input is required in terms of large-scale equipment, facilities, capital and land. Thus, edible mushroom cultivation is particularly applicable to situations where large-scale capital-intensive operations are inappropriate. Cheap, locally available lignocellulosic materials, such as straw, sugar cane bagasse, corn cobs, cottonseed hulls, peanut hulls, coffee wastes from agriculture, as well as waste cotton fibres, waste-paper products, and sawdust available from industrial activities can be used as growth substrates. In addition, harvesting and post-harvest processing requirements are minimal, and the overall process employs relatively simple technology. Furthermore, since edible fungi usually reduce the lignin component of the lignocellulosic growth substrate and thereby increase the accessibility of polysaccharide components, a spent substrate residue can be used as an animal feedstock. Alternatively, the spent residue may serve as a valuable soil conditioner. There is a growing realization that edible mushrooms represent a source of high-value metabolites (e.g. flavour compounds, anti-tumour and immunopotentiating agents, and hypocholesterolemic compounds), and as such, they also have considerable potential for future industrial development. Wide-scale introduction of bioconversion technology is perceived to be of particular relevance to the immediate and long-term needs of many developing countries in many parts of the world.

Professor S. T. Chang is an internationally-recognized authority in the field of edible mushroom cultivation and has received several international awards for his contribution to mushroom biology. He is considered to be largely responsible for the successful development of mushroom cultivation techniques in China during recent years. He will serve as consultant to UNIDO in the creation of an international network for mushroom cultivation and bioconversion technology, with special emphasis for helping developing countries.

A MUSHNET column about activities, including mushroom cultures collections, research in progress, and

commercial and industrial applications, that are taking place in the UNIDO MUSH network will be regularly included in future issues of the UNIDO *Genetic Engineering and Biotechnology Monitor*. Groups interested in participating in the network are invited to write to UNIDO's Biotechnology and Genetic Engineering Unit in Vienna, Austria.

Bioconversion and mushroom cultivation technology

The huge quantities of lignocellulosic wastes that are generated annually through the activities of the agricultural, forest and food-processing industries constitute a valuable resource if the appropriate bioconversion technology is applied. One highly efficient form of bioconversion occurs when these agricultural wastes are used as substrates to grow different types of edible mushrooms. Mushrooms represent a source of high-quality protein, and are also reported to contain numerous high-value metabolites (e.g. anti-tumour and immunopotentiating agents, hypocholesterolemic compounds and flavourants). Moreover, the spent substrate residue left after mushroom harvesting can be used as an animal feedstock and/or a soil conditioner.

UNIDO recognized that bioconversion and mushroom cultivation technology have important roles to play in the economies of less developed countries and commissioned a report on the creation of a "Bioconversion and Mushroom Cultivation Technology Centre/Network". Listed among the suggested locations for the centre/network headquarters was Hong Kong and the territory will host the First International Conference on Mushroom Biology and Mushroom products, 23-26 August 1993. The Conference, organized jointly by the UNESCO Network for Microbial Resource Centres (MIRCENS) and the Chinese University of Hong Kong, is expected to attract between 300-400 participants from over 50 countries. UNIDO will contribute resource persons to the Conference.

Enactment procedures for the international centre/network will be initiated as an immediate follow-up to the Conference, the first step in this process being the setting up of a Steering Committee to undertake the detailed planning involved in establishing the centre/network and its future operation. Countries/institutions interested in participating in the Network are encouraged to send a letter of intent to Technology Development and Promotion Division, UNIDO, Vienna.

A special article on trends in production and technological development of mushrooms by Prof. S. T. Chang and Prof. P. G. Miles is found in this issue of the monitor. ("The Creation of an International Centre/network for Mushroom Cultivation Technology", S. T. Chang and J. A. Buswell, UNIDO, July 1992, 67 pp.)

Ghana's success in mushroom cultivation

Under the guidance of an expert from Thailand, Ghana began to produce mushrooms on a commercial scale two years ago. The success of the scheme should encourage other developing countries to embark on similar projects through South-South cooperation.

The expertise acquired by South-East Asian countries in mushroom cultivation is now being disseminated through South-South cooperation, and one of the countries to benefit is Ghana. Mushrooms have always grown wild in Ghana, and Ghanaians have for centuries used them as a meat substitute.

Ghana's humid, tropical climate is very favourable for mushroom farming, and the country is much in need of the additional supply of protein that mushrooms can provide. Consequently Ghanaians are taking enthusiastically to mushroom cultivation. Many of them have received training from the National Mushroom Development Project (NMDP), which is directed by Mr. Leslie Sawyeer.

In Ghana, as elsewhere, the advantages of mushrooms over other food sources include the following:

1. Mushrooms in their dried form have a higher protein content than any other vegetable product. They also contain a high concentration of essential vitamins and minerals, and are valued for their benefits to health, including the capacity to reduce blood cholesterol.

2. Mushrooms can be grown on a variety of waste products from agriculture or industry, such as straw, sawdust, coconut coir, corn cobs, cotton waste and banana leaves. Subsequently, these materials can be used as compost for other plants.

3. Once the technology has been mastered, cultivation requires relatively simple techniques and equipment.

4. A very small amount of land is needed for cultivation.

5. Mushrooms require a minimum of water and sunlight.

6. Mushroom cultivation can be done either as a full-time job or as a hobby.

The Ghanaian mushroom project uses six varieties: Indian oyster (*Pleurotus sajor-caju*), Bhutanese oyster (*Pleurotus cous*), abalone (*Pleurotus*

cystidiosus), American oyster (*Pleurotus ostreatus*), Jew's ear mushroom (*Auricularia polytricha*) and straw or oil palm mushroom (*Volvariella volvacea*).

The cultivation system adopted in Ghana is a standard method used in many parts of the world. The procedure begins with the preparation of compost. The most popular material is sawdust, which ideally should first be decomposed for two or three weeks by the addition of substances that encourage fermentation. The compost is then put into heat-resistant plastic bags about 13 inches long, and is heated to kill off any micro-organisms that might compete with the mushrooms for nutrition. When the compost is fully sterilized, the mushroom spawn is inserted. The bags are then kept in a darkened room for several weeks. When the mycelium has spread over the compost, the room is ventilated and a small amount of light is let in, causing the mycelium to develop into mushrooms. Finally the bags are opened and the mushrooms cropped.

Ongoing technical advice and support is provided to growers by the NMDP. For example, the project supports its graduate farmers by supplying them with bags containing the mixture necessary for mushroom production - although currently the demand for bags exceeds the supply.

It would be misleading to give the impression that mushroom cultivation is an instant solution to a country's protein problems. The initial capital outlay can present difficulties for an individual grower, and the growing process requires careful monitoring. However, provided there is adequate government support and supervision, the mushroom industry offers great hopes to developing countries, as the case of Ghana shows.

Although sorghum and cassava are important subsistence crops in Ghana, biotechnology research is mainly directed to the country's export crops (oil palm, cocoa and coffee). According to a recent survey by John Mugabe (ACTS Biopolicy Institute, Maastricht, the Netherlands), applications remain very moderate.

The Faculty of Agriculture of the University of Ghana currently concentrates on multiplying disease-resistant and high-yielding cocoa plantlets through clonal propagation. The Faculty also applies somatic cell culture techniques on the regeneration of cassava. Furthermore, thermotherapy is applied to eliminate viral and bacterial diseases of cassava.

At the National Agricultural Research Institute work is being conducted on the conservation of various indigenous crops through *in vitro* culture.

The Department of Veterinary Services of the University of Ghana develops vaccines against some of the prevalent cattle diseases, such as foot-and-mouth disease. (Extracted from *Cooperation South*, December 1992)

Mushroom growing: Learning the trade secrets

Anyone wishing to begin producing mushrooms will find a wealth of useful information in the recently published *Manual of Mushroom Cultivation* by Peter Oei (Tool Publications, Sarphistraat 650, 1018 AV Amsterdam, Netherlands). Topics covered by this comprehensive book include the basic biology of mushrooms, techniques of propagation, which species are suitable for particular climatic conditions, how to perform a feasibility study and how to find markets. The book is illustrated by numerous drawings and photographs.

For those seeking technical training or expertise in mushroom production, these are available from a number of sources in the developing world. Professor Anon Auetragul, who advised the Ghanaians on their mushroom project, remains happy to share his unique knowledge of the subject. His organization, the International Mushroom Society (Thailand), offers study tours of mushroom farms and on-the-job training for groups or individuals. The society provides expertise and equipment and prepares project proposals for mushroom development. It will supply free of charge Professor Auetragul's manuals on the cultivation of oyster, Jew's ear and straw mushrooms, published by the Food and Agriculture Organization of the United Nations (FAO). The address of the society is:

International Mushroom Society (Thailand)
2306 Phaholyothin Road
Bangkhen
Bangkok 10900
Thailand
Tel: (662) 579-4418
Fax: (662) 561-2591

Other developing country institutions offering training and expertise in mushroom cultivation include the following:

International Mushroom Society for the Tropics
Contact: Professor S. T. Chang
c/o Department of Biology
The Chinese University of Hong Kong
Tel: (852) 609-6286
Fax: (852) 603-5646

Indian Agricultural Research Institute
Division of Mycology and Plant Pathology
New Delhi 110 012
India
Tel: (91 11) 581474
Fax: (91 11) 575-2006

Institute of Applied Neotropical
Mycology (IMINAP)
Apartado Postal 701
Puebla 72001, Puebla
Mexico

College of Postgraduates
Department of Mushroom Biotechnology
Apartado Postal I-12
Puebla 72130, Puebla
Mexico

Quality Control and Training Centre
Department of Plant Pathology, Mushroom Unit
University of the Philippines
Los Baños, Laguna
Philippines

Atatürk Horticultural Research Institute
P.K. 15 Yalova
Turkey

An informative scientific journal in the field is *Micologia Neotropical Aplicada*, published in Mexico, which contains original papers on the cultivation and uses of tropical fungi. Inquiries should be addressed to:

D. Martínez-Carrera
Editor-in-Chief
Apartado Postal 701
Puebla 72001, Puebla
Mexico

UN and other organizations' news

Effective alternative to AIDS cure

While the search for a cure for AIDS continues, activists around the world are emphasizing programmes to slow the spread of the pandemic. The World Health Organization (WHO), which has led the effort to monitor the epidemic and the number of people infected globally, is working to identify those programmes which help countries slow the spread of the disease and effectively support those who are infected at a community level.

WHO, one of the co-sponsors of the Eighth International Conference on AIDS in Amsterdam last July, now has a staff of 400 working with more than 160 countries and territories. Its mandate is to coordinate a unified international strategy for the prevention and control of the human immunodeficiency virus (HIV) which leads to AIDS and to reduce the personal and social impact of HIV.

The evaluation of the 15 projects found that they brought about significant changes in behaviour and five revealed measurable reductions of HIV infection or sexually transmitted diseases, which make people especially vulnerable to infection with HIV.

The diagnosis and treatment of sexually transmitted diseases is one of the six new priorities of the WHO strategy, which has been greatly expanded to meet the epidemic's new challenges. The five other priorities are:

- Adequate and equitable health care for the growing number of HIV-infected people falling ill;
- Reduction of women's social vulnerability to HIV infection by improving their health, education, legal status and economic prospects;
- A more supportive social and policy environment for AIDS prevention;
- Immediate planning in anticipation of the epidemic's social and economic impact;
- A greater focus on conveying the compelling public health rationale for overcoming stigmatization and discrimination.

In an effort to promote community awareness and involvement to counter the disease, WHO has made the theme of World AIDS Day on 1 December "AIDS - A Community Commitment", stressing how vital it is for each community to pledge itself wholeheartedly to the fight against AIDS.

The human immunodeficiency virus has infected some 10 to 12 million men, women and children since the start of the AIDS pandemic, and around 2 million have developed AIDS. Some 500,000 cases in 186 countries have been officially reported to WHO. The figures are expected to multiply several times by the year 2000. As most of the men and women afflicted are in the prime of life, the results will devastate many communities, especially in parts of the world least able to cope. World wide, AIDS could deprive 10 million children of one or both of their parents by the turn of the century.

Researchers have found that about one third of babies born to HIV-infected women become infected themselves. Although this occurs mainly during pregnancy or birth, there is recent evidence that HIV can be transmitted from a mother to her child through breast milk. However, the majority of babies breast-fed by HIV-infected mothers do not become infected. Therefore, WHO and the United Nations Children's Fund reaffirm that breast-feeding should be the standard advice to all pregnant women, including those who are HIV-infected, in areas where the primary

causes of infant deaths are infectious diseases and malnutrition. (Source: *Development Forum*, September-October 1992)

An emergency health kit

United Nations agencies and other bodies are increasingly called upon to respond to large-scale emergencies and disasters that may occur anywhere in the world, and which may pose a serious threat to public health. All too often emergency appeals for drugs produce an avalanche of inappropriate, expired or poorly identified drugs from concerned citizens' medicine cabinets or the pharmaceutical industry itself.

In order to facilitate a swift and effective response with supplies to meet priority needs in the event of disasters, the World Health Organization (WHO), together with other aid agencies, has developed standard lists of the essential drugs and medical supplies that an emergency kit should contain.

The WHO-recommended kit has been adopted by many organizations and national authorities as a reliable, appropriate and quickly available source of essential medicines and equipment needed for basic medical care of displaced populations.

In collaboration with a wide range of international partners, and after field testing, the kit was revised. WHO has now produced a revised list of drugs and medical supplies to meet the needs of 10,000 people for about three months, under the title *The New Emergency Health Kit*. This publication is available in English, French and Spanish from WHO, Distribution and Sales, 1211 Geneva 27, Switzerland. Price: SW.Fr. 8/$7.20. Special price for developing countries SW.Fr. 5.60. (Source: *Development Forum*, September-October 1992)

United Nations Environment Programme (UNEP)

Press release, September 1992

From regulations to industry compliance: Building institutional capabilities

Most countries now have environmental laws and regulations to provide at least minimum environmental standards for industry. The environmental performance of companies which go above and beyond these should always be encouraged. But Governments also need to make sure that all companies, local or multinational, are equally complying with these standards to ensure the effectiveness and equity of environmental protection laws.

This new publication provides government officials and other concerned actors with some guidance on building institutional capabilities to implement their environmental laws with an integrated approach so that waste and pollutants are not simply transferred between air, water and land, but are actually reduced at source. It offers some ideas and concepts that can be adapted to local, social, economic and political situations to legally bind industrial facilities to established environmental standards and to check that they are meeting them. It shows, through examples of some countries' experiences, that incremental steps can be taken with even minimal personnel and resources when there is sufficient political will.

The report is divided into six sections. Part 1 provides a brief introduction. Part 2 sets the background of the policy planning, legislation, standard setting, permitting, implementing, enforcing cycle. Part 3 introduces the concept of integrated pollution control. Part 4 examines more closely the stage of establishing a permitting procedure. Part 5 looks at checking that the industrial facility is meeting the standards elaborated upon in its pollution permit and some of the essential elements of effective industrial inspectorates. Part 6 gives a general idea of the minimum resources an inspectorate requires, and some ways in which its costs can be covered.

Examples of the types of industrial activities which are controlled by certain countries and the European Community are given in the appendices. Actual examples of permits and procedures are also provided.

It is UNEP IE/PAC's hope that this technical report will help countries in their implementation of Agenda 21 and other decisions taken by Governments at the UNCED Earth Summit in June 1992.

ISBN 92-807-1342-X; UN Sales No. E92-III-D-11. 62 pages. Price: FF 200. Available from UNEP IE/PAC, 39-43 quai André Citroën, 75739 Paris, France. Telex: 204997; Fax: (33-1) 40588874. Also available from UN Publications, CH 1211 Geneva 10, Switzerland, or New York, NY 10017, USA.

Regulatory issues

Australian planned release: Canola - Protoplast fusion breeding lines, Pacific Seeds Pty Ltd.

A series of field trials is planned using canola lines derived from a protoplast fusion experiment. The protoplast fusion involved cytoplasm of *Brassica napus* (canola) and *Raphanus sativus* (radish). The material has been studied extensively in contained experiments and is known to only contain nuclear genetic material of *B. napus*.

It is anticipated that the varieties derived from the protoplast fusion experiment will show superior yield particularly under adverse conditions to the original parent line. The field trials are essential to establish if the lines show the expected advantages. If a significant

advantage is demonstrated over other canola lines then the material will be generally released in hybrid varieties.

The trials will take place in Queensland and New South Wales. Each site will be less than a hectare and will contain both varieties derived from the protoplast fusion work and varieties from Pacific Seeds' conventional breeding programme. If the trials are successful, more extensive work will be carried out in 1993 with a view to commercial release in 1994.

Because the plants are genetically identical to conventional canola, there is no anticipated impact on the environment in the short term associated with these trials nor in the longer term with a general release. The safety of the product for human or animal consumption is identical to conventional canola.

The work is part of a long-term canola breeding programme which Pacific Seeds has been conducting in Australia for 12 years. Close collaborative links have recently been established with programmes in North America and Europe, which complement the Australian programme. It is expected the work will substantially improve the performance of hybrid parent lines and hybrids and lead to greater productivity and profitability for Australian canola growers. (Contact: Jim McDonald or Greg Buzza, Tel.: (076) 301666) (Source: *Australasian Biotechnology*, Vol. 2, No. 5, October 1992)

Yeast Industry Platform recommends changes in EC rDNA regulations

According to the Yeast Industry Platform (YIP), "the current regulatory framework aimed at controlling recombinant-DNA activities in the (European) Community treats them in the same manner as the most dangerous processes and products, when no such danger is indicated by any evidence".

YIP - whose members include such companies as Alko (Finland), Boehringer Mannheim (Germany), Champagne Moet & Chandon, Pernod Ricard and Transgene (France), SmithKline Beecham Biologicals and Interbrew (Belgium), Guinness Brewing Worldwide (UK) and Unilever (Netherlands) - argues that "the regulatory framework for placing a product on the market must be based on the assessment of the characteristics of the final product - and not on the specific technology used in the production process."

YIP was formed in January 1991 and actively supports the current EC BRIDGE R&D programme, especially the project involved with sequencing the entire yeast genome. The total annual sales of YIP member companies are 180 billion ECUs and they employ 600,000 people. A short publication, *Yeast products, processes, prospects, impacts*, is available. Details from: The Yeast Industry Platform, c/o Tech-Know, Avenue de l'Observatoire, 2, B-1180 Brussels, Belgium. (Source: *Biotechnology Bulletin*, August 1992)

Guidelines on the use of animals in research

The Agricultural and Food Research Council (AFRC) has published a useful set of guidelines on this subject covering topics such as current legislation, genetic modifications, planning and design of experiments, education and training and conditions for funding research.

The chapter on genetic modification draws largely on the Advisory Committee on Genetic Manipulation (ACGM) Guidelines on work with transgenic animals (1989). Genetically modified animals or their products must not enter the food chain unless evaluated by the Advisory Committee on Novel Foods and Processes (ACNFP).

Details from: Agricultural and Food Research Council, Central Office, Polaris House, North Star Avenue, Swindon SN2 1UH. (Source: *EBIS*, Vol. 2, No. 3 (1992))

Social and ethical issues

Bioethics: A French approach

For a country with a relatively relaxed approach to most aspects of biotechnology regulation, France has been quick to adopt a clear position in the recent debate on bioethics. Given that several of the biotechnologies have direct consequences on human procreation and ownership of body parts and secretions, the French are to be applauded for their efforts to rush through this legislation.

Simultaneously, in the Council of Europe, Mme. Catherine Lalumière has proposed the drafting of a European Convention on Bioethics, ready for the common market in 1993. The French are keen to play a leading role in this sensitive area by attempting to implement legislation which follows the tenets of common sense as well as justice. Those areas directly involving biotechnology are relatively uncontroversial, for example an individual's genome is sacrosanct and must be protected except in the case of therapeutic intervention. Genetic fingerprinting is restricted to application by the courts of law. (Extracted from *BFE*, Vol. 9, No. 6, June 1992)

Ethics lobby forces rethink on growth hormones

After persistent pressure and a threat of legal action from an eminent critic of genetic engineering, the US National Institutes of Health agreed to suspend the

enrolment of children in two clinical trials of synthetic human growth hormone.

In a legal petition delivered to the NIH at the end of June 1992, Jeremy Rifkin's Foundation on Economic Trends, and the Physician's Committee for Responsible Medicine, threatened legal action if the NIH did not respond within 20 days to their concerns about the safety and ethics of the trials. In a letter delivered to the foundation, the director of the NIH said that after considering the issues raised in the petition, the NIH would call on independent experts to review its research on human growth hormone who will report their findings within three months. In the meantime, the trials will continue, but no new children will be enrolled.

Synthetic versions of the human growth hormone produced by genetically engineered bacteria are marketed in the US by Genentech and Eli Lilly. The Food and Drug Administration has approved the drug only for the treatment of children with pituitary dwarfism, who do not produce enough of the hormone themselves, but some paediatricians are giving the drug to children who are simply short.

The NIH is supporting two separate trials of the hormone. One is a study of the effect of growth hormone on girls with Turner's syndrome, a chromosomal abnormality which results in extremely short stature. The other trial is designed to test the effects on children who are very short for their age but have normal levels of growth hormone and normal growth hormone receptors. Boys in the study are projected to reach an adult height of no more than 160 centimetres, and girls no more than 145 centimetres, putting them in the bottom percentile for their age group.

In the trial, the children are given three injections a week of either the hormone or a saline placebo. The children are also given regular X-rays, blood tests and psychological testing. They are photographed naked each year to record growth. The study continues for each child for 10 years or until they reach their adult height.

The foundation's petition calls for a complete halt of the trial of healthy short children, and of the placebo arm of the Turner's syndrome trial. Lawyers for the foundation argue that giving these children a placebo violates federal regulations governing the participation of children in clinical trials.

The foundation's legal reasoning is modelled on a report published in 1989 by a team from the University of Nebraska Medical Center's Institutional Review Board, the body which reviews all research on human subjects. Researchers at the university had been asked to participate in a multicentre trial of human growth hormone in girls with Turner's syndrome, similar to the trial at NIH. Nebraska's review board concluded that the research did not comply with federal regulations, because the risks to the children given a placebo were greater than minimal, the placebo offered no benefit, and the research was not likely to yield vital knowledge. (Extracted from *New Scientist*, 15 August 1992)

General

Vaccines for Peace

An international vaccine-development programme could reduce the threat of biological warfare while improving health care in developing countries, a German scientist suggests in the current issue of *Politics and the Life Sciences*.

The proposed programme, called Vaccines for Peace, is the creation of Dr. Erhard Geissler, professor of genetics and head of the Peace Research Group at the Max Delbrück Centre for Molecular Medicine, Berlin. The programme would produce and distribute vaccines against bacteria, viruses and toxins that pose natural threats to health in many developing countries but that also could be used as weapons of biological warfare. There are dozens of such "dual-threat" agents, the more familiar of which include anthrax, several varieties of encephalitis and hepatitis A.

Rapid advances in molecular biotechnology and the break-up of the Soviet Union have increased the risk of biological and toxin warfare, Dr. Geissler warns. Vaccines for Peace could help minimize that risk, he argues, by providing incentives for participation in the Biological Weapons Convention (BWC), a treaty that bans the production or use of biological and toxin weapons. Participation in the BWC would be a prerequisite for joining Vaccines for Peace. The programme's vaccines and shared research would provide a powerful motive for developing nations to become parties to the treaty.

In the former Soviet Union, many scientists once employed by that country's 70 biological defence research institutes now are jobless and at risk of being recruited by countries interested in developing biological weapons. Vaccines for Peace could employ those scientists and make use of the institutes for peaceful purposes.

Vaccines for Peace would be administered by the World Health Organization and paid for by members of the United Nations with money saved through reduced defence spending and the elimination of redundant national vaccine programmes.

Dr. Geissler's proposal was the subject of an international workshop held in Biesenthal, Germany, in September 1992. The workshop, attended by scientists, doctors, diplomats and military affairs experts, was co-sponsored by the Max Delbrück Center for Molecular

Medicine and the Stockholm International Peace Research Institute (SIPRI). (Source: *Press release*, 2 September 1992)

Disease surveillance to expose biological warfare

If cholera broke out next week in Sarajevo, how would United Nations observers know whether the outbreak occurred naturally or was part of a destabilization campaign?

Covert use of biological weapons for sabotage poses a threat that could be reduced through a global system of disease reporting and investigation, microbiologist Marl. L. Wheelis of the University of California at Davis argues in the current issue of *Politics and the Life Sciences*.

While existing national surveillance technologies already can assure the world that no large-scale production of biological weapons goes undetected, small-scale development and use of such weapons could occur, Dr. Wheelis writes. Fear of exposure would deter such small-scale actions, Dr. Wheelis believes. What is needed, therefore, is a mechanism to detect hostile use of biological agents.

"We do not know enough yet about disease ecology to be able to predict most natural outbreaks", Dr. Wheelis writes. His proposal would build scientists' understanding of how diseases emerge and spread to enable them to distinguish between natural epidemics and hostile acts.

Dr. Wheelis's proposal would require developed countries to keep track of diseases in a manner similar to that of the US Centers for Disease Control, with doctors and health centres reporting all cases of certain diseases and providing field teams to investigate outbreaks at short notice. In developing countries, cooperating regional centres would be established to perform a similar function.

An investigating team would have reason to suspect warfare if molecular analysis shows the infectious agent to be a strain not known in that part of the world and unlikely to have been introduced there naturally, or if the disease exists in the absence of the required vectors or spreads in an unusual way.

In addition to reducing the likelihood of biological war, Dr. Wheelis concludes, "enhanced understanding of the ecology of human, veterinary, and crop diseases would result in a dramatic improvement in public health world wide, and it would suggest strategies for reducing crop and livestock loss that precipitate human starvation".

Politics and the Life Sciences is the journal of the Association for Politics and the Life Sciences. Editorial offices are located at Lake Superior State University. (Source: *Press release*, 2 September 1992)

Gene therapy gets green light in US

The first gene therapy treatment for lung cancer has received the unanimous approval of an important federal panel, bringing the once-rarified and experimental science of manipulating human genes to bear on the most common cause of cancer death in America.

The M. D. Anderson Cancer Center in Houston received permission from the Federal Recombinant DNA Advisory Committee to treat 14 patients suffering from non-small cell carcinoma, a disease often caused by smoking. Much remains to be learned before anybody will know how effective the approach is, experts said. The method devised is another first in the field of gene therapy, an attempt to add molecules that will switch off genes in the tumour cells thought to contribute to frenzied cell growth. (Source: *International Herald Tribune*, 17 September 1992)

Biorational insecticides grow while chemical products wane

While the overall world insecticide market will remain nearly stable during the next 15 years, sales of biorational insecticides are expected to grow rapidly, and at the expense of traditional chemical products.

The world insecticide market was worth an estimated $7.8 billion at the end-user level last year, with biorational products taking about $350 million of that. According to a new report from Decision Resources, an affiliate of Arthur D. Little Inc. in Burlington, Mass., the total insecticide market will actually decline to $7.4 billion by the year 2005, while biorationals will increase to over $900 million.

This scenario assumes the world-wide pesticide regulatory developments of the 1980s and 1990s will continue into the next decade. These incremental changes increase the cost of R&D and registration, more so for chemical insecticides than for most classes of biorational products.

The scenario also assumes that transgenic insect-resistant crops are not commercialized before 2005; these competitors to biorational insecticides do not require application by farmers and will eventually cut into all insecticide use.

If such crops are commercialized, Decision Resources estimate the total insecticide market will be slightly smaller than $7.3 billion. However, the difference in value would be more than compensated by the value of the insect resistance trait in transgenic crops.

Environmental pressures and consumer demands for healthy foods will promote these trends. Biorational insecticides are considered to be less hazardous to the

environment and safer to both pesticide handlers and the ultimate food consumer. Often, this more benign profile is reflected in less onerous regulatory requirements.

As a result, the R&D and product development expenditures necessary to meet registration requirements for a chemical insecticide may be ten times those for a microbial insecticide, the study finds.

Because of the major investments required, chemical insecticides are generally targeted at large markets, such as rice, wheat, corn, barley, soybeans and cotton. In contrast, biorationals are directed at specialties like vegetables, fruits and nuts.

Biorationals compete well in these niche crops where few chemicals are registered for use, Decision Resources say. They also enjoy success in markets where a single species of insect causes severe crop losses. (Source: *Chemical Marketing Reporter*, 28 September 1992)

Biotherapies to boost world anti-cancer market by 1997

With tremendous growth anticipated in immunotherapy and targeted-delivery pharmaceuticals, the world market for anti-cancer drugs could quadruple from $1.3 billion in 1991 to $5.4 billion in 1997 - at a compound annual growth rate of 26 per cent. According to *World Cancer Therapeutic Pharmaceuticals Market*, released by Market Intelligence of Mountain View, USA, immunotherapy drugs will grow from 30 per cent of the total anti-cancer market in 1990 to 53 per cent by 1997. Targeted-delivery treatments, currently in the research stage, are expected to reach the market in mid-decade and take a better than 20 per cent share within three years.

One of the most exciting advances, the report suggests, is the development of site-specific targeted delivery drugs, most notably monoclonal antibodies and liposome encapsulation agents. These carry therapeutics directly to malignant tissue, cutting the exposure of healthy cells to toxic chemicals. Immunotherapy drugs - such as interferons, interleukins and colony-stimulating and tumour-necrosis factors - are dramatically changing the market.

The market share of traditional chemotherapy agents will decline, from 61 per cent in 1991 to 26 per cent by 1997. Substitutes have been eagerly sought for these harsh drugs, which often seem to damage patients as much as they do tumours. Biotechnology companies, the report predicts, are likely to be earning more than half of that anti-cancer market revenues by 1997. Details of the report from RauCon Bioinformatics & Consulting GmbH, P.O. Box 1069, W-6912 Dielheim, Germany. (Source: *Biotechnology Bulletin*, September 1992)

Biotech firms show profits

The majority of biotechnology companies are shortening the time line to commercialization through alliances with major drug companies, which can bear some of the regulatory and marketing risks involved in launching a new drug. Chief executives responding to Ernst & Young's annual biotechnology survey say, in addition to R&D alliances, they favour giving big drug companies an equity stake in their firms.

Large to mid-sized companies, which are finding themselves lacking the overall resources to achieve profitability, often seek alliances with larger biotechnology companies. Unfortunately this year, regulatory setbacks killed the vast appetite for biotechnology initial public offerings, say Ernst & Young. After a large number of public offerings were accomplished over the last 18 months, with more than $5 billion raised, investors were put off by the derailment of several important products.

Despite the setbacks, the biotechnology industry had a record year for sales and revenues, which totalled $8.1 billion, up 28 per cent from 1991. The increase was driven by more than 20 therapeutic biotechnology products, 600 diagnostic products and new agricultural biotechnology products.

Product sales in 1991 and 1992 reached $5.9 billion, a 35 per cent increase from the previous year, while total revenues were $8.1 billion, up 28 per cent. Total market capitalization for the industry is about $50 billion, up from $35 billion in 1991 but down from a mid-year high of about $60 billion. (Extracted from *Chemical Marketing Reporter*, 28 September 1992)

Biotechnology: Key issues for the third world

The problem of mass poverty in the third world is essentially one of rural poverty. Biotechnology applications in rural areas could make a contribution to poverty alleviation if it is accompanied by widespread gains in purchasing power of the poor through the creation of increased employment opportunities in rural areas. The International Labour Office (ILO) has carried out a series of empirical case studies, which have shed light on a string of poverty-related issues and identified gaps in the knowledge base for future work.

Further information from: Iftikhar Ahmed, Technology and Employment Branch, International Labour Office, Geneva, Switzerland. (Source: *Biotechnology and Development Monitor No. 10*, March 1992)

Genetic diversity, profit for the developing world?

Professor Bob Thomas of Biotics Limited has since 1986 been promoting a phytochemical screening

programme with the objective of cataloguing commercially exploitable genetic resources in the developing world. Thomas is keen to see a repatriation of wealth to the developing world on the basis of royalty payments. The company was founded in 1983 as a spin-off from Thomas's activities at the School of Chemistry and Molecular Sciences at the University of Sussex, UK. Laboratory services are supplied on a contract basis by the University.

The European Commission has given its backing to the Biotics programme, supporting a number of regional screening programmes. Already Professor Thomas has secured the interest and financial participation of a number of major companies including Glaxo, the British Technology Group, SmithKline Beecham, and others. Biotics is supported by a University of Sussex programme which offers training facilities for scientists from the developing world.

Trainees might constitute the staff and managers of companies created in developing world countries with the objective of producing commercially interesting plant extracts. Biotics has supplied more than 2,000 samples of dried plants from Africa, Asia and Latin America to organizations concerned with the commercial screening of new biological activities. Biotics can support its commitment by offering a custom extraction service, which may tailor solvent extraction methods suitable for subsequent large-scale procedures. (Source: *BFE*, Vol. 9, No. 6, June 1992)

African AIDS toll

AIDS is expected to reduce the projected population in the African countries worst hit by the disease by 20 million during the next quarter-century, according to the latest United Nations world population projections.

Africa is the home of the 15 countries with the highest prevalence of HIV. By 2015, the UN projects that AIDS will be directly responsible for 13 million excess deaths in these countries (more than 13 million will die of AIDS but many of these would have died prematurely from other causes). In addition, AIDS deaths among women in their reproductive years will mean that about 7 million fewer children will be born.

In spite of this staggering toll, the UN says Africa's population is still expected to double by 2015. (Source: *Science*, Vol. 257, 18 September 1992, p. 1627)

Public perception of genetically manipulated organisms

When Europeans are asked about the risks of biotechnology, their concerns tend to focus on human safety and potential harm to the environment. In a useful review of the likely public reactions to the release of genetically manipulated organisms (GMOs), Dr. Shirley Lanning of Hill and Knowlton spotlights a series of question-marks. Jeremy Rifkin of the US Foundation on Economic Trends, she notes, argues that GMOs are potentially even more hazardous to the environment than chemicals because:

- They are alive and thus inherently more unpredictable when introduced into the environment;
- They can produce, grow, migrate and mutate;
- They cannot be recalled to the laboratory once released.

Specific risks which are perceived by the general public include the following. GMOs are seen as likely to:

- Be developed and controlled by a few large multinational corporations and cause harm to humans and/or the environment;
- Survive and spread;
- Transfer genetically engineered traits to wild or other species;
- Have unpredictable deleterious effects on the ecosystem;
- Result in reduced biodiversity;
- Adversely affect animal welfare, agricultural intensification, developing countries and other social and ethical issues.

Copies of *Biotechnology Update: Genetically Modified Organisms* from: Dr. Shirley Lanning, Eurosciences Communication, Hill and Knowlton (UK) Ltd., 5-11 Theobolds Road, London WC1X 8SH, UK. (Source: *Biotechnology Bulletin*, July 1992)

Central American network for cooperation in tropical diseases

This new network is being created within the Iberoamerican Science and Technology for Development Programme (CYTED-D), Biotechnology Subprogramme, under the acronym REDCEN. Its main aim is to stimulate interaction amongst Central American research groups in the use and standardization of new techniques for the diagnosis of some important tropical diseases present in the subregion. Some of the planned activities to be carried out by the network in the near future are: a Symposium on Tropical Diseases and Molecular Biology, to take place in Panama; and Advanced Course on Biotechnology Applied to Health, to be held in El Salvador; and a Workshop on Impacts of

Biotechnology Commercialization in Central America, to take place in Costa Rica. (Source: *Boletin de Biotecnologia*, Vol. 9, No. 1, July 1992)

Programme of agricultural research

The Cooperative Programme of Agricultural Research for the Andean Region (PROCIANDINO) originated in 1986 through an agreement between the Governments of Bolivia, Colombia, Ecuador, Peru and Venezuela and the Interamerican Development Bank. Its aim is to strengthen the capacity and quality of research and to transfer agricultural technology within the region. It has the support of the Interamerican Institute for Cooperation in Agriculture (IICA) as its administrator and co-financing agency. PROCIANDINO has recently started a second phase of its existence, which will continue until 1996. Its purposes will be to strengthen the exchange of experience and the training of manpower in areas such as biotechnology, informatics and electronics, as well as conducting studies on legislation and patents in this field. (Source: *Boletin de Biotecnologia*, Vol. 9, No. 1, July 1992)

HIV is making its mark in eastern Europe

HIV infection is following in the wake of the political and social upheavals of former communist countries of eastern Europe. The number of people with HIV is still small and, in general, AIDS in eastern Europe affects less than six people per million, compared to western European rates of about 100 per million. Nevertheless, all the conditions exist for rapid spread of the virus.

The patterns of infection across eastern Europe differ from country to country. In Czechoslovakia and Hungary, for example, the epidemic is mainly among homosexual and bisexual men. In Yugoslavia and Poland there has been a recent explosion of infection among intravenous drug users. This is in sharp contrast to the situation in Bulgaria, where only a very few cases have been reported, and the most likely route of transmission is heterosexual sex. Romania has seen an epidemic mainly among children, caused by the use of unsterilized needles and syringes and the once widespread practice of "microtransfusion", in which malnourished children were given small, repeated injections of blood or plasma as a tonic.

In general, official attitudes have changed greatly since the mid-1980s, when most of the communist Governments in eastern Europe were still denying the existence of a problem with AIDS in their countries. Governments now acknowledge the existence of prostitution and drug abuse and have abandoned their initial policies of mandatory testing of certain risk groups in favour of widespread voluntary testing and counselling.

The process of democratization has also made it possible for many marginalized and stigmatized groups to emerge and organize. Community-based organizations are now starting to play an important role in the response to the HIV crisis.

Government officials in Czechoslovakia and Hungary consider their large, indigent gypsy communities to be particularly susceptible to the spread of HIV. These groups are difficult to reach with information, because of the language barrier and their marginalization from mainstream society. Plans for outreach work have been thwarted by lack of funds.

The fundamental economic changes of the past few years have brought new difficulties threatening the effectiveness of national AIDS control programmes. Nations face severe economic crises as they struggle to introduce western-style market economies and update their industries. In addition, the old centralized health-care systems are rapidly being privatized.

In this atmosphere, AIDS is perceived as just one of many urgent problems, such as environmental pollution, competing for limited resources. Even the most basic medical equipment is in short supply, especially in Poland where the Government is immobilized by foreign debt and is struggling to afford HIV antibody tests. Few patients receive zidovudine. The limited supplies are reserved for those with most advanced HIV disease or for health-care staff who become infected at work. In a country where the typical working adult makes the equivalent of $500 a year, the idea of paying $5,000 a year for zidovudine is unrealistic. Even the prospect of being sponsored by western pharmaceuticals companies for taking part in clinical trials of anti-AIDS drugs is remote; the number of AIDS patients is still too small, and local clinical laboratory services too limited.

Many institutions have become heavily reliant on western charity for items such as disposable needles and syringes, HIV antibody test kits and supplies of zidovudine.

In Poland, many of the early phobias and negative attitudes among health-care staff, about working with HIV-positive people, are changing. Some of these anxieties are not entirely irrational. Poland has one of the highest incidences in Europe of hospital-acquired hepatitis-B infection. This situation appears to be improving slowly since the introduction of hepatitis-B

vaccination and better sterilization methods for medical instruments. Fortunately, HIV is not as infectious as the hepatitis-B virus. However, in the population at large, there still exists considerable intolerance towards infected people. At the grass-roots level, priests work closely with gay and HIV-positive people. A number of community centres and hospices for people with AIDS have been set up by the church.

What of the future? The WHO's Global Programme on AIDS has sent teams of specialists to help countries formulate and develop HIV education, testing and monitoring programmes. However, in many cases donors have failed to produce sufficient funds for the countries to implement the recommendations.

In the current economic climate, the chances of making significant progress in HIV prevention and care are not good. Not until the restructuring of these countries is complete, and the millstone of debt removed, can their prospects improve. (Extracted from *New Scientist*, 22 August 1992)

Genetically engineered foods get green light

The US Food and Drug Administration (FDA) has embraced the principle that the Government should regulate the products of genetic engineering, not the process by which they are created. Its proposed guidelines for the regulation of new varieties of foods, which had been expected for months, represent an unofficial endorsement of the idea that government agencies charged with preserving public health do not need special rules to oversee genetically engineered organisms.

The arguments that such special treatment is unnecessary has been made by scientists and the biotechnology industry in several reports over the past few years.* It has not convinced environmental groups, however, which argue that the safety of the nation's food supply is being compromised by an eagerness to help companies bring new products to market.

The proposed new guidelines state that foods developed using genetic engineering pose no new or special safety risks to the consumer and should be subject to the same standards of regulation as are applied to all other foods. The announcement said these new technologies will provide foods "that are tastier, more varied, more wholesome and that can be produced more efficiently".

The guidelines are consistent with the line taken by the competitiveness council, which has pushed for the elimination of unnecessary regulatory burdens on the industry. They are also in keeping with similar measures introduced earlier this year to streamline the approval process for biotechnology drugs.

The guidelines put the onus on industry officials to decide whether a new genetically engineered plant variety needs pre-market approval by FDA.

Several consumer protection groups are alarmed by the notion of industry policing itself. At the same time, the long-awaited guidelines are welcomed by the agricultural biotechnology industry, which lags far behind other sectors of the industry and has yet to bring a genetically engineered food to market in the United States. According to the industry's trade group, the Industrial Biotechnology Association, more than 50 crops produced through genetic engineering have been tested.

Under the new guidelines, foods developed through genetic engineering, including fruits, vegetables and grains, will be regulated within the existing framework of the federal Food, Drug and Cosmetic Act. The level of oversight will be based on the characteristics of the food and its intended use, rather than the method by which it was produced.

FDA expects that many of the gene-altered foods being introduced (as with most new plant varieties produced by more traditional breeding methods) will not require pre-market approval by the agency. However, pre-market approval and labelling will be required if the use of genetic engineering is shown to increase the concentration of a naturally occurring toxicant in the plant, to introduce an allergen (protein that can trigger an allergic response in some people) that is not commonly found in the plant or to alter the nutritional composition of the plant. Under the new guidelines, industry executives will need to pick their way through a series of "decision trees" to decide whether to consult

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* *Field testing genetically modified organisms: Framework for decision*, Report by the US National Academy of Sciences/National Research Council (Washington, DC, 1989); *Strategies for assessing the safety of foods produced by biotechnology*, report of a joint Food and Agricultural Organization (FAO)/World Health Organization (WHO) consultation (Geneva, 1991); *Exercise of federal oversight within scope of statutory authority: Planned introductions of biotechnology products into the environment*, document by the Office of Science and Technology Policy (OSTP) (Washington, DC, 1992).

the FDA when introducing a new genetically engineered plant variety.

One of the first genetically engineered foods to reach the grocery stores is likely to be the new Flavr Savr tomato from Calgene Inc. of Davis, California. Researchers at Calgene have isolated from tomatoes the gene that encodes the polygalacturonase enzyme, which causes fruit to soften. Reinserting the gene into tomatoes in a reverse or "antisense" orientation blocks as much as 99 per cent of the enzyme's production.

Interested parties have 90 days to submit comments to the FDA. But barring a groundswell of public opinion to the contrary, the proposed guidelines are likely to stand. (Extracted from *Nature*, Vol. 357, 4 June 1992)

Global pest resistance management training programme

Pest resistance is a serious global problem. Over 600 pests (insects, pathogens, weeds, etc.) are reported to have developed resistance to chemical pesticides. Several important pests have overcome or have potential to overcome resistance to plant defence mechanisms developed through conventional plant breeding and biotechnology. Durability of resistance is especially critical in the rapidly advancing area of plant genetic transformation, which is primarily focusing on the use of *Bacillus thuringiensis* genes to impart pest resistance in several important crops.

The pest resistance phenomenon often proceeds to overuse, misuse or mismanagement of chemical pesticides resulting in increased cost of control, environmental hazards, toxic residues in food and water, and loss of biological diversity. The overall negative ecological, economic and social impacts may in turn affect the long-term sustainability of global agro-ecosystems.

The need for pest resistance management therefore is urgent. Resistance management is the delaying or prevention of adaptation in pest species to any human health or plant protection mechanisms including chemical, cultural, biological or biotechnological control. Integrated Pest Management (IPM) is the comprehensive approach to pest management that utilizes multiple strategies including resistance management to reduce pest problems. Properly executed, resistance management within IPM programmes can lead to reduced pesticide inputs, long-term susceptibility of pest populations and a pest-stable ecosystem.

One possible approach to the growing pest resistance problem is to take advantage of what is already known. It has already been demonstrated that training of key personnel and technical cooperation can significantly reduce pest resistance risk. Through effective resistance management training, pesticide use patterns change and effective life-span of pesticides and host plant resistance technology increases. Effective resistance management can mean reduced pesticide use without loss of productivity of subsistence and commercial farmers.

With this realization, the Global Pest Resistance Management Training Programme at Michigan State University is planning to conduct a two-week summer institute from 25 July to 7 August 1992 to train scientists from developing countries. The summer institute will be the first formal international training programme which has ever been conducted to solve the serious and growing problem of pest resistance. The institute will attempt to create a dialogue among global scientists in developing and implementing resistance management actions or strategies within the context of IPM. In addition, participants will receive laboratory experience in resistance detection and diagnostic systems. Each participant will be provided with critical literature, institute monograph, monitoring tool kits, networking capabilities and "hand-on" resistance management experience.

Course content:

Concepts and principles of pest resistance management and integrated pest management (IPM);

Theoretical and applied evolution and population dynamics;

Pest resistance management to conventional pesticides:

- Insecticide resistance management
- Fungicide/bacteride resistance management
- Herbicide resistance management
- Nematicide resistance management
- Botanicals resistance management;

Pest resistance management in biotechnological pesticides;

Pest resistance management in germplasm developed through conventional plant breeding and transgenic plants;

Pest resistance management for biological and cultural control agents;

Pest resistance management and environment, human health and agricultural sustainability;

Collaborative project development and global networking in pest resistance management

For further details contact: Resistance Management Summer Institute, Michigan State University, 203 Pesticide Research Center, East Lansing, MI 48824, USA.

Science Innovation '93: New Techniques in Bimolecular Research

This meeting, to be held from 6 to 10 August 1993 in Boston, MA (Hynes Convention Center and Sheraton Boston) and sponsored by *Science* magazine and the American Association for the Advancement of Science (AAAS), will unite the innovators and end-users of problem-solving techniques and instruments at the forefront of biomedical research. Its mission is to stimulate discovery and foster communication and technology transfer among the increasingly interdependent scientific communities within academia, industry and Government.

Specific techniques and applications will be covered in plenary lectures and workshops covering the following: basic and clinical immunology, biomedical imaging, chemical and structural NMR, crop production, DNA amplification, DNA forensics, DNA sequencing, DNA structures, drug targeting/delivery/tracing, electrical measurements of mammalian cells in culture, fluorescent in situ hybridization (FISH), gene expression, gene therapy, gene transfer, high-speed liquid chromatography, computer identification of functional motifs, mass spectrometry, microscopy, non-isotropic detection, oncogenes and suppressor techniques, gene mapping, optical trapping (laser tweezers), preparative and analytical electrophoresis, protein structure determination, biomedical engineering and biomaterials, RNA, X-ray crystallography, tobotics, neural networks, nano technology, peptide technology, drug design, biosensors, pheromones, ESCA and surface analysis, patentins, automated workstations, organ culture, glycoproteins, and chaos analysis of biological rhythms. (Source: *Press Release*, AAAS)

International Conference on the Convention on Biological Diversity: National Interests and Global Imperatives

The Biopolicy Institute of the African Centre for Technology Studies (ACTS), with support from the Finnish International Development Agency (FINNIDA) and the Pew Scholars Programme in Conservation and the Environment, held a four-day International Conference on the Convention on Biological Diversity: National Interests and Global Imperatives on 26-29 January, 1993 in Nairobi, Kenya. The papers for the conference were prepared by leading researchers, scholars, policy analysts and practitioners in the field of biodiversity conservation and biotechnology.

The conference built on the findings of the 1991 Nairobi Experts' Workshop on Property Rights, Biotechnology and Genetic Resources organized by ACTS and the World Resources Institute (WRI) as well as research supported by the Pew Scholars Programme in Conservation and the Environment. The Nairobi workshop was held under the auspices of the Biodiversity Conservation Strategy Programme of WRI, the United Nations Environment Programme (UNEP) and the World Conservation Union (IUCN).

The conference addressed topics such as national sovereignty, new developments in international environmental law, *ex situ* conservation, *in situ* conservation, incentives for conservation, access to biological diversity, access to biotechnology, technology transfer, sharing of biotechnology benefits, biotechnoloy trade, intellectual property protection, biosafety, indigenous knowledge, biodiversity exploration, research and training, education and public awareness, information exchange, global lists, financial resources and mechanisms, implementation measures, technical and scientific cooperation, relationships between Parties and non-Parties, relationship with other conventions and agreements, relationship with other initiatives such as Agenda 21 and the Global Biodiversity Strategy, gaps in the convention and options for protocols.

The conference provided an opportunity to researchers, policy-makers, entrepreneurs and practitioners to review the outcome of the global negotiations on biodiversity and the future of the convention. The conference report and individual papers will be published through the *Biopolicy International* series. (Source: *Press Release*, ACTS)

Biodiversity Information Network: Call for further participation

Within the context of the Biodiversity Convention and Agenda 21, an international group established a Biodiversity Information Network to solve the problem of managing global diversity information. The network will disseminate and facilitate access to biodiversity information world wide. It will encourage the active involvement of all regions of the world. The first mission of the initiative is to ensure participation of the entire biodiversity community.

The workshop, sponsored by the International Union of Biological Sciences, the International Union of Microbiological Societies and the World Federation for Culture Collections, was held at the Tropical Data Base, Campinas, Brazil, 26-31 July 1992. Initial participants included scientists, non-governmental and governmental organizations.

The sustainable management of the environment and conservation of the biodiversity of plants, animals, micro-organisms and all living things depends on reliable and readily accessible information. Without information on the names, the location, activity and interactions of organisms in the ecosystem, appropriate policies, conservation strategies or remedial actions cannot succeed.

The amount of information currently in existence and soon to be developed is vast. It is scattered around the world and is not easily obtained. There is a clear need for a network to link these resources and make them readily available. The participants invite the active involvement of all individuals and organizations with an interest in the aims of the network.

The network to be established will be primarily electronic - linking databases and providing a communications system - but will use all other means of distributing information. The network will encourage exchange of data and ensure that the needs of developing countries are met. The information resource will be global and the participation of the developing world will be actively sought.

An interim steering group will provide support for the initiative and seek funding and sponsorship. Working groups have been formed to give technical, educational and administrative support to start the process of establishing the network.

Simultaneously with the workshop, on-line bulletin boards were set up in which several hundred interested people participated. From this it is clear that the initiative is attracting world-wide interest, reflecting the general recognition that information is an essential element in the underpinning of the Rio Convention.

The workshop was funded by the United Nations Environment Programme, Instituto Brasiliero do Meio Ambiente e dos Recursos Naturais Renovaveis, Programa de Formacao de Recursos Humanos para Areas Estrategicas, Conselho Nacional de Desenvolvimento Cientifico e Tecnológico, Financiadora de Estudos e Projetos and the British Council.

For further information contact:

Vanderlei Canhos, Base de Dados Tropical, Fundacao Tropical de Pesquisas e Tecnologia "André Tosello", Rua Latino Coelho, 1301-Parque Taquaral, 13087-010 Campinas, SP, Brazil. Tel: +55 192 427022, Email: dora@bdt.ftpt.ansp.br.

John McComb, World Conservation Monitoring Centre, 201 Huntingdon Road, Cambridge CB3 0DL, UK. Tel: +44 223 277314, Email: johnm@wcmc.co.uk, BT Gold 75: DBI0710.

Barbara Kirsop, Microbial Strain Data Network, 307 Huntingdon Road, Cambridge CB3 0JX, UK. Tel: +44 223 276622, Email: msdn@cgnet.com or BT Gold 75:DBI0005.

Anthony Whitworth, Association for Progressive Communications, 2284 Railroad Drive, Fairbanks, AK 99709. Tel: +1 907 4798129, Email: anthony@igc.apc.org or anthony@gis.lter.alaska.edu.

Hideaki Sugawara, World Data Center for Microorganisms, The Institute of Physical and Chemical Research, RIKEN, Saitama, Japan. Tel: +81 48 4621111, Email: r35118@rkna50.riken.go.jp.

(Source: *Press Release*, September 1992)

First Arab Exhibit and Second Arab Conference on Perspectives of Modern Biotechnology

The above events are scheduled to take place between 24 and 28 April 1993 in Amman, Jordan. The objectives are to enhance interest in biotechnology-related research and applications, investment opportunities in Arab countries in industry, agriculture, environment, etc., and on barriers facing such investment projects, as well as to enhance efforts in the Arab countries to develop biotechnology-related infrastructure and regulations and assist in developing mechanisms of regional cooperation.

Conference themes will cover world-wide biotechnology-based innovations, with emphasis on what is most relevant to Arab countries, i.e. agricultural and industrial applications, R&D in these areas and promotion and commercialization of biotechnology-based investment projects.

Further details may be obtained from Mr. Hassan Charif, Organizing Committee, Second Arab Conference on Perspectives of Modern Biotechnology, ESCWA, P.O. Box 927115, Amman, Jordan. (Source: *News Release*, 9 December 1992)

First International Conference on Mushroom Biology and Mushroom products

The United Nations Educational, Scientific and Cultural Organization (UNESCO), the Network for Microbial Resource Centres (MIRCENS) and the Department of Biology of the Chinese University of Hong Kong have organized the above conference for 23 to 26 August 1993 to take place at the Shatin Town Hall, Hong Kong.

The conference will be jointly sponsored by international agencies and industrial corporations with an interest in mushrooms and their products. It will serve as a forum for participants from both developed and less-developed countries to present and share the most recent advances in mushroom biology and mushroom products, and to explore opportunities for future research and cooperation. The conference will also allow participants from academic, industrial and government sectors to interact in identifying the needs and potential for wide-ranging exploitation of mushrooms in such areas as food production, nutrition and health care, as well as waste bioconversion.

The conference will cover all aspects of mushroom biology and mushroom products and will consist of plenary sessions, oral and poster presentations and round-table discussions. Full details will be published in a second announcement later in 1993.

Further information may be obtained from: Professor S.T. Chang, Chairman, Organizing Committee, 1st International Conference on Mushroom Biology and Mushroom products, Department of Biology, The Chinese University of Hong Kong, Shatin, NT, Hong Kong. Tel: (852) 609 6286/609 6348, Fax: (852) 603 5646. (Source: *Press Release*, November 1992)

IUMS congresses: 7th International Congress of Bacteriology and Applied Microbiology Division; 7th International Congress of Mycology Division

The Czechoslovak Society for Microbiology has announced the holding of the above congresses to take place from 3 to 8 July 1994 in Prague. The general structure will consist of symposia and poster sessions in bacteriology and applied microbiology and mycology, while selected topics will be organized as interdivisional symposia and/or in the form of workshops or colloquia. A call for abstracts will be made during the summer of 1993 when the second announcement will be published, which will also contain the final congress programme, social events, etc. Further details may be had from: Secretariat IUMS Congresses '94, Institute of Microbiology, Videnska 1083, CS - 142 20 Prague 4, Czechoslovakia. (Source: *Press Release*, November 1992)

Eleventh Australian Biotechnology Conference

The 11th Australian Biotechnology Conference will be held from 20 to 24 September 1993 at Observation City Resort Hotel, Perth, and is sponsored by the Australian Biotechnology Association.

The Conference is being planned to attract all those interested in the science and the commercial development of biotechnology. The theme is "Asian-Australian Biotechnology Cooperation", reflecting the growing importance of biotechnology in Asia and Australia, and will foster collaboration in both research and commercialization. Major areas of interest in scientific and commercial aspects of biotechnology will be covered. The programme includes keynote lectures by invited speakers who are leaders in their fields, colloquia, workshops and poster sessions. The Nancy Millis Oration, sponsored by CSL, will also be delivered. UNESCO will sponsor a symposium on applications of biotechnology in tropical agriculture.

Major themes include:

- Biosensors
- Plant biotechnology in agriculture, forestry and horticulture
- Applications of biotechnology to medicine and animal production
- Food, fermentation and bioprocessing
- Biotechnology for environmental management
- Biotechnology and minerals
- Marine and algal biotechnology
- Policy and regulation
- Investment strategies and case studies

Workshops are planned on the latest developments in:

- Ribozymes
- Polymerase chain reaction
- DNA sequencing and diagnostics
- Gene sequencing and computer management
- Automated micropropagation (plants)

- Fermentation

- Hybridomas

Further details may be obtained from Judy Sargeant, 11th ABA Conference, School of Biological and Environmental Sciences, Murdoch University, Murdoch, Perth, Western Australia 6150. Fax:+61 9 310 3505,Email: mgkjones@murdoch.edu.au.

Plant collections endangered in eastern Europe and Russia

More than half a million varieties of 2,500 plant species stored in gene banks in eastern Europe and the former Soviet Union are at risk, according to a report issued by the Food and Agriculture Organization and the International Board for Plant Genetic Resources. Immediate international assistance is needed to avoid the damage that could be caused from a depressed economy and a series of decisions to privatize plant breeding institutes without providing continued public funding for the gene banks associated with them.

The Soviets have collections unmatched elsewhere because of the work of Nikolai Vavilov, the first president of the Academy of Agricultural Sciences, beginning in the 1920s. But with funding for agricultural research programmes being reduced by as much as 80 per cent since the break-up of the Soviet Union, his emphasis on plant genetic resources is being abandoned.

Gene banks in the former Soviet Union are most at risk because of the lack of long-term storage facilities, at -20° C, for nearly 350,000 accessions at the Vavilov Institute in St. Petersburg and its 17 experimental stations. More than half the collection is kept in paper bags at room temperature in St. Petersburg, and another 120,000 items are stored at 5-8° C at Kuban. These accessions must be regrown, multiplied and dried every five years, a process that is labour-intensive, and there are insufficient funds for equipment to extend their life.

The fate of a quarter of the Soviet collection, mostly subtropical species, is even more uncertain. These stations are owned by the newly independent States but are poorly equipped compared with gene banks at Kuban and St. Petersburg. Moreover, the new Governments are unlikely to have either the resources or the interest to maintain this germplasm.

There is less risk that the eastern European collections will disappear because most are held in long-term storage facilities. But the harsh economic conditions still pose a serious threat: for example, at the Institute for Plant Genetic Resources in Sadovo, Bulgaria, with tens of thousands of accessions, compressors in one of the three cold rooms are broken and those in a second room are unreliable. If the remaining cold room ceases to function, the Institute does not have hard currency to buy the needed Russian spare parts.

In addition, most of the collections do not have funding commitments beyond the end of the year. With the institutes now obliged to produce and to sell seed to pay for essential staff and operating expenses, many are terminating support for gene banks. The idea that such facilities should be supported by the Government has not been embraced by the Governments of eastern Europe.

Although the situation appears grim, a relatively small infusion of cash could reap large dividends. Emile Frison, group leader in Europe for the plant genetics resources board, estimates that "$2.5 million over four to five years" would protect a multi-billion-dollar investment. He says that such a rescue package might buy enough time to persuade the relevant Governments that germplasm collections require public funds. (Source: *Nature*, Vol. 360, 19 November 1992)

Biodiversity Convention a "lousy deal", say US

America's biotechnology companies claim that the Biodiversity Convention signed at the Earth Summit in Rio will undermine the patents and licences which give them intellectual property rights over products and processes. They also fear that approval of the convention would have undermined their Government's tough stance on intellectual property rights in the latest round of negotiations for the General Agreement on Tariffs and Trade (GATT). The convention is intended to preserve the Earth's great variety of species, but it also has provisions for transferring technology from rich to poor countries.

Biotechnology companies in Britain have a different interpretation of the convention. They see it as recognizing that intellectual property rights must be respected. In the rest of Europe, the industry is undecided. (Extracted from *New Scientist*, 4 July 1992)

Pyrethum and biotechnology

AgriDyne Technologies, a Utah, USA-based biotechnology company, received in April 1992 a US$1.2 million grant from the United States Department of Commerce to develop and produce a genetically engineered pyrethum to enable the United States to become self-sufficient in the supply of this natural pesticide.

Pyrethum is extracted from the flower heads of pyrethum (*Chrysanthemum cinerariaefolium*) plants grown by some 195,000 farmers in East Africa. The growing environmental concerns about the harmful effects of synthetic pesticides have greatly expanded the demand for pyrethrins. To benefit from the booming demand, Kenya, the major exporter of pyrethrums, has attempted to boost production with the help of micro-propagation on superior clones.

The United States has been importing pyrethrums worth about US$ 100 million. The objective of the Department of Commerce grant is to develop a natural pyrethrin substitute through cell culture.

This research if successful has the potential of adversely affecting the export earnings and a source of livelihood of nearly 200,000 small farmers in a number of East African developing countries, *viz.* Kenya, Tanzania and Rwanda. (Source: *RAFI Communique*, June 1992)

B. COUNTRY NEWS

Australia

New commercialization group starts

The government-backed Australian Technology Group is now getting under way following the $30 million investment by the Government announced in February 1992. The objective of the Australian Technology Group is to provide the range of services required to translate Australian research and technology into products and services that can be delivered to the Australian and international markets on a fully commercial basis.

The Australian Technology Group arises from the recommendations of the Block Task Force on Commercialization of Research. That task force found that the existing technology transfer bodies did not possess the resources, expertise, nor charter to widely source, supply and negotiate technology transfer and lacked adequate finances. The Australian Technology Group plans to provide the full range of services involved in the commercialization of technology.

CSIRO's commercialization arm, Sirotech, is to be wound up early in 1993. It is understood that its patent and legal services will become part of the CSIRO corporate structure and the commercialization activities of science and technology will be transferred to the six CSIRO Institutes. (Source: *Australasian Biotechnology*, Vol. 2, No. 6, December 1992)

European Community

The Concertation Unit for Biotechnology in Europe (CUBE) is no more

Under the umbrella of wide-ranging changes in the organization of R&D within the European Commission, the Concertation Unit for Biotechnology in Europe, CUBE, has been dissolved, its staff dispersed and its responsibilities taken under the wing of the Biotechnology Coordination Committee headed by Mr. David Williamson, Secretary General of the EC.

As the biotechnologies have grown from an R&D-based activity to an increasingly important component of global economic activities, it became increasingly difficult to maintain a cross-disciplinary mandate from within the shell of Directorate General XII of the European Commission (Research and Technology). The move rationalizes the situation and deflates a number of inter-service tensions.

CUBE was conceived in 1984, officially entering the world in 1985 as a component of the Biotechnology Action Programme. CUBE is effectively a direct consequence of the FAST chapter, especially as its director throughout its existence was Mark Cantley, author of the "Towards a Bio-Society" report.

CUBE has used its limited resources to act as a catalyst for action by more wealthy structures both inside and beyond the European Commission. Under Cantley's leadership, CUBE has been influential beyond its means, cherishing transparency even though this runs counter to the prevailing practices of the EC.

Mark Cantley did a great deal for European biotechnology. Among the achievements of his team was the creation of a framework for setting sugar and starch prices as feedstocks for industrial processes. This move, at a stroke, made the EC internationally competitive for carbohydrate feedstock-dependent biotechnologies. (Source: *BFE*, Vol. 9, No. 9, September 1992)

EC paves way for law on genetically altered foods

The Commission of the European Communities has signalled that it intends to introduce new controls on genetically altered foods. Under proposals approved by the Commission earlier in the year, all genetically altered substances - used to alter the taste, smell or texture of food and to improve production, storage and manufacturing methods - will need to be screened before they are introduced into the food chain.

If the proposed law is adopted by the 12 Member States, the EC would have powers to ban some substances - or to insist that food products containing them should be labelled.

The Commission says that patent applications have already been filed covering novel foods such as low calorie fats, virus-resistant mushrooms and potatoes, and fast fermenting yeast. (Source: *Biotechnology Bulletin*, July 1992)

Proposed novel foods directive

The text of the Commission Proposal for a Council Regulation on novel foods and novel food ingredients has been published. (Official Journal of the European Communities (92, C190/04)).

Article 7 will be of particular interest to biotechnologists:

The Regulation places a duty of care on those marketing a food containing a new substance or organism with no established history of food use to carry out a safety assessment.

Where it is necessary to submit for authorization the Scientific Committee for Food (SCF) which is constituted of 17 independent eminent scientists will be asked to give an opinion. The SCF is currently developing an approach to novel foods, including foods from biotechnology.

Under a proposal for scientific cooperation on which the Council recently agreed a Common Position national scientific bodies are required to give support to the SCF and institutes in non-EC countries can be involved.

Where the food or food ingredient falling under the scope of this Regulation contains or consists of a genetically modified organism within the meaning of article 2, paragraphs 1 and 2 of Council Directive 90/220/EEC on the deliberate release of genetically modified organisms, the information required in the request for authorization mentioned in article 6 shall be accompanied by:

- A copy of the written consent, from the competent authority, to the deliberate release of the genetically modified organisms for research and development purposes provided for in article 6(4) of Directive 90/220/EEC, together with the results of the release(s) with respect to any risk to human health and the environment;

- The complete technical dossier supplying the information requested in annexes II and III of Directive 90/220/EEC and the environmental risk assessment resulting from this information.

Articles 11 to 18 of Directive 90/220/EEC shall not apply to food or food ingredients falling under the scope of article 6 which contain or consist of a genetically modified organism.

In the case of food or food ingredients falling under the scope of this Regulation containing or consisting of a genetically modified organism, the decision mentioned in article 6 paragraph 2 shall take account of the environmental safety requirements laid down by Directive 90/220/EEC.

The Commission is currently examining the relationship between the novel foods proposal and a draft under consideration updating current seed directives with a view to implementing the "one-door one-key" policy so that novel food considerations can be dealt with at the time of application for registration of a variety. (Source: *EBIS*, Vol. 2, No. 4, 1992)

Implementation of Directives 90/219/EEC on Contained Use of GMMs and Directive 90/220/EEC on Deliberate Release of GMOs

Since the adoption of both Directives in April 1990, experts on biotechnology from the 12 Member States have met regularly, at first as the Group of National Experts on Biotechnology and then as the Committees of Competent Authorities, to discuss details of implementing the Directives (see *EBIS* 6, p.7). The objective has been to reach agreement by consensus on a uniform and clear interpretation of the text, and also to prepare a number of documents referred to in the Directives. Handbooks for both Directives have now been published by DGXI, which bring together the results so far achieved.

The handbooks provide guidance for the implementation of the Directives and are intended to assist the competent authorities in their work, to guide those intending to work with GMMs or release GMOs and generally to inform interested groups and the public at large. (Source: *EBIS*, Vol. 2, No. 3, 1992)

Biofuel subsidies loom as opponents battle on

Encouragement of biofuel use in Europe is a long-standing Commission aim, but its commitment to the issue has accelerated visibly since the GATT negotiations forced a compromise on agricultural policy earlier this year. The latest draft Directive emerged in March 1992 with clear emphasis on raising farm incomes and ensuring continued employment of land forced out of use under Common Agricultural Policy reforms.

The Directive proposes tax incentives on biofuels to encourage their development. The excise duty on bioethanol and biodiesel is to be limited to 10 per cent of the corresponding levy on mineral oils. The intention is to lift use of biofuels in gasoline to 10 per cent from the current 5 per cent ceiling. This will require additional capacity of 5m ton/year of bioethanol, almost ten times the existing 600-650,000 ton/year industrial ethanol market according to one estimate.

The implications of the directive are serious for existing ethanol, MTBE and fatty acid markets. Though ethanol is not currently used directly in gasoline to any great extent, its established markets could be seriously distorted as seasonal surpluses and shortfalls in agriculturally generated feed force bioethanol producers to seek short-term alternatives. Crop variations of as much as 2m ton could arise on the volumes envisaged by the EC.

The EC also argues the measures will reduce energy imports and bring environmental benefits associated with lower carbon dioxide emissions. Opponents argue that there are no scientific grounds for environmental claims, while similar subsidy programmes in the United States and Brazil do not bear out the European market expectations and have generated significant technical difficulties (Extracted from *European Chemical News*, 29 June 1992)

France

Transgenic plants ready for approval in France

France may be the first nation to opt for the wholesale approval of transgenic animals and plants. Projects concerned will involve the release of engineered viral vaccines, food industry bacteria and both food plants and animals. France has approved over 100 field releases of transgenic plants, against 230 or so in the USA. Amongst the plants tested in France are rape, beetroot, maize and potatoes, about half genetically engineered treated for herbicide resistance. Given the stringency of the Commission du Génie Biomoléculaire's (CGB's) oversight mandate, this pronouncement is an encouraging result for European biotechnology. So far about two thirds of the proposed studies have been authorized without objection by the CGB. The remaining proposals were approved after changes had been made. Such changes often involved no more than the provision of detailed data on the genetic constructs used.

The positive attitude of France is likely to be respected in a new law concerning "control of use and dissemination of genetically modified organisms" which is now under discussion in the Senate. The law should put France in a position of adherence within the context of the recent European directives. (Extracted from *BFE*, Vol. 9, No. 6, June 1992)

Germany

Information Centre for European Culture Collections (ICECC)

A major resource for biologists and biotechnologists has been set up with EC support at Braunschweig, Germany. The Information Centre for European Culture Collections (ICECC) is hosted by the DSM-Deutsche Sammlung von Mikroorganismen und Zellkulturen GmbH.

The ICECC provides a permanent secretariat for Community culture collections and a focal point for European scientists to seek advice and information on cultures and culture collections generally. It will coordinate the exchange of information between culture collections and provide an information service to users throughout the world.

Further information from: Katja Fröhlich, Information Centre for European Culture Collections, Mascheroder Weg, 1b, D-3300 Braunschweig. Tel.: +49 531 6187 15, Fax: +49 531 618718. (Source: *EBIS*, Vol. 2, No. 3, 1992)

Germany links biology centres

Germany has taken its first step towards improving its biomedical research by linking five large research centres. These include the large cancer research centre in Heidelberg and the Max-Delbrück Centre for Molecular Medicine in Berlin-Buch, Germany.

The network of institutes will share committees to oversee appointments and to evaluate the research done in each unit. Evaluation committees will be international and research activities in the institutes will be loosely coordinated.

The German Ministry of Research, the BMFT, which adopted the recommendations of its advisory committee on biological research, has donated US$ 2.6 million to get the project going. Harald zur Hausen, director of the Heidelberg Centre, hopes that this marks the start of a more extensive national cooperation involving other research institutes, but university departments are expected to resist the idea because of their concern about a loss ofindependence. (Source: *Nature*, Vol. 358, 23 July 1992)

Germans wary of DNA fingerprinting

Criminal convictions cannot be made on the evidence of DNA fingerprints alone, according to a ruling by the German Federal Court of Justice at Karlsruhe. Although DNA fingerprints are still admissible, judges must ensure that the prosecution has supporting evidence.

The decision overturns a 1990 conviction for rape handed down by Lower Saxony's state court in Hanover. The Court of Justice now says research has brought the reliability of genetic fingerprinting into question. The probability that anyone else carried out the rape is only 0.014, says Christoph Zülch, a spokesman for the court. "But when you project that onto Hanover's male population, it means there are 35 other men out there who could have the same genetic material. That's 35 too many", he says.

DNA fingerprints taken from the suspect and the sperm were analysed at the Institute for Forensic Medicine in Hanover and found to match. They were then compared with DNA fingerprints from a random sample of "possible assailants" to determine the probability that another man in the area might have the same genetic make-up. The court also found this step lacking by the court. Zülch says the random sample may

not have accurately represented the true statistical average of Hanover's population. (Source: *New Scientist*, 19 September 1992)

Hungary

AGC in Hungary

AGC, the Cambridge-based agricultural biotechnology concern, is studying the possibility of establishing a Hungarian joint venture with the Gödöllö-based Agricultural Biotechnology Centre. The company has already completed a pre-investment feasibility study and believes there are grounds for collaboration.

Peter Barfoot, AGC's business planning manager, is hoping to establish a technology-for-equity swap which involves the UK company supplying its portfolio of insect resistance and other plant-derived genes in return for a stake in a new Hungarian company. Barfoot expects the new venture will produce a wide range of transgenic crop plants including rice, potato, sunflower, chili, and oilseed rape.

The Hungarians will conduct research using AGC technology with a view to developing transgenic versions of indigenous crops. The joint venture will conduct field trials of the new crops. "We will get royalties from sales of new varieties and will license transgenic germplasm to plant breeders", Barfoot says.

Hungary is very keen to develop biotechnology and has said that it will make funds available for joint ventures with Western companies. Nevertheless, Barfoot does not expect AGC's plans to advance until cast iron guarantees of financing are given. AGC expects a decision on the financing by the end of 1992. "If all goes well we would hope to start the joint venture in January 1993 and start the first field trials of transgenic potatoes in the summer". (Source: *Chemistry & Industry*, 15 June 1992)

India

India to produce ESCAgenetics' true potatoes

India will join ESCAgenetics Corp.'s hybrid true potato seed (TPS) producer/distributor programme. One kilo of TPS can yield about ten acres of virtually disease-free potatoes, while traditionally propagated tubers must be grown in cool climates, inevitably carry a certain percentage of viral infections and must be exported to hot climates at a rate of 20 tons of tuber seed to get an equal yield. If field trials are successful, India's Government is calling for a 15-million ton increase in production. India is one of 11 nations world wide that ESCAgenetics plans to collaborate with in TPS trials. (Source: McGraw Hill's *Biotechnology Newswatch*, 3 August 1992)

New national seed bank

India is setting up one of the largest national gene banks in the world to protect its plant genetic resources. But the project, a collaboration with the United States Government, has brought charges that India has sold out to foreign interests.

The gene bank, due to be completed in 1994, will be able to hold up to 800,000 seed samples, according to Rai Singh Rana, director of India's National Bureau of Plant Genetic Resources. Its purpose is "to undertake all aspects of exploration, collection, preservation and exchange of plant germplasm". Much of its work will involve building a national database of the extensive collections of plants held in laboratories, seed banks and botanic gardens all over India.

The Indian Government is paying 40 per cent of the cost and the rest is coming from the US Agency for International Development. In return, American scientists have access to seed and data for research.

India is the home of the original wild varieties of many major agricultural crops, including rice, beans, mango, banana and yam. Commercial varieties frequently need infusions of genes from wild varieties to maintain their productivity and to build resistance to disease. One estimate by independent ecologist Robert Prescott-Allen puts the annual value to the American economy of wild germplasm taken freely from other countries at $66 billion.

Conservationists warn that the Indo-US agreement establishing the project, which was signed in 1988, gives American seed companies open access to the gene bank but contains no rules on intellectual property rights. As a result, they say, strains developed using India's wild germplasm could be patented by Western companies without India receiving a penny.

At the Earth Summit and during negotiations for the Biodiversity Convention, India was among the most vocal nations asserting the right of nations to maintain control of their genetic resources. The convention contains clauses that encourage third world countries to demand both cash and access to biotechnological know-how in return for sharing their genetic wealth with other countries. This was one reason why the United States, alone among Western nations, refused to sign the convention.

However, the convention refers only to wild plants and excludes germplasm held in national seed collections. (Source: *New Scientist*, 11 September 1992)

Japan

MITI increases biotech R&D

The Ministry of International Trade and Industry (MITI) recently announced several new biotechnology-based programmes involving a wide range of chemical and pharmaceutical companies, who share the project's costs, contribute researchers and facilities, and - significantly, from the standpoint of international competition - get to commercialize the research results.

One of the key institutions through which MITI promotes the development of environmental conservation technologies is the Research Institute of Innovative Technology for the Earth (RITE), established in 1990. One RITE project is concerned with the development of high-performance bioreactor technology for the production of biochemicals. The bioreactors utilize the synthetic capacity of cellular reactions that occur under ambient temperature and pressure conditions. In this project, genes isolated from the energy-supplying systems of useful microorganisms are modified to optimize the production of cellulites and other desired substances.

The three newest projects show the increasing importance of DNA research. They include a project to apply genetic engineering to environmental monitoring. A second project involves sequencing DNA at high rates with high accuracy. The third project focuses on developing computer software to process "genetic information", including DNA sequencing and homology testing.

In the DNA sequencing project, Hideatsu Maeda, research scientist at the Research Institute for Polymers and Textiles (Tsukuba), says that the project will study carbon dioxide fixation by microorganisms.

In terms of computerization, says Masaaki Yamamoto, assistant director of MITI's Biochemical Industry Division, "there is currently little information technology concerned with biotechnology in Japan". That could change. The project will use a 1,000-processing-element parallel-processing computer developed as a result of MITI's recently concluded Fifth Generation Computer Project. (Source: *Biotechnology*, Vol. 10, October 1992)

Japan buys into gene project

The Government announced its decision to contribute $600,000 to the Genome Data Base in Baltimore in August 1992.

The Genome Data Base is the linchpin of international efforts in gene mapping, locating genes on the human chromosomes. Researchers working within the various national research programmes that make up the human genome project send their discoveries to the library. In return, they can see the "landmarks" found by others, their exact positions and the probes needed to locate them.

However, Japan's investment will not make it immediately easier for Japanese scientists to gain access to the database; although there is a GDB "node" in Tokyo, it is not yet linked to the academic network. This should happen in 1993. The domestic network will be run by a new body called the Japan Information Centre of Science and Technology, and will be linked to research centres such as the University of Tokyo's Institute of Medical Science and the Institute of Physical and Chemical Research. (Extracted from: *New Scientist*, 29 August 1992)

AIDS spending increase

Japan is at last waking up to the dangers of AIDS. The Ministry of Health and Welfare responded to a sharp rise in the number of reported cases of infection by human immunodeficiency virus (HIV) by requesting a fivefold increase in fiscal year 1993, starting on 1 April, for its tiny budget to fight AIDS. Nearly half of the proposed budget would go to research, with the rest invested in public education, screening, treatment and counselling.

Japan has few AIDS patients compared with the United States, Europe and some South-East Asian nations. The official total, including those who have died, stands at just under 500, but many cases are said to go unreported because of fear of discrimination. However, in the first six months of 1992, 226 new cases of HIV infection were reported, almost the same number as in the whole of 1991.

A change in the affected population is also driving the increased support. Many of those newly infected are believed to have contracted the virus through heterosexual sex, whereas in the past the majority of reported cases were among haemophiliacs and homosexuals. This development has heightened public concern and awareness of AIDS.

A significant portion of the increased budget will be used for public education. Ignorance and prejudice about AIDS are widespread: many hospitals refuse to treat those with AIDS for fear of frightening away other patients, while others refuse to acknowledge that they care for patients with HIV.

Only two hospitals, both in Tokyo, specialize in the treatment of AIDS patients - the Institute of Medical

Science of Tokyo University and Tokyo Komagome Hospital. The Ministry would like to establish similar centres in other parts of the country. Officials also plan to establish Japan's first hospice for the treatment of terminally ill AIDS patients, although critics say that the 20-bed facility falls woefully short of what is needed. (Source: *Nature*, Vol. 358, 27 August 1992)

Environment agency considers impacts of biotechnology

The Central Council for Environmental Pollution Control at Japan's Environment Agency set up an Expert Committee on Biotechnology in June 1989. After 16 meetings, the Committee produced a report on the environmental aspects of the deliberate release of recombinant organisms into the environment. The 50-page report, available in English, notes that there was a wide disparity of views among the Expert Committee's members on the risks and on the need to involve the public. Details from: Environment Agency Global Environment Department, Planning Division, 1-2-2-Kasumigaseki, Chiyoda-ku, Tokyo 100, Japan. (Source: *Biotechnology Bulletin*, July 1992)

Guidelines on gene therapy

Japan took its first step towards gene therapy in June 1992 when a committee of the Ministry of Health and Welfare (MHW) recommended the establishment of guidelines and the creation of a central committee to review research and clinical trials involving humans. But, although Japanese medical researchers are eager to follow the lead of the United States in this field, the Japanese must overcome fundamental weaknesses in the system of reviewing recombinant DNA research before they can begin gene therapy.

In Japan, there are almost as many guidelines and committees for recombinant DNA research as there are government ministries and agencies. The Ministry of Education, Science and Culture (MESC) has a committee to review proposals from universities, while the Science and Technology Agency (STA) has a parallel committee to deal with all other national research laboratories. On top of this, the Health Ministry, the Ministry of International Trade and Industry and the Ministry of Agriculture, Forestry and Fisheries each have guidelines for industrial applications that fall within their respective territories.

None of these committees or guidelines has so far addressed gene transfer in humans because the issue has been considered "taboo", but pressure from the medical research community and the pharmaceutical industry is expected to spur action by other government agencies.

The movement towards gene therapy highlights the problems that Japan faces in handling the ethical, social and legal issues arising from genetic research. The Government invests a tiny amount in these issues compared with what is spent in the United States, Europe, Canada and Australia. Japan has few lawyers, ethicists or social scientists familiar with the rapidly evolving field and those who do take an interest are "extremely conservative".

The Health Ministry produced more detailed guidelines at the end of 1992. In the meantime, the reactions of other government ministries and agencies to the preliminary plan are eagerly awaited. (Source: *Nature*, Vol. 358, 2 July 1992)

Kenya

Pyrethrin producing microbes threaten Kenya's exports

The United States plant biotechnology company, AgriDyne Technologies, recently announced that it will spend over US$ 3 million in the next three years to produce "natural" pyrethrins. These will be derived from a genetically engineered microbe containing a plant gene from *Chrysanthemum cinerariaefolium* (Pyrethrum). The flowers of this daisy-like perennial contain six insecticidal compounds collectively called pyrethrins. The compounds are extracted and used as a natural insecticide that is relatively safe for humans and mammals. Pyrethrum is currently mainly grown in East African countries, but also in Ecuador and Tasmania (Australia). The company claims that it will produce bio-pyrethrum within a price range of US$ 55-75 per pound, while the current wholesale price for technical grade pyrethrum extract is US$ 187.50 per pound.

If successful, this technique may enable the United States to become self-sufficient in the supply of this insecticide. According to the Rural Advancement Foundation International (RAFI), this technological development could prove economically devastating to some 195,000 East African farmers who cultivate pyrethrum flowers, given the fact that the United States are by far the world's largest buyer of pyrethrum. Especially Kenya's exports may be hit. Currently, over two-thirds of the world's pyrethrum production (amounting to approximately US$ 100 million) comes from flowers grown or dried in Kenya. Global demand for the environment-friendly insecticide exceeds supply. In recent years, the Kenyan Pyrethrum Board administered a tissue culture programme for the rapid expansion of high-quality Pyrethrum production. As a result of the superior clones, production in Kenya is projected to expand to record levels in the next few years, while the producer price continues to climb. AgriDyne's pyrethrin technology may rigorously limit the projected expansion, while the world market price for pyrethrum will certainly drop.

Rural Advancement Foundation International (1992), "Genetic Engineering of Pyrethrins: Early

Warning for East African Pyrethrum Farmers". *RAFI Communique*, June 1992.

African Centre for Technology Studies (1992), "New Threat to Kenya's Pyrethrum Exports". *ACTS Technology Alert*, 8 July 1992. (Source: *Biotechnology and Development Monitor* No. 12, September 1992)

Mexico

New sorghum release

ICRISAT's Latin American Sorghum Improvement Program (LASIP) has announced that another sorghum line developed jointly by ICRISAT and Mexico's national scientists has been officially released. Cultivar Istmeño was released in 1991 by the Instituto Nacional de Investigaciones Forestales y Agropecuarias (INIFAP) for cultivation in the drought-prone lowlands of the state of Oaxaca in southern Mexico. Istmeño is a white-grained dwarf variety suitable for manual or mechanized harvesting. Istmeño, which means "of the isthmus" in Spanish, was sown on about 5,000 ha during the 1992 season. Istmeño has been well accepted by farmers in this region due to its excellent grain quality, tolerance for drought, resistance to lodging, and high grain yield potential. (Source: *SAT News*, No. 11, July-September 1992)

The Netherlands

Biotech vandals strike again

The Dutch biotechnology industry is still bedevilled by a fringe of destructive activities, who are continuing to attack experimental plots and other industry projects.

Last September, a group calling itself "Fiery Virus" said it was responsible for the destruction of an experimental field of genetically manipulated maize plants. The group also claimed credit for an attack on a biotechnology exhibit at a major flower and agricultural show. The action will delay the research programme by at least a year.

Last year, similar attacks were carried out on fields of genetically engineered potatoes. Groups with similarly quaint names, such as the "Seething Potatoes", claimed responsibility. The Dutch home affairs minister then vowed to put a stop to the actions, and ordered the secret service to infiltrate the groups. This strategy has yet to bear fruit. (Source: *Chemistry & Industry*, 7 September 1992)

Pakistan

Collection in the wilderness

Pakistan's National Agricultural Research Centre and ICRISAT joined forces in a successful collection trip of wild species of chickpea in the far reaches of northern Pakistan. Seeds were collected from *Cicer microphyllum*, *Cicer nuristanicum*, and *Cicer macranthum*. This effort will make seeds of the two latter species available to researchers for the first time. Biodiversity and preservation of germplasm, as emphasized at the recent UNCED meeting in Rio de Janeiro, are of global concern. Such collection trips are therefore important. Dr. van Rheenen reported that, despite their isolation, the area's inhabitants of this rugged but beautiful area enthusiastically greeted the collection team. (Source: *SAT News*, No. 11, July-September 1992)

Peru

Genetic resources of Andean tubers

In cooperation with national institutes from Peru, Ecuador and Bolivia, the International Potato Centre (CIP) recently started to develop a gene bank for the less known Andean tuber crops *oca*, *olluco*, *mashua* and *arracacha*. In cooperation with the Research Centre of Andean Crops (CICA) of the University of Cuzco (Peru), for instance, a collection of more than 700 accessions of Andean tubers from southern Peru is maintained and characterized. CIP has applied electrophoresis to determine the genetic variation in this collection. It was found that the genetic diversity in some of the Andean root and tuber crops was very small in comparison to that found in potatoes or sweet potatoes. Interviews with local farmers confirmed that crop diversity in Andean tubers has decreased over the last decades.

The work on *oca*, *olluco*, *mashua* and *arracacha* complements CIP's activities on the conservation of potato and sweet potato germplasm. At present, seeds are maintained from more than 1,000 accessions of about 100 different wild potato species. The *in vitro* cultivated potato germplasm collection originally consisted of more than 13,000 samples. Through the application of electrophoresis, duplicate accessions could be identified and the collection reduced to 3,500 samples. Accordingly, the management of the collection has been significantly simplified.

CIP's recent involvement with the conservation of sweet potato germplasm required the construction of

additional storage space for *in vitro* cultures. At present, the sweet potato collection now consists of more than 2,300 accessions. Duplicates have been verified using the electrophoretic technique. Training in this technique applied to sweet potato germplasm has been provided to scientists from Peru, Jamaica and Colombia. (Source: *Biotechnology and Development Monitor* No. 12, September 1992)

Switzerland

Ciba renews genetic request

Ciba-Geigy (Basel) has renewed its request to Swiss authorities to test-plant a gene-manipulated corn. The company withdrew an earlier application in May 1992, but says it decided to resubmit the request after Switzerland's national referendum clearing biotechnology experiments. Plantings of the corn, which is resistant to the corn borer, have already been carried out in the United States of America, Argentina and France. (Source: *Chemical Week*, 21 October 1992)

Gene rules

Following a recent national referendum in which nearly 74 per cent of the voters called for regulation, the Swiss Government is drawing up a constitutional amendment aimed at preventing the abuse of genetic engineering. The Swiss chemical industry supports the proposed amendment and says it is in accordance with guidelines and practices already adopted. (Source: *Chemical Week*, 27 May 1992)

Uganda

Uganda to host AIDS vaccine therapy trials

Uganda will likely be the first developing country to test AIDS vaccines in a population at high risk of HIV infection. The initial trial will be a therapeutic vaccine, meant to boost the immune response of people who are already infected. Uganda is also first in line for a test of a vaccine designed to prevent HIV infection, the World Health Organization's ultimate goal.

WHO, together with several other health organizations, said it had identified four sites for efficacy trials of AIDS-prevention vaccines: Uganda, Thailand, Rwanda and Brazil. These countries have the high HIV-infection rates needed to judge a vaccine's efficacy and have shown they are eager to host trials. Last July, Uganda became the first country to present WHO with its "national plan" for such a trial. Thailand also is expected to offer a plan shortly.

In each case, WHO has pledged to test therapeutic vaccines first. Although WHO "emphasizes preventive vaccines", there is "strong pressure from all countries to start with therapeutic vaccines ... In areas where one-third of the people are infected, the population expects something that will have an effect within their lifetime".

A therapeutic vaccine trial in Uganda may start in Spring 1993. Researchers first will test the vaccine in small groups of people to ensure that it is safe, then conduct a wider trial. (Source: *Science*, Vol. 257, 7 August 1992)

United Kingdom

Guidelines on the use of animals in research

The Agricultural and Food Research Council (AFRC) has published a useful set of guidelines on this subject covering topics such as current legislation, genetic modifications, planning and design of experiments, education and training and conditions for funding research.

The chapter on genetic modification draws largely on the Advisory Committee on Genetic Manipulation (ACGM) Guidelines on work with transgenic animals (1989). Genetically modified animals or their products must not enter the food chain unless evaluated by the Advisory Committee on Novel Foods and Processes (ACNFP).

Details: Agricultural and Food Research Council, Central Office, Polaris House, North Star Avenue, Swindon SN2 1UH. (Source: *EBIS*, Vol. 2, No. 3, 1992)

Biotechnology Forward Plan published

The Biotechnology Directorate of the Science and Engineering Research Council (SERC) has published its "Forward Plan" which sets out their priorities for research and post-graduate training in biotechnology over the next ten years. The plan identifies four key areas related to bioprocesses and bioprocessing. It also reviews the state of the art in the following areas:

- Bioactive molecules and biocatalysis;
- Control and use of metabolism;
- Bioprocess operation and performance;
- Bioprocess monitoring and control.

The Forward Plan may be obtained without charge from: Dr. Doug Yarrow, Director, Biotechnology Directorate, Science and Engineering Research Council, Polaris House, North Star Avenue, Swindon, Wilts. SN2 1ET, United Kingdom. Tel.: +44 793411410, Fax: +44 793411033. (Source: *EBIS*, Vol. 2, No. 4, 1992)

United States of America

Agricultural Biotechnology for Sustainable Productivity project

New research opportunities have rapidly advanced among industrialized countries, while developing countries are often unable to keep pace. The US Agency for International Development (AID) addresses the discrepancy in national science and technology capabilities through collaborative programmes that seek to enhance the agricultural productivity of developing countries. The agency's first centrally-funded initiative in this area was the Tissue Culture for Crops Project (TCCP) based at Colorado State University (CSU).

TCCP-sponsored research sought to produce crops (wheat, rice and sorghum) tolerant to an array of stresses, including salinity, drought and acid/aluminium soil conditions. TCCP scientists and breeders in universities and international and national programmes developed research teams for each objective. Two of the most significant accomplishments from these teams were the registration and release of sorghum germplasm with improved tolerance to fall armyworm and to acid/aluminium soil conditions. Other work is ongoing regarding salt and drought tolerance.

TCCP also initiated a plant tissue culture network (IPBNet), which produced the first world-wide directory of tissue culture and biotechnology scientists working on crops and problems of immediate importance to developing countries. Networking activities also provided training at CSU in basic and advanced tissue culture and micropropagation techniques.

TCCP research programmes relied primarily upon somaclonal variation, tissue culture and *in vitro* selection to produce novel sources of genetic variation to be tested for agronomic fitness through field and statistical analysis. The approaches and the institutions involved were, however, found to be limited in their ability to successfully derive germplasm tolerant to the complex range of multi-genic, abiotic stresses, which the project proposal was originally written to address.

With these findings in mind, AID's Office of Agriculture began a multi-stage review of opportunities to support biotechnology, using both external as well as internal mechanisms. External evaluation of TCCP was undertaken, followed by the convening of an experts' panel under the direction of the National Research Council. This panel produced a report, *Plant Biotechnology Research for the Developing World*, published by the NRC in 1990, which looked at constraints on productivity in the developing world and relevant technologies to address these constraints in the near-term future, meaning three to five years.

The combined results of these investigations were then reviewed by in-country AID missions and national and international agricultural programmes. Based upon information from comprehensive review, it was decided to design a new project in plant biotechnology which would bring together public sector and commercial research efforts in an integrated product-development programme. The new project would be awarded following the peer review of proposals submitted to AID based upon a formal request for applications.

The proposal review process resulted in the award by AID of a cooperative agreement to Michigan State University in September 1991, to implement a new phase in its support for plant biotechnology. This project, titled "Agricultural Biotechnology for Sustainable Productivity (ABSP)", presents a change in research targets from those of TCCP. The purpose of ABSP is to mutually enhance US and developing country institutional capacity for the use and management of biotechnology research to develop environmentally-compatible, improved germplasm. The production of novel genes for resistance is now focused on biotic instead of abiotic stress; tissue culture research has shifted from somaclonal variation to rapid propagation of commercially important germplasm; and new direction has been given to efforts in genetic engineering.

Progress made by TCCP has been incorporated into the ABSP project. The IPBNet is being reinstated with new emphases; distribution of germplasm will be continued; and developing country collaborators are being sought from TCCP's original network. In this regard, ABSP is a direct follow-on effort to TCCP, adding to its foundation new aspects of biotechnology which include direct linkages with the private sector, expertise in biosafety and intellectual property rights, and proven abilities in various methods of plant transformation.

The establishment of ABSP's network and research collaborations will build upon the local network of scientists assembled through regional meetings held by TCCP in Thailand, Kenya and Costa Rica. ABSP thus becomes the first and only comprehensive biotechnology programme to utilize collaborative research teams which encompass the public and private sectors, field agronomists and breeders, expertise in biosafety and intellectual property protection, and a dedicated team of international specialists committed to the equitable use of biotechnology in global agricultural research. These teams provide ABSP with the flexibility to implement partnerships in commercially-oriented research as easily as research at land-grant institutions, and through national and international agricultural research centres.

The ABSP project envisages the integration of new technologies, such as plant genetic transformation and bioreactor propagation, into the mainstream of international agriculture. With a primary emphasis on genetically-engineered pest and pathogen resistance, ABSP focuses on the potential to reduce chemical input

and produce high-quality plant material at a lower economic and environmental cost than conventional methods alone.

Unlike basic research programmes, ABSP takes an integrated management approach to the development of specific research products and their transfer to developing country partners. ABSP has set for itself the following guiding principles:

- Maintain a highly focused research programme concentrating on specific crops and technologies;
- Implement a product-oriented research style, which links public and private sector institutions in the USA and developing countries;
- Link product-oriented research to policy analysis of intellectual property and biosafety to ensure product commercialization in an environmentally responsible manner;
- Maintain a geographical focus on specific centres of expertise; develop a critical mass for the multi-disciplinary team which will transfer technology to national programmes;
- Build a far-reaching network that provides access to information for developing and developed countries world wide. Serve as a forum for the exchange of ideas and information on biotechnology in relation to sustainable agriculture;
- Establish linkages with other organizations such as the CGIAR Agricultural Research System and the Association of Biotechnology Companies (ABC).

ABSP is a project in which biotechnologists will interact as a team with other disciplines of agricultural science to produce specific products, in close collaboration with developing country partners.

Further information is available from: Bruce Bedford, ABSP Networking Specialist, 412 Plant and Soil Sciences Building, East Lansing, MI 48824-1325, USA. (Source: *Bio Link*, Vol. 1, No. 1, 1992)

The research approach of the ABSP project

By the beginning of the 21st century, plant biotechnology could play a major role in world markets and become one of the most important technical forces in the economies of the industrialized nations. If speculation becomes reality, this revolutionary technology will contribute significantly to the sustainability of agricultural production systems through increased crop yields, a reduced reliance upon chemical pest control and increased marketing alternatives for producers. Biotechnology may enhance nutritional content, lengthen post-harvest storage duration, improve resistance to biotic and abiotic stress factors, substitute one crop for another or a synthetic product for a crop product, and lead to the substitution of renewable energy sources for fossil fuel.

Except for plant cell and tissue culture techniques, which are the foundation of plant genetic engineering, somaclonal variation, cell selection and other techniques of *in vitro* culture, plant biotechnology has not been transferred to a majority of developing countries. The goal of ABSP project research is to assist developing countries in adopting a wider application of biotechnology in order to address priority problems which represent specific constraints on agricultural productivity. In achieving this goal, the sustainability of agricultural production systems will be improved by reducing the need for synthetic pesticide application and the quality of life enhanced by increasing the availability of food for consumption and marketing.

The research problems identified for inclusion in ABSP are those which conventional plant breeding alone cannot resolve. From the three regions of collaboration, Asia, Africa and Latin America, crops were chosen based on economic and nutritional significance coupled with severe pest or pathogen constraints on productivity. Targeted crops include: potato, for which the constraint is potato tuber moth; sweet potato, which is constrained by sweet potato weevil; maize, constrained by the corn stem borer; and cucurbits, which are constrained by several viruses.

ABSP has set several research objectives which, when considered in their entirety, will reduce the constraints on productivity and broaden the application of biotechnology in developing countries:

- Assemble minigenes containing insect resistance genes (Bt and proteinase inhibitor), driven by plant-specific regulatory elements;
- Genetically engineer potato, sweet potato and maize for resistance to insect pests in developing countries;
- Genetically engineer cucurbits with a virus coat protein gene for development of resistance to potyviruses;
- Demonstrate pest resistance of transgenic crops at the laboratory, greenhouse and field level, and integrate this into sustainable agricultural systems via collaborations with plant breeders, agronomists, statisticians, virologists and entomologists (with expertise in insect resistance management and integrated pest management);

- Transfer scientific knowledge and techniques to developing countries through postdoctoral fellowships.

A consortium of three universities (Michigan State, Cornell, Texas A&M) has developed a team of scientists with considerable expertise, who will lead the research and training components set forth in the project objectives. The team includes Dr. Mariam Sticklen, research director for the ABSP project and faculty member in the Departments of Crop and Soil Sciences and Entomology at Michigan State University; Dr. Ray Wu, faculty member in the Section of Biochemistry, Molecular and Cell Biology at Cornell University; Dr. Roberta Smith, the Eugene Butler Professor in the Department of Soil and Crop Sciences at Texas A&M; Dr. Rebecca Grumet, faculty member in the Department of Horticulture at Michigan State University; and Dr. David Douches, faculty member in the Department of Crop and Soil Sciences at Michigan State University.

The success of the research programme will be measured in the achievement of its objectives and goals. That achievement will mean significant progress also has been made in the management and networking aspects of the programme. The components of ABSP, by virtue of the project's integrative approach, cannot be segregated. Public private sector relationships, consultancies and internships in intellectual property and biosafety, the transfer of knowledge and expertise through developing country post-doctoral fellowships in US laboratories, and the dissemination of information via *BioLink* (the quarterly newsletter of the ABSP project), workshops, conferences and symposia, will all be built upon good cience. (Source: *BioLink*, Vol. 1, No. 1, 1992)

DNAP: Unique opportunities through ABSP

The Agricultural Biotechnology for Sustainable Productivity (ABSP) project is creating a unique opportunity for interaction between private biotechnology companies located in the United States and developing countries. Each partner contributes capital, technology and marketing expertise; ABSP provides matching funds and a permanent linkage role. The outcome of this new approach can be very beneficial to the agricultural sector by providing conditions for stability and or increased productivity. In addition, it will create new business opportunities between producing and consuming countries.

The private sector will focus on first-generation products that are in higher demand for local and export markets, concentrating on technologies that are more effective, short-term and less costly. If profitable, the partnership would be motivated to move to second- and third-generation products that require a higher level of sophistication and development costs. This association can provide an ideal partnership whereby technology can flow from one company to another to improve the availability of food in producing countries and lead to the production of value-added products to be marketed in consuming-country markets.

DNA Plant Technology Corporation, in Cinnaminson, New Jersey, USA, has established two joint projects with private biotechnology companies under the ABSP project. The first is a partnership with Agribiotechnologia de Costa Rica SA, to explore advanced micropropagation methods (bioreactor cloning) for banana, pineapple, coffee and ornamental palms. The second involves a micropropagation company in Indonesia, FITOTEK, and focuses on pineapple micropropagation.

Both companies have been in business for over eight years and are being operated in a profitable mode. The goal of these partnerships is to reduce the unit cost of the cloned plants by improving the micropropagation efficiency in each target species. If successful, these associations will create an opportunity for expansion of the micropropagation business and open the doors toward vertical integration between producing and consuming markets. (Source: *BioLink*, Vol. 1, No. 1, 1992)

Proposal to relax rules on biotech crops trials

Proposed rules that would loosen regulation of US field tests of genetically engineered crops have angered environmentalists and set industry executives worrying about a patchwork of state and federal policies. Both groups expect President Bill Clinton to take a close look at the issue.

The proposal, published in the *Federal Register*, would allow US biotechnology companies to avoid a lengthy permit process and to begin certain field trials of corn, cotton, tomato, potato, soybean and tobacco with a simple notification to the US Department of Agriculture (USDA) on the same day they plant. Companies and researchers would decide whether their experiment satisfied USDA guidelines on allowable genetic constructs and their characteristics. The public has 60 days to comment.

Crops not on the list also could avoid the permit process if an institutional biosafety committee or state officials, reviewing data under the guidance of the USDA, decided that federal scrutiny was unnecessary. The final proposal omits transgenic plants grown to harvest pharmaceuticals but recommends cautious treatment for plants incorporating functionally intact genes from human or animal pathogens. (Extracted from *Nature*, Vol. 360, 12 November 1992)

Report on emerging infections

In October 1992, the Centers for Disease Control (CDC) announced that a man in Tucson, Arizona, had

died of pneumonic plague, apparently after being infected with the disease by a cat during a trip to Colorado. He was the first person to die of this type of plague in the United States in five years. Although plague is unlikely to make a big comeback in the USA, this incident, like the recent resurgence of tuberculosis and measles, is one more sobering reminder that infectious diseases once thought to be firmly under control cannot be written off. And that message was underscored in a report issued by a panel of the Institute of Medicine (IOM),* which warned of a general "mood of complacency" in the scientific community towards the dangers of emerging infectious diseases.

The bulk of the panel's recommendations are directed at the CDC, which the report calls on to increase both its US and international disease surveillance with the goal to identify new diseases or resistant pathogens early on so that health officials can develop new vaccines or antimicrobial drugs before an infection races out of control. (Extracted from *Science*, Vol. 258, 23 October 1992)

Combining economics with biodiversity

Three government agencies are starting an experimental programme to encourage the conservation and exploration of rare plants and animals around the world. One goal is to look for compounds useful for new pharmaceuticals. Called the International Cooperative Biodiversity Groups programme, it is making available $1.5 million for projects that will involve inventorying, collecting and research on organisms from endangered ecosystems such as rain forests, coral reefs and deserts.

The initiative sprang from existing activities at the National Science Foundation, which has a large biodiversity programme, the Agency for International Development, and the National Institutes of Health, where the National Cancer Institute has been collecting compounds to test for anti-cancer and anti-AIDS activity.

The new programme is designed to encourage the use of indigenous knowledge and the training of local experts. Provisions on intellectual property rights are included so that countries will share in the profits from any commercial products that are developed from their flora and fauna. (Source: *Science*, Vol. 258, 23 October 1992)

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* "Emerging Infections: Microbial Threats to Health in the United States", Institute of Medicine, 1992.

Over-regulation could damage US biotechnology, says report

Existing US regulations for field tests of genetically engineered organisms are stifling research, according to a new report by the National Biotechnology Policy Board that recommends strict regulation of deliberate releases only for products posing the greatest risk to public safety.

The document emphasizes the social costs of regulatory delays and recommends a pilot study to measure the benefits of new products. This practice would help to quantify the impact of regulatory delays, provide data about the safety of new products, educate the public about the potential of biotechnology and reward federal agencies for prompt review, says the report, which was approved last week by the policy board at its meeting in Washington, DC.

The board's recommendations follow a study by the congressional Office of Technology Assessment that warned regulators not to relax biotechnology regulation so much that public concerns are ignored. But the report points out that "intense government oversight tends to confirm public perceptions that biotechnology processes pose significant and unique dangers".

The report also recommends financial incentives for the industry, including government participation in joint ventures, technology transfer from universities with patent rights attached in some cases and changes in the US tax code that would encourage investment in research. (Source: *Nature*, Vol. 359, 15 October 1992)

Majority in US back gene-based therapy

The vast majority of Americans (89 per cent) support the use of gene therapy to treat genetic diseases, a new survey reveals. The same percentage also favour continuing research in this field. A similar proportion would support gene therapy on their children, and only slightly less (79 per cent) would be willing to have it performed on themselves. The survey was sponsored by the March of Dimes Birth Defects Foundation, which opposes gene-based treatments for non-therapeutic purposes. Gene therapy corrects a disorder by replacing or counteracting a faulty gene. (Source: *European Bio News*, No. 1, October 1992)

Courts reject DNA fingerprinting after NAS report

Four months after the National Academy of Sciences (NAS) released a report intended to end the controversy over DNA forensic fingerprinting, the

situation is as muddled as ever. At least three state courts have ruled that DNA evidence is inadmissible despite the report's conclusion that it should be accepted. The situation has deteriorated to the point where one DNA fingerprinting company - the Maryland-based Cellmark Diagnostics Inc. - would like the NAS panel to clarify its conclusions.

The courts have rejected DNA evidence for reasons not foreseen when the report was released in April 1992. One of its recommendations was for better laboratory quality-control standards and certification procedures, and some DNA fingerprinting critics have argued that DNA evidence should be inadmissible until such procedures are established. But the issue that most bothered the courts relates to statistics, not standards. The California Court of Appeals, the Massachusetts Supreme Judicial Court and the US District Court of Guam have all ruled (citing the NAS report and the accompanying controversy) that the scientific uncertainty over the role of population substructure in calculating the chance of DNA matches is too great to pass the so-called *Frye* test, a measure of scientific acceptance needed for legal acceptability set out in a 1923 decision by the US Supreme Court. As a result, DNA evidence using all but the most conservative statistics is now inadmissible in Massachusetts, some districts of California and Guam.

Most people agree that the current confusion is temporary and that the introduction of DNA evidence will some day become routine in the courtroom. But many of the scientists who follow the issue are disappointed that the NAS study did not resolve it. Cellmark wants the panel members to draft a letter discussing - and presumably rejecting - some of the recent court decisions. But the NAS committee has formally disbanded, making that unlikely. (Extracted from *Nature*, Vol. 359, 1 October 1992)

NAS plan to protect US biotechnology

The National Academy of Sciences predicts global markets for biotechnology products will grow by at least $50 billion per year over the next decade. In a report issued in August 1992, NAS warned that Europe and Japan are making stronger efforts to turn basic biotechnology research into marketable end products.

The academy expects the US to continue its domination of the biopharmaceutical market, but it warns that the US was very weak in bioprocess engineering and the ability to produce biotechnology products on a large scale. Japan has already surpassed the US in applied microbiology, and Europe and Japan are making strong efforts to help their companies take advantage of university research. Patents on insulin, tissue plasminogen activator and erythropoietin are expiring, and improved manufacturing technologies will be needed to lower the costs of these products and keep them competitive with generics manufactured overseas. Such products will also be used in greater quantities and will need to be manufactured on a much larger scale.

The academy would like the US to adopt a long-term plan to coordinate research, development and training. The academy sees a skilled workforce as essential for the industry's future. It wants government to spend more on education and the encouragement of cross-disciplinary exchanges among scientists and engineers. Such spending would speed the development of new products, protect emerging technologies and help corporations capitalize on ideas being developed by universities. (Extracted from *Chemical Marketing Reporter*, 24 August 1992)

Zimbabwe

Pearl millet release in Zimbabwe

The efforts of a collaborative effort between ICRISAT scientists and their counterparts in Zimbabwe's Department of Research and Specialist Services have culminated in the release of the first pearl millet variety developed in southern Africa with ICRISAT participation. The variety SDMV 89004, now named PMV 2, was developed out of a composite population initiated in 1985. Throughout the trials SDMV 89004 proved superior to all other cultivars. Equally important, it was accepted by farmers.

PMV 2 has been widely tested for superiority in yield and resistance to the major pests and diseases in over 25 trials across eight research station sites for four years, and over ten communal area sites for two years. On research stations, PMV 2 was 40 per cent better than the local variety grown by farmers. On tests carried out in the communal areas, PMV 2 more than doubled the yields of the local variety. Apart from superiority in yield, this variety is early-maturing, requiring only about 85 days to mature. It is ideal for the short season and frequent droughts that lead to crop failure in most of the communal areas where this crop is grown. PMV 2 has also been positively received in Namibia, Malawi and Botswana, where it has been extensively tested. It is still under on-farm trials in Namibia and Botswana. The decision to release PMV 2 by the Government of Zimbabwe comes at a time when the whole of southern Africa is experiencing a terrible drought, reportedly the worst this century. (Source: *SAT News*, No. 11, July-September 1992)

C. RESEARCH

Human genes

Gene test may assess chance of conceiving a handicapped child

Geneticists from the Netherlands and the United States have discovered how the most commonly

inherited form of handicap, Fragile X syndrome, is caused. The condition affects 1 in 1,200 boys and 1 in 2,000 girls.

By cloning the gene, known as the Fragile Mental Retardation gene (FMR-1), that causes the syndrome when it is altered, researchers have discovered the mechanism of the mutation.

Ben Oostra of the Erasmus University in Rotterdam and his colleagues have shown that the mutation causing Fragile X syndrome results from a change in the size of a certain gene fragment at the fragile site of the X chromosome. The first sequence of the FMR-1 gene which is transcribed into a protein contains a number of repeats made of three nucleotides: CGG. In the normal population there are between 6 and 51 CGG repeats in this part of the gene. People with between 48 and 200 repeats are carriers of a premutation, but the gene is still expressed normally in the brain and they are free of any symptoms. People with between 200 and 2,000 CGG repeats have a full mutation and show the symptoms of Fragile X syndrome.

It is very important to distinguish between the normal gene and a premutation because tests carried out on the parents and grandparents of children with Fragile X syndrome have shown that a normal FMR-1 gene never changes directly into a full mutation, but passes through a premutation stage in at least one generation. Research has also shown that full mutations are inherited from women, whereas premutations can be inherited from both sexes.

By studying a woman and her parents, geneticists can determine the woman's risk of passing a full mutation to her child - even if her number of CGG repeats is within the borderline region of 48 to 51 repeats, where the gene can be either normal or in the premutation stage. If the parents have the same number of CGG repeats in the FMR-1 gene as the woman, the gene is stable and normal. But if there is a difference in the number of repeats in the two parents and the woman, the gene is changing, and the woman may carry a premutation.

A premutation can change into a full mutation during the formation of ova in the ovary, and, again, the risk depends on the number of CGG repeats.

On the other hand, if a pregnant woman has a premutation of between 48 and 65 repeats, there is only a small risk that her foetus will develop a full mutation. But the risk is much higher if, say, the woman carries a premutation of between 65 and 200 repeats. (Source: *New Scientist*, 18 July 1992)

Unfettered protein is culprit in osteoporosis

Hormone replacement therapy - the controversial treatment that prevents osteoporosis in older women - may soon be replaced by an alternative with fewer side effects. Experiments on mice in the United States have demonstrated for the first time the mechanism of osteoporosis, opening the way for targeted treatments of the disease.

Scientists have known for years that the process begins when the ovaries stop producing the hormone oestrogen, but they were unable to explain why. Doctors prescribe oestrogen to women to prevent the condition, but this therapy has risks such as cancer of the lining of the uterus.

Research at the Veterans Affairs Medical Center in Indianapolis have shown that oestrogen suppresses a protein which stimulates the development of bone-destroying cells. When oestrogen stops circulating, these cells flourish. The team knew that adding oestrogen to laboratory cultures of mouse bone cells held back the production of IL-6. Adding IL-6 to the culture stimulated the production of osteoclasts. The team studied mice whose ovaries had been removed. Compared with a group of control animals, these mice produced twice as many osteoclasts and their bones also became thinner. One group of mice received implants of oestrogen; another received an antibody that blocks IL-6. Both treatments prevented the increase in osteoclasts and the thinning of bone. The antibody had no effect on control animals.

Gene therapy could target the production of IL-6 in bone marrow without suppressing its useful effects elsewhere in the body. Another possibility is to use refined oestrogens that do not have the side effects of the current therapy. (Source: *New Scientist*, 11 July 1992)

Enzyme structure revealed

Scientists at Texas A&M (College Station, TX) report they have determined the structure of an enzyme that is critical to regulating blood pressure. The compound, kininogenase, helps maintain the hormonal balance that governs blood pressure. The scientists say the structural information - found using X-ray crystallography - is key to future molecular modelling work and could help lead to the rational design of better blood pressure drugs. The Texas researchers used

advanced molecular graphics to help analyse the X-ray data. (Source: *Chemical Week*, 20 May 1992)

Genetic possibility for alcoholism in women

Women's genes may play an important role in the development of alcoholism, according to the largest-ever study of female twins.

Since alcoholism often takes a different form in women, and is far less prevalent than among men, many researchers thought the causes of alcoholism might be largely environmental, but in a study of 1,033 pairs of identical and fraternal female twins psychiatrist Kenneth Kendler at Virginia Commonwealth University in Richmond and a team of geneticists found that the tendency to alcoholism was 40 to 60 per cent inherited.

Kendler's group based their conclusions on a statistical analysis of the degree to which alcoholism is shared by identical and fraternal twins. Compared to the fraternal twins, the identical twins, who have identical genes, were far more likely to both be alcoholics or both to have no problem with alcohol.

To make sure they were not observing an environmental effect caused by identical twins being treated more equally, the researchers interviewed each of the twins, asking them if their parents dressed them in the same clothes as children, if they were in the same school class, and similar questions. They found that those with common environmental factors were no more likely to share a tendency to alcoholism. This strengthened Kendler's argument that there is at least a moderate genetic component to alcoholism in women. (Source: *New Scientist*, 24 October 1992)

Pulling genes from cancer cells

Recent studies have revealed that the myc gene, a segment of DNA important to cell division, may foster cancer growth when reproduced in excess amounts. Surplus copies of the gene are located on tiny specks of genetic material that float around tumour cells. Examining these specks is not easy, but a scientist at the University of Texas Health Science Center at San Antonio is the only person in the world performing a technique to grab the myc genes out of cancer cells. Using a glass instrument that measures one ten-thousandth of an inch, the scientist is able to remove the specks from cancer cells for study at his laboratory at the Cancer Therapy and Research Center. By targeting specks on DNA rather than the whole cancer cell, doctors may be able to develop less toxic therapy. Instead of killing the cancer cell through radiation or other treatments, it may be possible to change its aggressive behaviour, thereby turning the cancerous cell into a benign one. (Source: *Bio Bytes*, July 1992)

TB researchers build hopes on "missing" gene

Scientists in Britain and France have pinpointed a gene that makes the TB bacterium resistant to its principal enemy, a drug known as INH. The discovery should enable hospitals to diagnose dangerous drug-resistant strains of TB more rapidly, and could help in the development of desperately needed new drugs.

Since the arrival of HIV, the number of cases of TB has risen sharply, with an estimated 8 million new cases in 1991. HIV triggers active TB disease in those already infected with the bacterium, as well as increasing uninfected people's susceptibility to it. In the United States there have been recent outbreaks of infection with strains of *M. tuberculosis* that are resistant to all the available drugs. These untreatable strains have killed most of their victims.

Ying Zhang at the Medical Research Council's TB unit at the Hammersmith Hospital, London, Stewart Cole at the Pasteur Institute in Paris, and their colleagues have shown how the bacterium resists INH. They began with a related bacterium, *Mycobacterium smegmatis*, which was easier to study, but have since confirmed their results in *M. tuberculosis*.

The team took a mutant strain of the bacterium that was resistant to INH. Bit by bit, they inserted stretches of DNA from a normal, drug-sensitive strain of *M. tuberculosis* into a series of copies of the resistant strain. Each copy was tested for its response to the drug. One copy was highly sensitive. The gene that was inserted in this copy is responsible for production of an enzyme, catalase, which the bacterium uses normally to convert hydrogen peroxide to oxygen and water. It appears to convert the drug into an active form that kills the bacterium. Strains that lack catalase are unscathed by the drug.

The findings do not explain how the bacterium resists any of the other drugs for TB, but Zhang believes the findings could be exploited to design a drug based on the active form of INH. This would attack strains of TB that lack catalase. It is surprising, says the team, that the mutant strain completely lacks the gene for catalase, rather than having a defective copy. Of three highly resistant strains, says Zhang, two had completely deleted catalase genes, and a third had a "silent" copy of the gene that did not make the enzyme. (Source: *New Scientist*, 22 August 1992)

More effective anti-cancer compound

Compounds to selectively invade cancer cells have been developed by K. C. Nicolaou of Scripps Research Institute (La Jolla, CA). The compounds are modified enediynes, natural antibiotics. The modified enediynes enter the cells and there create free radicals that kill the

cells. Nicalaou claims the new compounds are more effective than existing anti-cancer compounds such as cisplatin, doxorubicin or taxol. The enediynes are chains of six carbon atoms linked by two triple bonds and one double bond. The chain can form a benzene ring with two missing hydrogen atoms. This ring acts as a powerful free radical, scavenging hydrogen. In tests, the 11 designer enediynes made so far have been able to invade cancer cells while leaving normal cells untouched. The invaded cells suffer so much DNA damage that they die. The compounds seem especially effective against leukaemias. (Extracted from *New Scientist*, 20 June 1992)

Teaching the body to tolerate transplants

Ways of preventing the immune system from rejecting tissue transplants are being tested by American researchers. Their goal is to selectively turn off the recipient's immune response to the donor's cells, rather than to suppress the entire immune response.

The researchers inject T-cells from the donor into the recipient's thymus, the organ that mediates the response of the white blood cells which attack foreign tissue in the body. They have found this can greatly increase the time that transplants survive in rats and mice, although the use of the technique in humans is a long way off.

T-cells normally attack tissue they do not recognize as "self", causing organs transplanted from other donors to be rejected. Surgeons carrying out transplants prevent rejection by using drugs that suppress the response to T-cells, but these drugs cause serious complications because they inhibit all T-cell response and can affect other parts of the immune system. Three American groups are trying to "educate" the thymus to prevent T-cells attacking the transplanted tissue, without inhibiting other immune response.

Their approach is based on the role of the thymus in "teaching" T-cells to recognize the body's own cells. The researchers inject cells from the donor, so that T-cells in the thymus are exposed to donor cells as well as "self" cells. They hope that this exposure in the thymus will prevent T-cells from attacking the transplant, just as they do not attack the body's own cells.

Results so far are encouraging. Hiroki Ohzato and Anthony Monaco of the Harvard Medical School have succeeded in making mice accept skin grafts from a different strain of mouse - a tough test of transplant acceptance. They achieved this tolerance by injecting spleen cells from the donor strain into the thymus of adult mice; injection into the blood proved to be less effective.

Monaco believes that the spleen injections may have worked well because they are rich in dendritic cells, which are thought to be involved in teaching T-cells to recognize "self" in the thymus.

Also encouraging is the survival of pancreatic islets transplanted into rats by Andrew Posselt and Ali Naji of the Hospital of the University of Pennsylvania. They found the islets survived better if bone marrow was injected into the thymus rather than into the blood. Some injected cells survived in the thymus (*Diabetes*, Vol. 41, p. 771)

In similar experiments at Washington University in St. Louis, John Goss and Wayne Flye injected white blood cells from the spleen of donors into the thymus of rats and mice. According to Goss, this raised the survival rate to 85 per cent for heart and islet transplants where tolerance is easier to obtain than for skin grafts.

The results are encouraging because the technique works for adult recipients and donors. It might one day lead to clinical use, in which patients would receive an injection of donor tissue in the thymus as well as a transplant. However, important questions, such as how long donor tissue can survive in the thymus, remain to be answered before human trials begin. (Source: *New Scientist*, 5 September 1992)

MS gene link

Finnish researchers have linked a gene with multiple sclerosis. The gene, on chromosome 18, encodes a protein called MBP, which forms part of the myelin sheath surrounding nerves. Multiple sclerosis causes progressive damage to the nervous system and the breakdown of myelin. Scientists have long suspected that MBP might be implicated in MS.

The Finnish team studied 21 families with a history of MS, as well as other MS patients and healthy controls. They found that a particular variant of the MBP gene was significantly more common in the MS patients than in the controls. The team concludes that the variant gene plays a role in MS. (Source: *New Scientist*, 31 October 1992)

Genetically engineered growth hormone

Fujisawa Pharmaceuticals (Osaka, Japan) has genetically engineered a growth hormone found in 1984, providing a treatment for a rare type of dwarfism. Known as Laron Syndrome after Professor Zvi Laron who described it, the dwarfism affects Sephardi Jews and Arabs, limiting growth to 1.3 metres. Victims are also over-weight, have low blood sugar and weak bones. The disease is caused by a molecular defect of the liver's growth hormone receptor, rendering hormone secretion

ineffective. The disease is thought to have originated from a mutation in the Mediterranean region centuries ago. There are 41 known patients, of whom 13 Israeli children have been treated with the hormone in Japanese clinical studies. They have lost excess fat and grown 12 cm/y. (Extracted from *Jerusalem Post*, 22 July 1992)

Engineered cells fight cancers

Cells engineered to produce interleukin-2 can help fight cancers, based on experiments with mice, according to Robert E. Sobol of the San Diego Regional Cancer Center. The researchers introduced the altered cells and some tumour cells into mice. Two weeks later, a small tumour was implanted in each mouse. One months later, six of the 10 mice showed no sign of cancer. Mice that received the preliminary injection of tumour cells without any interleukin-producing cells also showed some immune response to the implanted tumour. But in control mice that received only the implanted tumour, the cancer grew larger. (Extracted from *Science News*, 30 May 1992)

Role of p53 gene in fight against cancer

A molecule that blocks the activity of the p53 gene might halt the progression of leukaemia, according to Jorge Spinolo of the University of Nebraska Medical Center (Omaha). p53 has been implicated in the development of many cancers, including acute myelogenous leukaemia (AML). The new treatment was able to slow the growth of cultured cells from AML patients. The antisense molecules used to block p53 have shown no adverse effects in seven monkeys. FDA approval for tests on 10-15 AML patients is being sought.

The p53 gene is essential in maintaining chromosomes in good repair, and may thus be essential in preventing cancer. p53 may be able to detect chromosomal damage, and can prevent replication until repair enzymes have corrected the problem. This helps to prevent genetic abnormalities from being passed on to new cellular generations. Dr. Michael B. Kastan of Johns Hopkins says that p53 has long been known as a tumour-suppressing gene. The new research indicates how p53 actually works. The research could help understand how to time cancer treatment. The work suggests that DNA-damaging treatment might be the best first approach, to be followed some time later with chemotherapies. Dr. Thea D. Tisty of the University of North Carolina (Chapel Hill) says that a loss of p53 activity is one of the first steps in the development of cancer. Maintaining p53 activity could thus prevent tumour development. (Extracted from *Science News*, 6 June 1992 and *New York Times*, 22 September 1992)

Test to detect CF gene in embryos

Embryos with the gene for cystic fibrosis can be detected when they are just days old, according to Dr. Alan H. Handyside of Hammersmith Hospital (London). A single cell is removed from the embryo and examined for the potentially flawed gene. The technique has been used to examine the embryo of a female embryo for cystic fibrosis. The girl has now been born, without cystic fibrosis, as predicted by the test. Cornell Medical Center researchers say they also have a pregnancy in progress after a pre-implantation examination for cystic fibrosis. The test at the moment can be used only with *in vitro* fertilization, making the procedure expensive, even though the test itself is not very expensive. Some researchers predict that it will eventually be possible to replace malfunctioning genes in an embryo only 4-8 cells large.

Examination of the DNA of the single cell removed from the embryo was done with nested primer polymerase chain reaction. The technique was used to examine embryos from three couples, in which both father and mother carried the CF gene. Only one pregnancy resulted from the various IVF attempts. (Extracted from *New York Times*, 24 September 1992)

Making monoclonals

Steenbakkers, working for Akzo, is claiming a new, improved method for the production of human monoclonal antibodies.

In the system, β-lymphocytes are harvested from a donor, subjected to clonal expansion, immortalized and cultured. The monoclonals can then be isolated from the culture. Alternatively, after clonal expansion the mRNA can be isolated, amplified (as cDNA) and expressed in a suitable host.

Both procedures include a selection step for antibody-producing lymphocytes (selecting for antibodies with the desired specificity) before the expansion.

The main advantage of this technique lies in the combination of clonal expansion and immortalization or amplification. Through the expansion, enough β-lymphocytes can be produced from "one to a few" originals to allow fusion or transformation - from one lymphocyte up to 500 can be grown. Thus the technique allows antibody-producing cells to be made from "every possible lymphocyte source".

"The combination of clonal expansion and electrofusion offers a new method of monoclonal antibody development which has the potential to generate hybridoma cell lines from single β-cells. In this respect, the method can at least compete with the PCR technique for Ig genes", Steenbakkers says. The method also produces affinity matured antibodies, he adds. The technique is claimed to be suitable for use with human β-lymphocytes since it circumvents the selectivity problems of Epstein-Barr virus transformation associated

with human monoclonals. (Source: *Chemistry and Industry*, 15 June 1992)

Parasitic proteins provide key to malaria vaccine

Prospects for a malaria vaccine have brightened with a discovery by researchers in Britain and the Gambia. The team has pinpointed a protein from the malaria parasite, which triggers a strong response from the killer T-cells of the immune system. The scientists hope that the protein could be used as the basis for a vaccine.

The new findings will not lead immediately to a vaccine, but the scientists are excited by the results for several reasons. First, they provide the only convincing evidence so far that people in malarial regions make killer T-cells against the parasites - a part of the immune response that many scientists believe is vital for protection against disease. Secondly, they demonstrate a new method that could be used to design vaccines against many diseases, including HIV and tuberculosis.

But best of all for the scientists, the results confirm their earlier suspicions that an important family of genes called the HLA genes are involved in protection against malaria. The HLA genes, which vary enormously from person to person, code for proteins, or antigens, on the surface of cells. These HLA antigens are vital in enabling cells of the immune system to "recognize" foreign proteins entering the body: T-cells recognize foreign proteins only when they are bound to the antigens. Because different people have different HLA antigens, their immune systems will "see" and respond to different parts of foreign proteins.

The team, led by Adrian Hill at the Institute of Molecular Medicine in Oxford, discovered that two HLA genes common in West Africans protect people from severe malaria. The researchers wondered whether the HLA antigens encoded by these genes might be particularly efficient at "offering" proteins from the malaria parasite to the immune system. The precise shape of the specific HLA antigen will determine which stretch of a foreign protein can be bound to it, and some shapes will trigger a better T-cell response than others.

The new findings suggest that their suspicions were right. The team looked at stretches of protein from the parasite that were bound to one of the two important HLA antigens, called HLA-B53. They found one stretch of a protein that produced a strong reaction of killer T-cells against the parasite. They studied the T-cells in the laboratory using blood samples from healthy Gambians who carried the HLA-B53 gene.

The results show that individuals with the gene have a natural protection that could be mimicked and boosted to make a protective vaccine. So far, the protein has not been tested in any experimental vaccine, but it has a clear advantage over many others that have: it is not highly variable from one strain of the parasite to another. In theory at least, this means that it might protect people in many different areas and for long periods.

No one knows, says Hill, whether the parasite protein will stimulate a strong immune response in people who do not have the HLA-B53 gene. This gene is present in about four out of ten Nigerians and in a quarter of Gambians, but it is absent from people in Thailand and other areas of South-East Asia where malaria is endemic. This is the next question the team wants to answer, says Hill. (Source: *New Scientist*, 29 August 1992)

Genetic factor of Parkinsonism found

Researchers at the Imperial Cancer Research Fund (ICRF) and the Institute of Psychiatry, both in London, have discovered a genetic factor in Parkinsonism. One in every 20 people has a defect in the gene for an enzyme known as cytochrome p450; this defect apparently increases the chances of developing Parkinson's disease by 2½ times. Cytochrome p450 helps to ensure that toxic chemicals are removed from the brain, and so its role in the disease was not a complete surprise. As Nigel Leigh of the Institute of Psychiatry points out, the genetic discovery provides the first clear evidence for the long-standing idea that environmental toxins may be a cause of Parkinson's disease.

Molecular modelling by scientists at ICRF and elsewhere has shown that the drug MPTP looks like dopamine. The same is true of a number of chemicals known to be potentially carcinogenic if inhaled over a long period, and widely present in the environment at very low concentrations. The genetic defect may allow these toxins, normally swept away by cytochrome p450, to accumulate in the brain and clog up dopamine receptors. With the receptors blocked, the brain cells cannot respond to dopamine. Eventually they give up making it, too; the result is Parkinsonism.

If this theory is correct, then it may be possible both to identify and protect those especially at risk of Parkinson's disease, and to offer a new treatment to those already affected by the condition. Scientists are already beginning to design appropriate molecular mops, but such therapy, if feasible at all, is years away. (Extracted from *The Economist*, 29 August 1992)

Trojan horse targets leukaemia

Mouse antibodies, genetically altered to mimic those of humans, may provide the key to treating acute myeloid leukaemia (AML). Genetic engineers at Celltech and American Cyanamid have managed to link up the naturally occurring anti-tumour antibiotic, calicheamicin, with "humanized" mouse antibodies.

Between one and ten molecules of calicheamicin will kill a cancer cell. Humanized mouse antibodies are not attacked by the human immune system but recognized CD33, a protein on the surface of leukaemic cells. Linked together, they act as a "trojan horse", bypassing the defence system and proving fatal only to the leukaemia cells.

Mouse antibodies are used because an immune response can be induced in mice and the mouse's antibodies removed. The humanization involves replacing everything with the human body counterparts except the region that binds to CD33, effectively producing something that the body recognizes as human with the ability to bind in the AML cell.

Almost all AML patients are struck down with the disease after their mid-forties, when bone-marrow transplants are considered to be high-risk. Most respond to conventional therapy but relapse. Some 90 per cent die within two years of being diagnosed.

David Bloxham, research director at Celltech, thinks the new antibody/antibiotic will best be used to reduce the bulk of the tumour in patients unlikely to respond to bone-marrow transplants, and will also be able to purge tumour cells from bone-marrow transplants.

The new drug will begin clinical trials in 1993, and could be in use within three years. (Source: *Chemistry & Industry*, 21 September 1992)

Amphibians offer a taste of their own medicine

Australian tree frogs exude an antimicrobial compound, which might make an antibiotic and antiviral drug, say chemists. The compound, dubbed caerin 1.1, is a peptide, a short chain of amino acids.

Chemists John Bowie and David Stone and zoologists Michael Tyler and John Wallace at the University of Adelaide isolated the compound from the skin secretions of three types of tree frog: *Litoria caerulea*, *L. splendida* and *L. gilleni*. They found that the compound kills *Staphylococcus aureus*, the bacterium that often causes boils and abscesses. It is also active against *Herpes simplex*, the virus which causes cold sores.

The researchers "milked" the frogs by applying a mild electrical stimulus. They were able to obtain about 70 milligrams of peptide a month from each frog, an impressive amount considering the size of the animal. They found that the compound has a molecular mass of 2,582 units, and that the chain contains 25 amino acids. The researchers built a molecular model of the compound, and from this deduced that it is about 0.4 nanometres long and shaped like a bent rod.

Bowie and his colleagues say that caerin 1.1 is the major component of a mixture of 35 peptides they have extracted from the frog secretions. One of these peptides, caerulein, had been discovered earlier by other researchers. They found that the molecule lowered the blood pressure. The remainder are yet to be evaluated for biological activity. As the list of possible pharmaceutical products extracted from amphibians grows it seems that amphibians are carrying a potential medicine chest on their backs. (Source: *New Scientist*, 5 September 1992)

Treacherous gene makes cows immune to mastitis

Genetically engineered cattle with resistance to a common type of mastitis may soon be with us.
Christine Williamson and her colleagues at the Agricultural and Food Research Council's Institute for Animal Health at Compton in Berkshire, United Kingdom, aim to tackle mastitis by fortifying the cow's own armoury against the bacteria that cause the infections.

As a first step, Williamson's team, in collaboration with other institutes, have produced eight mice whose milk contains lysostaphin, an enzyme which kills staphylococcal bacteria by dissolving their cell walls. Its effect is specific to staphylococcal bacteria.

The researchers isolated and cloned the gene which produces lysostaphin from a tiny loop of DNA which was derived from a strain of staphylococcal bacteria called *Staphylococcus simulans*.

First, they managed to make the bacterial lysostaphin gene function effectively in cultures of mammalian cells. But to ensure that the mice only produced lysostaphin in their mammary glands, Williamson's team spliced their gene to the control sequences of another gene which works only in the mammary glad. They then injected the amalgam of the two foreign genes into fertilized mouse eggs, producing eight transgenic mice.

One disappointment is that while all off-spring of the original eight mice carried the new gene, none seems capable, as yet, of producing lysostaphin. Nonetheless, the researchers are trying new approaches to get over this hurdle. (Source: *New Scientist*, 11 July 1992)

Hornless cattle gene

Scientists in Queensland (Australia) have found the gene which determines whether cattle grow horns or not, in all European or bos taurus breeds, according to CSIRO chief executive Dr. John Stocker. It may soon be possible for farmers to breed cattle without horns, which means that they are less vulnerable during transportation, and this development will save farmers the moral

dilemma of whether to de-horn or not. (Extracted from *Australian Finance*, 22 July 1992)

Powerful painkiller from Ecuadorian frog

Epibatidine from a poisonous frog (Epipedobates tricolor) in Ecuador is a very powerful painkiller, according to John Daly of the National Institute of Health (Bethesda, MD). The drug is 200 times more powerful than morphine. It apparently acts in a way different from any other painkiller, blocking hitherto unknown pain receptors in the brain. The compound has a formula C11H13N2C1. Its structure is a pyridine ring with a chlorine attached to one side. On the other side, the ring is attached to a 6-carbon ring that has a nitrogen bridge across the middle. Organochlorines are rarely found in animals. The compound is also a new class of alkaloid. Most alkaloids are also found in plants. The painkilling effect of the drug was assessed by dropping rats onto a hot plate. The rats will stay on the plate if given 1 mg of morphine/kg of body weight. The same painkilling effect is possible with only 5 micrograms of the new drug, kg of body weight. The new drug is not counteracted by naloxone, which neutralizes opiate alkaloids. (Extracted from *New Scientist, 30 May 1992*)

DNA from sabre-toothed cat fossil shows weak link to household cats

The 14,000 year-old leg bones of a sabre-toothed cat (*Smilodon fatalis*) have yielded two genes indicating that these animals are direct ancestors of today's lions and tigers, but not of the average household cat.

The DNA segments will help put to rest a long-standing controversy about where these extinct animals fit in the feline family tree. The genetic evidence suggests that *S. fatalis* falls in the same evolutionary branch as the large cats (pantherine lineage).

The scientists plan to use the DNA to determine if an ancient pathogen, much like the AIDS virus, was responsible for the species' extinction. The team at the National Cancer Institute will look for genetic evidence of a lentivirus present in many modern-day cat species in the *S. fatalis* fossil bones.

Using polymerase chain reaction, the NCI scientists isolated, cloned and sequenced two genes - the mitochondrial gene for 12S rRNA and nuclear FLA-I, the feline major histocompatibility complex gene, involved in immune responses. (Extracted from: McGraw Hill's *Biotechnology Newswatch*, 19 October 1992)

Molecule on metastasing rat pancreas cancer tumours found

Researchers at the German cancer research centre in Heidelberg have discovered a molecule on the surface of tumorous cells in the pancreas of rats, which is only found in metastasing cancer tumours and not in locally growing forms of the tumour. The molecule, called CD 44-v, has been found to be a close relative of the surface molecules of white blood cells. Initial tests on rats have succeeded in blocking the CD 44-v surface molecule with specific antibodies, and preventing secondary growths from forming on the pancreas tumour of the rat. (Extracted from *European Chemistry*, 10 September 1992)

Animal alternative for drug testing

Biotechnologists from Cranfield Institute of Technology, in collaboration with Pfizer Central Research, have successfully investigated a method of testing the metabolic stability of drugs using micro-organisms instead of live animals. Animal livers possess enzymes, which can increase the water solubility of such drugs, thereby helping their excretion. The fine tuning of this process is part of the procedure followed in designing new drugs with suitable retention and elimination characteristics. The scientists have discovered micro-organisms with enzyme systems, which break down drugs in similar ways to the enzyme systems which are present in animals, an area which has been under investigation by Cranfield Biotechnology Centre since 1988. To identify viable alternatives to some types of animal experimentation, the researchers - David Griffiths and Dr. Donald Brown, professor of biochemical engineering - screened more than 50 different micro-organisms for their ability to modify five drugs. The drugs tested were an anti-inflammatory (aminopyrine), a bronchodilator (theopylline), an anti-anxiety drug (diazepam), a steroid hormone (testosterone) and an anti-coagulant (warfarin). Many of the organisms could metabolize some of the drugs and, in particular, the fungus *Beauveria bassiana*, which was able to degrade all of the test drugs, was selected for further, more detailed studies. Details from: Professor Don Brown, Cranfield Biotechnology Centre, Central Business Exchange, Central Milton Keynes MK9 2EN or tel. +44 234 750111, ext. 2569. Or Dr. Serge Jezequel, Pfizer Ltd., +44 304 616082. (Source: *Biotechnology Bulletin*, August 1992)

Modification of mammalian development accomplished by gene manipulation

Researchers at the Institut Pasteur (Unité de génétique cellulaire) have succeeded in modifying the developmental process of mouse embryos, by engineering the Homeobox (Hox) genes. This family of Hox genes determines the sequential development of structures in animals, for example, limbs or the backbone in vertebrates or segmentation in flies. Using the technique of homologous recombination they have succeeded in overcoming the limitations of the random gene insertion, which has characterized transgenic animal research to date.

By taking embryonic stem (ES) cells, that is undifferentiated or totipotent cells from very early mouse embryos, the Pasteur team was able to replace the Hox-3 gene with a non-effective marker gene. Affected mice grew up with anomalies of the vertebra. In effect vertebrae at the rear of the animal had the morphological characters of those at the front.

This remarkable piece of gene engineering necessitated the grafting of the marker gene in the right copy number and in exactly the right position with regard to all control elements. This was achieved through the technique of homologous recombination. The success of this experiment marks an important first for the Pasteur and for the medical applications of gene manipulation. Gene therapy now becomes achievable by changing not the position but the identity of cells which express Hox genes.

For all concerned with the developmental process this publication marks one of the most important events of the decade, giving for the first time direct access to the processes of developmental control. Obvious first applications involve the development of animal models for a number of genetically determined developmental malfunctions. (Source: *BFE*, Vol. 9, No. 6, June 1992)

Plant genes

R-DNA bellflowers, melons enter hothouse

Tokyo-based Kirin Brewery Co., Ltd. will start hothouse cultivation tests of its recombinant Turkish bellflower.

Strong consumer demand exists in Japan for the Turkish bellflower, which is used extensively in floral arrangements. Kirin researchers developed a recombinant miniature form of the plant by introducing a gene encoding short height. Kirin will run the tests in an insect-proof 35-sq.m. hothouse within the facilities of its Plant Laboratory in Tochigi Prefecture.

In another plant test, a joint team of researchers at the National Institute of Agrobiological Resources (NIAR) and the National Agriculture Research Center (NARC), research arms of the Ministry of Agriculture, Forestry and Fisheries (MAFF), have begun hothouse cultivation tests of 50 transgenic melon plants. The tests are being conducted in NARC's cultivation facilities in Tsukuba.

The joint team genetically engineered the "Prince" variety of edible melon to contain genes encoding resistance to the cucumber mosaic virus (CMV). CMV causes extensive crop losses among melon growers in Japan each year. Having successfully completed closed-system cultivation tests, the team is now investigating potential environmental hazards arising from the new strain through the hothouse tests, and subsequently scheduled open-air cultivation tests.

Agracetus shoots genes into peanuts

Agracetus Inc. announced it has successfully implanted new genes into the peanut using its proprietary Accell gene gun. The company can now create germline transgenic elite varieties in six crops: peanut, corn, soybean, cotton, rice and beans.

New genes for herbicide tolerance and virus resistance were delivered into the Florunner variety of peanut, which makes up nearly half of the United States peanut crop. The resulting plants stably passed the genes to subsequent generations.

The advantage of the company's gene gun is that it can reach the germinal tissue of elite crops grown in the fields, not simply laboratory varieties. It also eliminates the need for tissue culture, which reduces product development time by two to three years.

The two model traits that were introduced to the peanut were resistance to an environmentally safe herbicide called Basta, and resistance to the tomato spotted wilt virus. (Source: McGraw Hill's *Biotechnology Newswatch*, 17 August 1992)

Gene gives resistance against European corn borer larvae

Monsanto has developed maize plants that produce a poison to kill European corn borer larvae. The plants are engineered with the kurstaki gene from *Bacillus thuringiensis*. The toxin is lethal to many agricultural pests, but is harmless to other animals. The gene itself has been engineered so that it produces 1,000 times more toxin than the natural gene. The corn borer does its damage by eating the maize stalk so that it is no longer strong enough to hold up the ears. In greenhouse tests, a heavy infestation of the corn borers causes negligible damage. Monsanto is now starting field trials of the engineered maize. It will be monitoring the trials to determine if the corn borer can develop resistance to the toxin. Monsanto's Mike Fromm says 0.1 per cent of total protein produced by the corn plant should be of the toxin to be effective. (Extracted from *New Scientist*, 18 July 1992)

Implanted gene "castrates" breeding plants

The ability to switch on and off the masculinity of plants is now possible because of a genetic system developed by Dutch researchers. They inserted genes into plants, which prevent them from producing pollen.

Breeders need to emasculate their premium plants, which have both male and female reproductive organs, to prevent them from breeding with neighbours at random and losing valuable characteristics.

Breeders improve crop varieties by crossing inbred plant lines. The offspring are often fitter and

more productive than either of the parental lines, a phenomenon called "hybrid vigour". But these advantages could be lost in the next generation if the hybrids were allowed to breed at random, creating offspring with mixed traits that are not necessarily the desired ones.

If breeders emasculate the plants, they can then pollinate them with pollen of their choice, ensuring that the original hybrid line with all its vigour is maintained.

Jan Leemans, the research director of Plant Genetic Systems in Ghent, Belgium, and his colleagues studied genes that regulate flower development in tobacco plants. They looked at a structure called the tapetum, which lines pollen sacs in the anther and forms first as the organ develops. They focused on the tapetal gene, which only works in the tapetum and seemed ideal for disrupting its development.

Next, the researchers spliced the tapetal gene to a second gene from the bacterium *Bacillus amyloliquefaciens*. This bacterial gene produces barnase, an enzyme that wrecks plant cells by breaking up their proteins.

The pair of genes was first incorporated into oilseed rape plants. The tapetal gene ensured that the barnase was only produced in the tapetum and the barnase caused the pollen sac to collapse. The plant developed normally but was male-sterile.

Then the researchers went a stage further and devised a further system for regenerating a line of male-fertile hybrids. This is important for breeders because they need access to pollen as well as female plants to generate flourishing hybrid lines with the same vigour as the original crossbreeds.

They isolated another gene from the same bacterium, which counteracts the barnase gene. The new gene produces a peptide called barstar, which blocks the action of barnase.

Again, they tagged the foreign gene to the tapetal gene to make sure that it would work only in the tapetum and incorporated the pair of genes into plants. The researchers crossed plants containing the barnase gene with those containing the barstar gene so that their offspring would inherit both.

Leemans said that his team had applied the system to corn, oilseed rape, brassica vegetables such as tomato, and cotton. (Source: *New Scientist*, 18 July 1992)

When beans means vaccines

A vaccine produced in a plant is being tested on guinea pigs and mice in Britain to see if it stimulates antibodies to foot-and-mouth disease. If the tests are successful, they will raise hopes that the vaccine could be used to immunize cattle. Growing vaccines in plants would be cheaper and easier than other production methods.

The vaccine is essentially a hybrid virus, which has been made to grow in the cowpea plant, the source of black-eyed beans. The Agricultural Genetics Company (AGC) in Cambridge plans to commercialize this pioneering technique by producing vaccines against other viruses that cause disease. Paul Bosely, research director of AGC, says the technique can produce proteins that could be used in a vaccine against HIV.

The work built on analyses of the structures of viruses by Jack Johnson at Purdue University in West Lafayette, Indiana. George Lomonossoff of the John Innes Institute in Norwich went on to grow a hybrid of the cowpea mosaic virus and the virus that causes foot-and-mouth disease.

When a hybrid virus is inserted into the cowpea plant, it multiplies in the leaves of the plant, and can be harvested in great quantities. "One cowpea leaf could provide vaccine for 200 doses", says Boseley.

Growing the vaccine is possible because of the close similarity between the cowpea mosaic virus - which infects the cowpea plant to produce flecks on the leaves - and the foot-and-mouth disease virus.

Lomonossoff and his colleagues at the John Innes Institute, who did most of the genetic manipulation work, claim that because the inserted loop pokes out from the cowpea mosaic virus in the same way that it would from the real foot-and-mouth disease virus, it should trigger strong immune responses in animals that are vaccinated.

In this respect, they say, the hybrid virus is likely to be superior to vaccines that rely on carriers such as yeasts, bacteria and animal viruses. In these carriers, say the researchers, the foreign material is less obvious to the body's immune system, so the response is likely to be weaker.

Bosely says that the virus grows quickly in the plant and can be harvested just a fortnight after insertion. He says that the plants are a very cheap source of vaccines: "All you need is a greenhouse". Other techniques require expensive fermentation equipment. Harvesting is cheap and simple too. You just grind up the leaves, centrifuge-out the virus particles, and purify them, says Bosely. AGC has applied for world-wide patent rights on the technology. (Source: *New Scientist*, 11 July 1992)

Transgenic wheat finally produced

Rice, corn and wheat - which together account for almost half of the world's food - have been prime targets for direct genetic manipulation since the first

plants expressing foreign genes were reported in 1983. Yet finding the appropriate combination of transformation and regeneration systems for these (and other) cereals has not been easy. The initial success came in 1988, when fertile transgenic rice plants were recovered. Two years later maize yielded its secrets. And now Indra and Vimla Vasil and their colleagues at the University of Florida (Gainesville) and Michael Fromm of Monsanto (St. Louis, MO) report the production of the first transgenic wheat.

Unlike many plants, which can be efficiently and routinely regenerated after transformation of somatic cells with the Ti plasmid system of *Agrobacterium*, cereals have proven recalcitrant to such manipulations.

Although the Vasils had pioneered the development of culture systems for cereals, had been able to regenerate wheat plants from protoplasts, and had obtained transformed wheat callus, until now the goal of obtaining transgenic wheat plants remained elusive. The Vasils decided to circumvent part of the very protocols they had been instrumental in developing. Instead of using embryogenic callus as a source of totipotent suspension cells, they delivered DNA, via particle gun bombardment, directly to such tissue. The hope was that this shortcut, although reducing the number of potential targets, would better preserve the embryogenic potential, which appeared to be lost during the long periods of time required to establish suspension cultures and select putatively transformed cells.

A second important component of the procedure was the choice of a selectable marker. The most commonly used gene in the recovery of transformed plants encodes an enzyme that inactivates the antibiotic kanamycin, to which wheat (almost predictably) displays a high natural resistance. Therefore the researchers chose a gene that inactivates a much less common antibiotic, phosphinothricin. Initially discovered as an antifungal drug, this bacterially produced agent has found its widest application as the active ingredient of the broad-spectrum herbicide Basta.

Bombardment of embryogenic wheat callus with a plasmid containing a phosphinothricin acetyltransferase gene (*bar*), followed by selection in the presence of Basta, allowed the recovery of plants from two different cultivars. That at least some of these were both stably transformed and fertile was demonstrated by enzymatic and functional assays of *bar* activity, hybridization analysis showing plasmid sequences in high molecular-weight chromosomal DNA, and, most significantly, the Mendelian inheritance of a functional *bar* gene in R1 and R2 progeny.

In common with many breakthrough demonstrations, these results do not yet represent an optimal system. Less than 1 per cent of the bombarded calli gave rise to transformed lines; the frequency with which mature, morphologically normal, self-pollinating plants were obtained was not high; establishing the regenerable callus lines (while easier and faster than suspension cultures) still requires many months; and Basta, even at high concentrations, did not completely inhibit the growth of control calli. (Extracted from *Bio Technology*, Vol. 10, June 1992)

Viral genes

White leaf virus of rice

This virus of the group of the Tenuiviruses, has been isolated and purified at the Centre for Research in Cellular and Molecular Biology of the University of Costa Rica. The genome has been cloned in a bacteria by a team of researchers under the leadership of Dr. Ana Mercedes Espinoza.

The group has also conducted studies on the life cycle of the virus in the Homopteran insect vector, on the epidaemiological characteristics of the disease and on the possibilities of its existence in bush plant hosts. Furthermore, the virus was observed together with some particular inclusions in the rice leaves under electron microscopy.

With the collaboration of Dr. Marta E. Valdez of the School of Biology of the same University, the development of a transgenic plant, resistant to the attack of the virus, is now being explored. (Source: *Boletin de Biotecnologia*, Vol. 9, No. 1, July 1992)

Simply enhancing

Improvements to biological insecticides may now be possible thanks to work done by Robert Granados and Yoshifumi Hashimoto for the Boyce Thompson Institute for Plant Research. Their work hinges on a gene that improves the action of baculoviruses.

Certain baculoviruses, such as *Trichoplusia ni* granulosis virus (TnGV) which attacks cabbage looper, have a virus enhancing factor (VEF), a unique protein which can improve infection of the insect, increasing mortality by up to 25 per cent. The VEF appears to enhance the infectivity of certain viral pesticides by degrading the insect's stomach lining, making it more permeable to the invading baculoviruses. Granados and Hashimoto have managed to clone and sequence the VEF gene in TnGV, and have subsequently identified it in two other baculoviruses, *Heliothis armigera* GV and *Pseudaletia unipuncta* GV-H.

The coded gene can be used to produce VEF in any microbial production system, for example *E. Coli*, and it could be introduced into plants to provide protection against insects, or into microbes to make biologically active agents, the inventors say. They also claim that it can be used for "engineering new viral pesticides with enhanced efficacy", as well as working on its own as a biopesticide or in combination with either a

biological or chemical insecticide. (Source: *Chemistry & Industry*, 21 September 1992)

Exploring other surrogate markers

Though CD4 counts are the best-known surrogate marker for AIDS, the body offers other clues about the rate at which HIV is dismantling the immune system, clues that may help researchers identify effective treatments. Here is a sampling of lesser-known surrogate markers that researchers are exploring.

β_2 microglobulin and neopterin. β_2 microglobulin is part of the class I major histocompatibility complex found on the surfaces of many cells; neopterin is produced when white blood cells called macrophages are stimulated. Both are elevated in HIV-infected people and in some studies have been better disease predictors than CD4 counts. Though they offer similar predictive value, β_2 microglobulin is more informative in late stages of the disease. A few AZT studies have shown that both can help evaluate therapies. Yet researchers are uneasy because neither seems directly implicated in the disease process.

Interferon. Interferon, a protein that carries signals to white blood cells, is elevated during HIV disease, especially in sicker patients. In the *Lancet* earlier this year, Donna Mildvan of New York's Beth Israel Medical Center and her colleagues reported a small study in which AZT markedly reduced levels of two types of interferon, an effect associated with decreased risk of death. "If confirmed in larger studies, it could be a very powerful marker in advanced disease", says Mildvan.

Delayed-Type Hypersensitivity (DTH). As their disease progresses, HIV-infected people lose the ability to respond to foreign antigens. DTH tests capitalize on this by injecting harmless antigens into a person and then measuring the resulting sore. DTH is a gauge of a type of immunity known as cell-mediated immunity (as distinct from the antibody response).

Early clinical symptoms. Symptoms like thrush, herpes zoster, weight loss and rashes do not define AIDS but can serve as useful markers of a treatment's effectiveness.

It is also more than possible that the best markers have not been discovered. "Surrogate markers are the clinical application of pathogenesis research", says Jonathan Kagan, head of clinical sciences at NIAID's Division of AIDS. "The more we understand athogenesis, the more we will find markers", and, as many researchers emphasize, markers become more powerful as they are combined. (Source: *Science*, Vol. 258, 16 October 1992)

Crystal structure of HIV reverse transcriptase discovered

The search for AIDS drugs could be boosted by the discovery of the crystal structure of the HIV's vital enzyme, reverse transcriptase. Lori Kohlstaedt and her colleagues at the Howard Hughes Medical Institute in Connecticut have built a detailed picture of the enzyme, which is the target of all the current HIV drugs because HIV cannot replicate without it. (Extracted from *New Scientist*, 4 July 1992)

Bacterial genes

Proteins from harmless bacteria could be used for malaria vaccine

A subunit vaccine - consisting only of the highly immunogenic parts of a pathogenic organism - for the type of malaria with the highest human mortality rate, could be the end result of research carried out by Dr. Stefan Ståhl in the Department of Biochemistry and Biotechnology at the Royal Institute of Technology in Stockholm. His thesis describes how harmless bacteria such as *Escherichia coli* have been used to produce immunogenic proteins from the malaria parasite *Plasmodium falciparum*.

The production systems described are general with a number of advantageous characteristics, Dr. Ståhl says. The proteins produced with the aid of modern gene technology have been programmed to be exported out of the bacterial cell. They are fusion proteins and one part consists of a "handle" that "grabs" an immobilized "counterpart". When the counterpart is tied to a solid surface, the fusion proteins can be efficiently purified from the bacteria's own multitude of proteins and used for further immunological studies.

This new type of strategy to produce subunit vaccines has been made possible through DNA technology. It is a combination of medical/ immunological research and high technology, Dr. Ståhl says. After identifying which parts of the pathogenic organism are required to create immunity, these are produced in another organism. The subunit vaccines are safer, and also possible to produce even when the required organism cannot be cultivated. (Source: *SIP* 230/92)

Mutant enzymes quicken the pace of chemical reactions

Genetic engineering is having an impact on chemistry as well as agriculture and medicine. Modified DNA is being used to produce mutant versions of enzymes, which are better than natural enzymes at speeding up chemical reactions.

Biologists at the University of Bristol used cloned DNA from the hot-spring bacterium *Bacillus stearothermophilus* to make a "mutant enzyme". This enzyme was then used by Guy Casy and his colleagues at the university's school of chemistry to catalyse the reactions of a group of compounds commonly used as building blocks in organic synthesis.

Casy and his colleagues at Bristol have studied the enzyme lactate dehydrogenase, produced by *B. stearothermophilus*. This enzyme catalyses the reduction of the keto (C=O) group in compounds such as α-keto acids to a hydroxy (OH) group, an important step in many chemical syntheses.

According to the researchers, the enzyme is ideally suited to being manipulated by genetic engineering because its three-dimensional structure is well known. They made a mutant version of the enzyme by first cloning the gene in the bacterium that codes the enzyme.

Using two short pieces of machine-synthesized DNA, the biologists made specific alterations in two regions of the gene. They then introduced the engineered gene into the bacterium *Escherichia coli* to "express", or produce, usable quantities of the mutant enzyme.

By changing the amino acid sequence of the enzyme in this way, the researchers altered its three-dimensional structure and hence its catalytic properties. The wild-type enzyme cannot cope with compounds such as α-keto acids, which have bulky side groups, but a similar human enzyme can. The researchers pinpointed which amino acids to change in order to make the bacterial enzyme act on these compounds.

The bulky groups are hydrophopic (greasy) and make the compounds very different from the enzyme's natural substrates. They prevent the compound from fitting into the active site of the wild-type ensyme, preventing catalysis. The researchers modified the enzyme in a way that made a region close to the active site more hydrophobic than that in the wild type; in this respect it resembled the same region in the human version of the enzyme. The substrate's bulky groups could then fit. By making further changes in the enzyme, the researchers increased its flexibility, making the active site even more accessible.

The lactate dehydrogenase from *B. stearothermophilus* has one further advantage, stemming from the micro-organism's ability to grow at 55° C, the temperature of many volcanic hot springs. Both the wild-type and the mutant enzyme survive at temperatures that will destroy many other enzymes, and retain their catalytic activity when heated to 90° C. Casy believes this makes them "ideal for use as synthesis catalysts". The enzymes in our bodies are rendered inactive above 40° C or 50° C. (Source: *New Scientist*, 4 July 1992)

Bacteria found to eat CFCs

Certain soil bacteria are able to break down chlorofluorocarbon-11 and -12, according to United States Geological Survey scientists. The bacteria have so far been found in pond, marsh, swamp and river sediments in the eastern United States and are presumed to destroy the CFCs only in the absence of oxygen. The researchers say the bacteria may break down CFCs in landfills - in air that circulates into the ground - and could be used by manufacturers or users seeking to destroy CFC supplies. (Source: *Chemical Week*, 20 May 1992)

Research instrumentation

New imaging diagnostics to be developed

The development of a new kind of pharmaceutical to diagnose diseases using radioisotopes is the subject of a joint venture between Allelix Biopharmaceuticals Inc. and Nordion International Inc., who have established Resolution Pharmaceuticals Inc. to develop and manufacture radioisotopically-labelled peptides.

The use of isotopically-labelled peptides represents the latest advance in the development of agents that allow physicians to diagnose internal disorders using imaging cameras. Peptides are less costly to produce, offer lower probability of immune reaction and clear from the blood faster, resulting in increased imaging sensitivity and superior image quality.

Initially, the joint venture will focus on the development of technetium 99m-labelled peptides offering superior imaging performance for disorders such as inflammation and associated infections. Technetium 99m is already the most preferred isotope for imaging, it and its precursor is supplied to world-wide markets by Nordion. The joint venture will employ peptides developed by Allelix to more effectively deliver technetium 99m to particular sites in the body.

Further information from Allelix Biopharmaceutical, 6850 Goreway Drive, Mississauga, Ontario L4V 1P1, Canada. (Source: *News release*, 9 October 1992)

Polymerase chain reaction used for antigen detection

A technique that harnesses the polymerase chain reaction (PCR) to detect vanishingly small amounts of an antigen has been developed by Charles R. Cantor, Cassandra L. Smith, and Takeshi Sano, of the University

of California, Berkeley, and Lawrence Berkeley Laboratory. In the technique, dubbed immuno-PCR, antigen is immobilized and exposed to an antibody specific for it. Then, a molecule that binds both DNA and antibodies is used to attach a DNA marker to the antigen-antibody complex, resulting in the formation of a specific antigen-antibody-DNA conjugate. The marker DNA is then amplified by PCR. The presence of PCR products demonstrates that marker DNA molecules have attached specifically to antigen-antibody complexes; the absence of PCR products shows that no antigen was present for binding to antibody. Using agarose gel electrophoresis to detect PCR products, the researchers were able to detect the presence of as few as 580 immobilized antigen molecules, a level of sensitivity about 100,000 times greater than that achievable with conventional enzyme-linked immunosorbent assays. The researchers suggest that relatively straightforward improvements in the technique could, in principle, allow the detection of a single antigen molecule. (Source: *C&EN*, 5 October 1992)

A new tool for chemists

Until now, neural networks have largely remained in the domain of computer science and artificial intelligence research. However, a recent collaboration between researchers from Merck, Sharp and Dohme and theoretical chemists at Imperial College, London, could soon make the "learning" ability of such systems an important new tool for understanding the workings of complex molecules such as enzymes.

Imperial College's Henry Rzepa and his team have "trained" a neural network, known as SONNIC, using three-dimensional electrostatic potential data, to "recognize" the pattern associated with 30 differently substituted imidazones. The team then fed the pattern calculated for the anomalous histidine-95 residue in the enzyme triosephosphate isomerase to the network.

This residue does not behave as expected because of the proximity of an α-helix portion of protein. This proximity alters the electrostatic potential pattern around the histidine, a change "recognized" by the trained neural network, and expressed as an accurate prediction of the residue's acid dissociation constant (pK_a). These values are important in determining the catalytic properties of the enzyme.

Predictions of dissociation constants and other physical data obtained using neural networks could help molecular biologists to target the right region of an enzyme to change in order to manipulate its properties. This could be especially useful in improving batch processing in the brewing industry, where raising the active temperature of fermenting enzymes from 37° C to near the boiling point of ethanol would allow for simpler "product" retrieval.

There are 33 such known enzymes other than triosephosphate isomerase and most of their pK_a values have not been measured experimentally. Predicting their properties on the basis of theoretical dissociation constants could remove the need for laborious measurements. The researchers are currently investigating the scope and accuracy of the technique. (Source: *Chemistry & Industry*, 21 September 1992)

New test for genetic markers

A faster method for detecting single molecules of DNA and other biologically important compounds has been developed by scientists at the Los Alamos National Laboratory in New Mexico. The group claims the technique has advantages over methods such as the polymerase chain reaction (PCR) and gel electrophoresis.

Alonso Castro, Frederic Fairfield and Brooks Shera use laser light to excite a fluorescent dye, ethidium bromide, bound to pieces of DNA. They pass the fragments by the laser beam quickly in a very thin stream of water, in a sheath flow cuvette.

As each fragment passes the laser, it emits a short burst of light, which can be detected and recorded as a sharp peak. The intensity of the light, or the height of the peak, is proportional to the length of the DNA molecule, because more dye molecules bind to longer DNA fragments.

The method does not determine specific nucleoside sequences, just the length of DNA fragments. However, Castro says that coupled with the use of restriction enzymes, which cut DNA at specific sequences, it can be used to detect particular genetic markers of known length.

Castro claims his method has advantages over PCR, which involves making many copies of - or "amplifying" - a DNA fragment.

The sheath flow cuvette method could be automated, in a clinical instrument for which little training would be needed, Castro believes. It currently has a detection limit of 10^{-16}M for large biological molecules, but can detect DNA fragments as small as 20 kilobases.

One drawback: it cannot distinguish between fragments of similar sizes. Castro hopes to improve the resolution to differentiate between DNA fragments that differ in size by only a few per cent. (Source: *Chemistry & Industry*, 21 September 1992)

Less time and money to produce cancer drugs

A start-up biotechnology company recently established in San Antonio is using computer power to

simulate the first 50 to 150 drug experiments to save time and money required to bring cancer drugs to critically ill patients. The company, BioNumerik, is teaming up with IBM, which is supplying computer workstations that provide microprocessing power to tackle large computing problems. Using a rational drug design approach, experiments usually performed in the laboratory can be simulated on speedy computers, eliminating blind alleys and saving time and money. The company is also developing new software that will incorporate virtual reality capabilities and allow the chemists, biologists and physicists to see molecules in several dimensions, and could forever change the way drugs are developed. IBM will provide the company with 20 workstations, giving BioNumerik one of the largest parallel networks in the world focused on biotechnology. (Source: *BioBytes*, August 1992)

Fast magnetic resonance imaging

Fast magnetic resonance imaging (fast MRI) can provide images of the brain to show changes in blood flow in split-second intervals, helping to provide information on the mechanism of brain activity. Fast MRI is much faster than positron emission tomography (PET) and requires no radioactive compounds. The research could eventually increase scientists' understanding of what goes wrong in epilepsy or psychiatric disorders. Fast MRI is based on the assumption that active nerve cells in the brain will demand more oxygen, and therefore more blood flow, than inactive cells. The chief benefit of fast MRI should be to help determine which areas of the brain are involved in what tasks. AT&T Bell Laboratories started developing fast MRI about two years ago. Research on fast MRI is also being done at Massachusetts General Hospital, the University of Minnesota and Yale University. Fast MRI so far has confirmed findings of PET, which images glucose metabolism in the brain. Dr. Robert Shulman of Yale admits that there is a great leap between blood flow levels and the interaction of individual nerve cells, but the two functions are apparently closely related. MRI detects signals from hydrogen atoms of water molecules. The hydrogen atoms are warped by a strong magnetic field. The radio waves given off when the realign themselves when the field is switched off are measured. Dr. Seiji Ogawa of AT&T Bell Laboratories discovered that the hydrogen in water molecules around blood vessels has slightly different magnetic properties depending on whether or not the blood is loaded with oxygen. Active areas of the brain become engorged with oxygen-rich blood, and this can be imaged with fast MRI. (Extracted from *New York Times*, 14 July 1992)

New additions to antibody range

Cambridge Research Biochemicals have added new products to their range of oncoprotein antibodies.

- Two rabbit polyclonal antibodies to p56lck recognizing different epitopes. p56lck is a tyrosine protein kinase which forms complexes with CD4 and CD8 in T-lymphocytes and NK cells.

- A rabbit polyclonal antibody to trk. trk belongs to the family of tyrosine protein kinase receptor molecules. The trk protooncogene product has been shown to be the high affinity Nerve Growth Factor receptor.

- A rabbit polyclonal antibody to the Retinoblastoma Gene Product. The retinoblastoma gene product is a nuclear phosphoprotein which is thought to regulate cell proliferation. Mutations in the retinoblastoma gene are found frequently in human sarcomas, lung, bladder and breast cancers and are the molecular basis for hereditary predisposition to retinoblastoma.

The antibodies have been raised to peptide immunogens and extensively characterized for use in Immunoblotting, Immunoprecipitation and Autophosphorylation assays. The immunizing peptides are also available for each of these antibodies.

- A sheep polyclonal antibody to fos and a rabbit polyclonal antibody to c-erbB2. The antibodies have been extensively characterized for use in Western Blotting, ICC and Immunoprecipitation.

For further information please contact: K. M. Price, Cambridge Research Biochemicals Ltd., Gadbrook Park, Northwich, Cheshire CW9 7RA, United Kingdom. (Source: *Press Release*, 13 July 1992)

Marker base improves diagnosis and treatment of inherited diseases

Scientists in various parts of the world are today working on projects to characterize and map the human genome (set of inherited chromosomes). It has been called the "biggest biological project in history", according to Dr. Claes Wadelius in the Department of Clinical Genetics at Uppsala University Hospital in Sweden. Dr. Wadelius has developed one of the world's more advanced marker bases for his doctoral thesis "Molecular studies of genes and mutations in families with genetic disorders". The genetic marker base at Uppsala serves as a resource centre for the whole of Scandinavia.

To be able to diagnose and treat genetic disorders better, it is important to locate the defective gene within the genome. This is where the genetic map comes in as it places the gene carrying a certain characteristic at a

specific point on one of the chromosomes. The scientists need well-known reference points - markers - to create and orient themselves on the map.

Dr. Wadelius' marker base currently contains more than 150 of the total 300 needed for a complete map of the genome. The markers consist of short synthetic DNA-pieces and are required for analysis using the PCR (Polymerase Chain Reaction) technique to multiply DNA. Dr. Wadelius has worked together with the Swedish biotechnological company Pharmacia on the development of special software for the analysis equipment. The Nordic Council of Ministers provided a grant for the project.

Dr. Wadelius used his own marker base to place the genes for some hereditary disorders - e.g. Lowe oculocerebrorenal syndrome, hyperkalemic periodic paralysis and properdine deficiency - on the map. The new discoveries in this field greatly improve diagnosis and even make it possible to trace genetic disorders in the unborn child and still healthy carriers of defective genes. They may also lead to more rational treatment in the future, Dr. Wadelius says. (Source: *SIP* 103/92)

New immunoassay system

PerSeptive Biosystems (Cambridge, MA) has launched the ImmunoDetection Sensor Cartridge immunoassay system which is simple to use and highly selective. The new immunoassay system performs analyses in a flow-through format by combining PerSeptive's Perfusion Chromatography technique with immobilized antibodies. The system is automated for greater accuracy and reproducibility. PerSeptive has successfully addressed problems that can limit the speed and efficiency of immunoassay and chromatography methods. Previous separation techniques represented a trade-off between speed and accuracy. Methods that yielded quick results were only capable of low resolutions and methods that achieved high resolutions were slower.

PerSeptive's ImmunoDetection (ID) assay allows scientists to measure the concentrations of target biomolecules such as proteins, peptides, oligosaccharides and antigens in real-time without the need for lengthy incubation procedures. New ID assays, including antibody mobilization and the standard curve, can be set up in under one hour as compared to two days to two weeks for setting up conventional assays. The assay itself can be performed in seconds or minutes, instead of two to four hours for conventional assays. The ID sensor has four basic components: an immobilized antibody that binds the target molecule, the flow-through bead, the flow-through cartridge that concentrates the target molecules, and the chromatography instrument. Each assay costs less because the antibody used for the separation can be reused hundreds of times. Moreover, more than one analyte from the same sample can be analysed by using the cartridges in series. ID Sensor Cartridges are available for either antigen or antibody assays. (Extracted from *Genetic Engineering News*, 15 May 1992)

Miscellaneous

New genetic tests

New genetic tests to determine the origins of natural materials, including fibres, timber and meat, are being developed at the British Textile Technology Group.

The BTTG tests could have far-reaching implications for activities ranging from clothes retailing to the control of trade in endangered species. The research started with the aim of finding a new way to distinguish between different fibres in clothing materials, which would be faster and more reliable than traditional examination by microscope. The textile industry needs such a test to detect the adulteration of expensive animal fibres like cashmere and mohair with cheaper wools. BTTG scientists have discovered how to extract the small amounts of DNA present in processed fibres and then identify the species from which it comes. They are now developing a kit, which will, for the first time, enable textile buyers to check quickly and accurately whether a particular fabric matches its specification. At the same time BTTG's Manchester and Leeds laboratories are working to extend genetic testing to a much wider range of natural materials.

One potential application is in the food industry, to test the origin of meat products. An inspector or buyer could then tell immediately whether a sausage contained the correct amount of pork, beef or venison - and had not been adulterated with kangaroo or horse meat.

BTTG sees the timber trade as another outlet. The genetic test could distinguish between woods which are difficult to tell apart with conventional methods.

The technology also has forensic applications, which would supplement the well-known role of human gene tests in rape and murder cases. For example, DNA analysis of stomach contents might identify a murder victim's last meal and a single fibre at the scene of the crime could provide evidence about the clothing worn by a murderer. (Extracted from *Financial Times*, 16 October 1992)

Landmark on human gene map

In a milestone for the human genome project, two separate teams have published the first two human chromosome maps of cloned DNA. Daniel Cohen at the Centre for the Study of Human Polymorphism in Paris, and a team that includes researchers from Japan and the United States, have mapped the long arm of chromosome 21. Meanwhile, David Page and his

colleagues at the Whitehead Institute in Cambridge, Massachusetts, have mapped the Y chromosome.

Both teams used the same basic method, by cloning overlapping sequences of human DNA in yeast cells. These yeast artificial chromosomes, or YACs, allow scientists to narrow the search for particular genes to within a few hundred thousand base pairs. By requesting specific YACs from the teams, researchers who need to "search" a region of DNA for a gene will now be able to hunt through precise stretches of DNA between known points on the chromosome. (Source: *New Scientist*, 3 October 1992)

Antisense agents

An emerging class of drugs known as antisense agents may make it possible by the turn of the century to avert several serious diseases of cellular or genetic origin.

Antisense agents, touted as the "second wave" of biotechnology, employ proteins to deliver a message to the DNA level of cells to redirect the RNA to produce "good" cells instead of disease-causing ones - that is, changing the "sense" of the original RNA message.

The proteins are made up of amino acids specifically sequenced to form peptides and oligonucleotides that target specific chains in diseased or disease-prone DNA and RNA.

For example, a patient with a precancerous lesion might be injected with an antisense drug. The protein would act to stop the patient's RNA from proliferating cancerous cells before uncontrolled growth even started, or at least early enough that those few cells which might already have formed would die off without causing further damage.

Such drugs could mean a burgeoning supply business for makers of amino acids and peptides. The research companies have the option of making their own oligonucleotides or having supply houses build chains researchers have designed for specific targets. Aside from cancer, researchers are interested in the effects this class of drugs may have on HIV, heart disease, arthritis and diabetes, among many other diseases. (Extracted from *Chemical Marketing Reporter*, 19 October 1992)

Nitrogen fixing micro-organisms

It is almost impossible to draw a complete state-of-the-art picture of *biological nitrogen fixation* (BNF). The number of varieties and strains of nitrogen fixing micro-organisms are immense. However, all have one characteristic in common: they are bacteria. No other organisms are able to fix nitrogen from the atmosphere. Nitrogen fixing organisms possess the enzyme *nitrogenase*, which converts atmospheric nitrogen to ammonia. Among the major fixers of atmospheric nitrogen are the following categories: *Rhizobia*, *Frankia*, *cyanobacteria*, *Azospirilla*, *Azotobacter*, and *Klebsiella*.

Ecologically as well as agriculturally the most important BNF systems are *symbioses*. *Rhizobia*, for instance, are bacteria that grow in nodules on the roots of leguminous food plants such as groundnut, lentils, peas and beans, fodder crops like clovers and alfalfa, and leguminous trees such as *Leucaena*. The plant and bacteria co-exist in a mutually beneficial relationship: the bacteria induce the plant to produce nodules, thereby providing them with nutrients and a protected environment, while the bacteria fix nitrogen from the air and make it available to the plant in the form of ammonia. *Frankia* strains also form nodules on host plants, primarily trees and shrubs of the *Casuarina* family.

Anabaena azollae (a cyanobacterium) forms a symbiosis with the water fern *Azolla*. Manuring paddy fields with *Azolla*, as practised for centuries in some Asian countries, has the potential to supply the entire nitrogen requirement for a high-yielding rice crop within a couple of weeks. Free-living (non-symbiotic) cyanobacteria can also be applied directly to paddy fields (*algalization*), but this has less potential. They retain most of the ammonia they fix and assimilate it into amino acids and proteins. *Klebsiella*, *Azotobacter* and *Azospirilla* are free-living nitrogen fixers. They associate with a plant's roots but do not enter into a true symbiosis. Used as seed inoculants, they are able to associate with a range of grasses, maize, and cereals such as wheat, rice, sorghum and millet. Their natural BNF levels, however, are modest: almost all the nitrogen they accumulate is assimilated. More research would be needed to boost their ability to accumulate and liberate nitrogen.

Crop rotation and intercropping with legumes are the most simple strategies to benefit from BNF. The BNF process in, for instance, clover often serves as fertilizer for a subsequent crop. Intercropping of grain legumes with cereal crops is common in tropical areas. When the indigenous nitrogen fixing bacteria are not effectively interacting with the host legume, inoculation can be a solution. Seeds are coated prior to planting with pure cultures of bacteria in a carrier, often peat. The peat allows the inoculant to be coated onto the surface of the seed, and also serves to protect the bacteria against dessication. In many regions, the byproducts of sugar

cane production, bagasse and molasse, can be used successfully for the production of inoculants. (Source: *Biotechnology and Development Monitor* No. 12, September 1992)

D. APPLICATIONS

Medical and pharmaceutical applications

Colombia's malaria vaccine approved for trials

A controversial malaria vaccine developed by a Colombian scientist began phase I safety trials in the United States in a joint venture with the US Army.

Manuel Patarroyo, a biochemist from the National University of Colombia in Bogota, developed an experimental vaccine in the late 1980s and has already conducted large-scale field trials of it in Latin America. The vaccine is based on four synthetic peptides, or segments of protein, which mimic the coat protein of *P. falciparum*.

Patarroyo, claims the vaccine is highly effective in protecting against malaria, but although other scientists are impressed with his laboratory data, many have questioned the results from his early clinical trials, which did not use control groups.

Researchers from the US Army, led by Jerry Sadoff at the Walter Reed Army Institute of Research in Washington, DC, have joined Patarroyo to test the vaccine. Because the FDA will only consider products made in American laboratories whose good manufacturing practice it had certified, the vaccine has been made in California instead of in Bogota. However, Sadoff stresses that the vaccine is "the same" and was made under Patarroyo's instruction.

In animal tests carried out at Walter Reed, the vaccine stimulated the same range of antibodies against the parasite as Patarroyo's original batches had done. The vaccine is now being tested in a small group of healthy civilians and military recruits in the United States, to check that it is safe and stimulates an immune response. If the tests go well, field trials could begin in early 1993 in Thailand to show whether the vaccine protects against infection. (Extracted from *New Scientist*, 26 September 1992)

New malaria hope

China's answer to malaria for the past 2,000 years or so has been artemisinin - known in China as *qinghaosu*. It is an extract of the wormwood plant, *Artemisia annua*, whose active compound was isolated and identified by Chinese scientists in 1972. Artemisinin is not easily dissolved in water, so for years manufacturers in China have been making and selling two derivatives, artemether and artesunate, that are more easily taken up in the body. This family of drugs is completely separate in structure - and, presumably, in action - from all other anti-malarials. Numerous trials have been published in Chinese journals, and now studies outside China are confirming that they are highly effective and act rapidly against the parasite.

Officials at WHO say no one outside China knew about the drug until 1979. WHO has been working with the Chinese Government since the early 1980s to obtain samples of the drugs and to translate the Chinese data on them. Meanwhile, WHO has also worked with the Walter Reed Army Institute of Research in the United States, and others, to produce an ethyl ether derivative of artemisinin, called artemether, which is now going through safety trials in Europe.

Artemether is said to have fewer toxic side-effects than artesunate, but the published data on both are still scant. While everyone waits, doctors in the worst-hit areas of South-East Asia, the Amazon and Africa are starting to treat people with Chinese artesunate.

Rhône-Poulenc Rorer expects to begin marketing their new anti-malarial drug, *Paluther*, during 1993. In clinical trials with severely ill patients, *Paluther* has acted faster than other anti-malarials when injected intramuscularly. Rhône-Poulenc Rorer say this offers hope that the new drug may be able to improve survival, particularly among children, who are frequently the most severely affected by malaria. (Extracted from *European Chemical News*, 7 September 1992, and *New Scientist*, 31 October 1991)

Anti HIV antibody trials

At the 8th International AIDS Conference in Amsterdam, Tanox Biosystems (Houston, Texas), the University Hospital of Zurich and Ciba-Geigy Ltd. presented the findings from a recently concluded human clinical trial of a monoclonal antibody against the human immunodeficiency virus (HIV). This was an open-label trial of a chimeric (humanized mouse) antibody, involving 12 volunteer viremic patients with advanced cases of AIDS. They were selected according to laboratory test results of antibody binding and were without anti-retroviral treatment for at least four weeks. The purpose of the study was to investigate the tolerability and behaviour of the antibody. Antibody therapy (or "passive immunity") is a concept which aims at controlling HIV by providing an infected person with antibodies that can neutralize or block the virus.

The results of the limited clinical study demonstrated that the antibody was well tolerated by the volunteer AIDS patients and had a biological half-life of 8-19 days. The antibody's half-life was markedly shorter in those patients with higher serum antibody binding activity. No side-effects were observed.

Ciba-Geigy plan to continue characterizing the antibody in further viremic disease conditions during the first half of 1993. Evidence of the therapeutic value of this treatment approach is unlikely to become available before the end of 1993. (Source: *Biotechnology Bulletin*, September 1992)

CEL-SCI completes safety testing of AIDS vaccine

Phase I studies of CEL-SCI's HGP-30 AIDS vaccine have been completed in healthy HIV-negative volunteers. Eighteen healthy volunteers safely tolerated the vaccine with no evidence of significant chemical or haematological toxicity attributable to the vaccine for periods of up to one year.

The HGP-30 vaccine is designed to overcome one of the major barriers to successful AIDS vaccine development. It is a synthetic copy of a region of the p17 core protein of the AIDS virus. Unlike the envelope of the AIDS virus, which undergoes frequent change, this core region is highly conserved from strain to strain. The vaccine was seen to elicit antibodies to HGP-30 in 17 of the 18 - and stimulated the production of HGP-30 specific T-cells in five of the nine volunteers tested. The patented rights to the HGP-30 AIDS vaccine are owned by Viral Technologies Inc., a joint venture of CEL-SCI Corp. and Alpha 1 Biomedicals Inc. Details from Dr. Vincent F. Simmon of Aipha 1 Biomedicals on +1 (301) 564 4400 or Geert Kersten of CEL-SCI Corp. on +1 (703) 549 5293. (Source: *Biotechnology Bulletin*, September 1992)

Testing blood for HIV infection in developing countries

Five years ago, the cost in some developing countries of testing each transfusion of donated blood for HIV infection was estimated at $30, compared with $1 allocated per person for health care in an entire year. Since then the situation has improved slightly: a preliminary test on a sample of donated blood can cost less than $1. But this is still a significant outlay for countries where the annual health budget per person is only $2 or $3.

In industrialized countries, donated blood is now routinely screened for HIV, making transmission by this route very rare. The same is not true elsewhere. The World Health Organization (WHO) estimates that in most developing countries, between 1 and 5 per cent of new HIV infections are due to infected blood transfusions, rising to 10 per cent in parts of sub-Saharan Africa.

When testing for HIV first began in the mid-1980s, the most commonly used test was the enzyme-linked immunosorbent assay, or ELISA. The test is laborious, involving adding many reagents and washing the plate of test wells after each one. It is intended for batch-testing more than 90 samples at once, not one or two at a time, and takes two to four hours.

In the late 1980s, health workers in Africa began asking for test kits that were not only cheaper, but also appropriate for use in small rural hospitals and medical centres. Such kits would not rely on reagents that needed refrigeration, would need no special skills to operate, could test one or two people at a time rather than batches of up to 100, and give results in a few minutes rather than hours.

These "rapid-simple" tests are now on the market, though the majority were intended for use in doctors' surgeries in industrialized countries, where patients would pay for an immediate answer. Many of them simply involve adding a drop of blood to a well, followed by a few drops of different reagents, and the result is available within a few minutes. Costs per sample range from below $1 to $4. However, both the United Kingdom and the United States have banned the sale of such kits to private individuals to protect people from testing without adequate counselling.

Few of these tests were designed with the needs of developing countries in mind. One exception is a test being developed by Cambridge Biotech Corporation in Worcester, Massachusetts. It uses the "latex agglutination" method: tiny beads of latex are coated with antigen proteins from HIV, making an initial mixture that looks like normal milk. When the patient's serum is added, any HIV antibodies in it attach to the antigens, making the beads "stickier", until eventually they hook together into clumps. If a test of this kind is positive, the final mixture will look like curdled milk.

The novel aspect of Cambridge Biotech's test is how the latex beads are agitated to bring them into contact with each other, an essential process if they are to agglutinate in the presence of antibodies. A plastic slide in the test kit is made from two pieces of plastic ultrasonically welded together with a narrow, tube-like channel running through the centre. The tester mixes the patient's sample with the latex in a well at one end of the slide, and drags the mixture to that end of the channel with a pipette. Capillary action then draws the liquid along the channel towards the other end of the slide, and so keeps mixing and agitating the beads. A result takes five minutes.

The test can be read by eye, but to avoid errors, Cambridge Biotech has developed a battery-operated slide reader small enough to fit into a briefcase. This has a photodiode that can detect agglutinated particles, and according to the result the reader displays a plus or a minus sign. Cambridge Biotech says the test is very reliable, giving few false-negative and false-positive results. The company plans to launch it in Europe and the developing countries. No price has yet been set, though the slide reader will cost about $500.

Health workers who have used the test in Africa are enthusiastic about it. This method is ideal for screening donated blood, especially in areas without blood banks where person-to-person donation is customary. Blood that tests positive is thrown away and the donor told it is unsuitable. However, if the person being tested is to be told the result, and the initial test is positive, the small risk that it is a false-positive makes a second and sometimes third test necessary for confirmation.

WHO used to recommend carrying out an ELISA first, and then a test called the Western blot. But while an ELISA costs only $0.75 to $1.75 per sample, the Western blot (which requires nitrocellulose gells, radioactive chemicals and photographic emulsions) is extremely expensive, at around $40 each.

The new tests let WHO change its recommendations. It now suggests using specific combinations of the ELISA with rapid-simple assays to confirm presence of HIV with maximum accuracy at the lowest cost (*Weekly Epidemiological Record*, Vol. 67, p. 145).

Most people working in the field agree that when used in these combinations the rapid tests are simple and accurate. So now the problem is not devising the technology for HIV testing in developing countries, but getting the tests to those who need them, at an affordable price.

Some companies charge higher prices to buyers in industrialized countries, who thus subsidize those in developing countries. Patrick Leonard, chief executive officer of Cambridge Biotech, says single-sample tests produced by his company have been bulk-bought by Governments and pharmaceutical companies and sold to developing countries for between $1 and $1.50 each, while their price to developed countries ranges between $3 and $4.

WHO successfully negotiated bulk purchase agreements which enable it to sell tests for $0.65 or $0.70 each - cutting the price by over 50 per cent. Further evidence that tests can be produced very cheaply also comes from the Program for Appropriate Technology in Health (PATH), a non-profit medical organization based in Seattle. In 1991 it developed a test that should cost about $0.20 and take 20 minutes to give a result (*New Scientist*, 9 March 1991).

Robert Downing of the Uganda Virus Research Institute, in Entebbe, says there is a large potential market in Uganda among people who want to know whether they are infected with HIV before marrying or starting a family. But kits are not available on the local market, and many potential users have trouble getting foreign currency. He thinks companies should examine ways of distributing kits priced in local currency: many Ugandans could afford to pay clinics or hospitals 2,000 shillings (about $2) for one-off tests, he says. It would be up to the company to convert that money back into dollars - easier in some African countries than in others.

With this in mind, PATH tried to set up manufacture of its test in Zimbabwe. It was to collaborate with an African company in Harare, but the company pulled out.

WHO supports initiatives such as that by PATH and will help check the quality of locally produced test kits. Although some private hospitals and clinics in developing countries can afford to buy their own test kits and charge their patients for them, many tests carried out in developing countries are paid for by grants from research projects and international bodies such as WHO. (Extracted from *New Scientist*, 5 September 1992)

Herbal disinfectant kills HIV virus

Herbal medical disinfectants that can kill the HIV virus in 30 secords have been recently developed by the Beijing Zhonglian Corp. The new disinfectants, named TG901 and TG901A, were developed by scientists at the New Technology Development Institute of Beijing Zhonglian Corp. with reference to ancient Chinese prescriptions and folk remedies. Tests by the AIDS Research and Test Centre of the Chinese Academy of Preventive Medicine Science, the Microorganism Epidemic Institute of the Chinese Academy of Military Medical Science and Beijing Venereal Disease Research Institute show that the diluted solution of the disinfectants kill the HIV virus in 30 seconds. In addition, the new drugs can also kill *syphilis spirochaete*, *gonorrhoea diplococci* and pathogenic fungus and mould in a very short time. This new breakthrough in medical science is of great significance in the prevention of AIDS and many other venereal diseases. (Extracted from *Chinese Chemical Research*, June 1992)

Enzymes kill AIDS virus on contact

A San Antonio biomedical company has found an affordable way to manufacture a product that selectively destroys the AIDS virus and other pathogens on contact. "Exact" is the trade name for two highly potent, purified enzymes, Myeloperoxidase (MPO) and Eosinophil Peroxidase (EPO), manufactured by ExOxEmis, Inc. Because it kills the AIDS virus but does not harm surrounding tissue or helpful bacteria which occur normally in the body, Exact could be used prophylactically in douches, creams, suppositories or lozenges. Although the antiseptic benefits of these enzymes have been known for 25 years, the cost of producing them on a large scale prohibited their entry on the consumer market until ExOxEmis made the process viable. Other possible uses for Exact include coating

donor blood bags to prevent HIV infection and treating other sexually transmitted diseases. (Source: *BioBytes*, November 1992)

P24-VLP AIDS drug to go on trial

British Biotechnologies AIDS treatment p24-VLP has been recommended by the US National Institute for Allergy and Infectious Diseases (NIAID) for evaluation in US clinical trials. Trials in HIV-positive patients are expected to start in the United States in 1993, and will be organized and funded by NIAID subject to its final approval procedure.

P24-VLP will be the first of British Biotechnology's four products currently in clinical trials to be studied in the United States. The drug has successfully completed a Phase I clinical trial supported by the UK Medical Research Council in healthy volunteers in the United Kingdom.

The drug, designed to prevent or slow down the progression of HIV-positive patients to AIDS, is genetically engineered using British Biotechnology's proprietary *Virus-like Particle* technology.

P24-VLP is designed to stimulate immunity to the core HIV virus protein, p24. Patients with high immunity to p24 show a slower progression to full-blown AIDS. (Source: *European Chemical News*, 2 November 1992)

Biotechnology used to create new molecule for cancer treatment

By tailoring a molecule using biotechnological methods, Swedish researchers are claimed to have developed a new method of producing a pharmaceutical for treating cancer, reports Kabi Pharmacia, the Swedish pharmaceutical group, with headquarters in Uppsala, north of Stockholm. The method was developed jointly by the BioScience Centre, recently opened in Stockholm, and the company's research unit in Lund, south Sweden.

The new molecule consists partly of an antibody, partly of a substance that stimulates the immune system. Because of its tailor-made structure it can be induced to directly identify and seek the type of cancer cells in question. It then proceeds to stimulate the body's own immune system to combat the cancer, Kabi Pharmacia says.

Professor Staffan Josephson, head of the BioScience Centre, says that biotechnology makes it possible to design pharmaceuticals that home in on their target, in other words, to affect the pathogenic cells only and nothing else. This sharply reduces the risk of side-effects. Treatment by irradiation and cytostatic agents, on the other hand, not only acts on the tumour but also has effects on the whole body.

Kabi Pharmacia's resources for molecular and structural biology and cell culture, which are considered to be the most important basis for the company's long-term pharmaceutical research will henceforth be concentrated to the BioScience Centre. It has a staff of 120 people, including 30 post-doctoral researchers.

According to Professor Josephson, the Centre is one of the leading establishments of its kind in Europe, partly because of its size, partly because of the competence in biotechnology assembled there. Extensive cooperation is also taking place with universities both in Sweden and abroad.

Another research project concerns factor VIII, which is used in cases of haemophilia. It is currently produced from human plasma but since this is in short supply the preparation is costly. Work is therefore in progress on cultivating cells that produce factor VIII in refined form. The research programme also includes the development of agents for treating atherosclerosis and glaucoma. (Source: *SIP*, 281/92)

Drug opens up second front against breast cancer

More effective treatments for breast cancer may follow now that researchers have discovered a second mode of action for the anti-cancer drug tamoxifen. The compound, which is widely prescribed for breast cancer, is known to block oestrogen receptors on many cancer cells, so inhibiting their growth.

A team working at the Institute of Cancer Research and the Royal Marsden Hospital in London, in collaboration with scientists at the National Cancer Institute in Bethesda, Maryland, has found that tamoxifen also works by encouraging the cells surrounding a tumour to produce a "growth factor".

Anthony Colletta, leader of the team, says studies had shown that women benefited from taking tamoxifen even if their breast cancer cells had no oestrogen receptors. So the team began to look for alternative modes of action for the drug.

Colletta's group compared samples of tumours from women who had been taking tamoxifen with those who had never taken the drug. The team found a "massive quantity" of TGF beta-1 in all 10 samples from the women who had been taking tamoxifen, says Colletta. The TGF beta-1 was produced by the stromal fibroblasts which surrounded the tumour cells.

TGF beta-1 is found everywhere in the body, being concentrated mainly in the platelets and the bone. Its normal functions include the repair of wounds, healing, embryogenesis and organ manufacture. Laboratory work has also shown that it strongly inhibits most types of epithelial tumour, including those of the breast.

The gene for this growth factor has been cloned and several companies manufacture its recombinant form, but Colletta says injections of TGF beta-1 are unlikely to prove an appropriate treatment for human cancers because of possible side-effects. However, because it has a very short half-life in the body, of about five minutes, "most people believe that the way to utilize the TGF beta-1 response therapeutically is to find ways of inducing it locally using other pharmacological agents", he says. (Extracted from *New Scientist*, 15 August 1992)

Non-invasive 12 mutation cystic fibrosis test

An advancement in technology to detect carriers or to diagnose cystic fibrosis by identifying 12 of the most common mutations associated with cystic fibrosis using a simple CF/12 Cheek Brush Test will be available by Integrated Genetics® (IG) after late 1992. The new test can be performed on cells obtained by brushing the inside of the cheek, thus replacing the traditional method of obtaining cells from a blood sample. The CF/12 CB test will cost less than $100 and is expected to be used as a prototype for other genetic disorders such as Duchenne Muscular Dystrophy and Beta-Thalassemia.

The CF/12 Cheek Brush Test is an easy and non-invasive procedure that begins by twirling a small brush vigorously on the inner cheek of the mouth for 30 seconds; returning the brush into a plastic tube; and mailing it back to the laboratory for analysis. IG uses PCR technology to amplify CFTR gene segments in each sample simultaneously for 12 mutations before analysing.

Further information available from IG Laboratories, Inc., P.O. Box 9322, One Mountain Road, Framingham, MA 01701-9322, USA. (Source: *News Release*, 24 August 1992)

Approval for use of hepatitis B product

Schering-Plough has won US Food and Drug Administration (FDA) approval for a biotechnology product to treat chronic hepatitis B. The drug, recombinant interferon alfa-2b, mimics a naturally occurring protein that serves as an antiviral agent in the body. The drug is already used to treat hairy cell leukaemia, AIDS-related Kaposi's sarcoma, genital warts and hepatitis C under the name Intron A for Injection. Sales of the drug totalled $251 million in 1991. The FDA approval marks the first treatment for hepatitis B, although several vaccines are available for preventative purposes. Schering-Plough is also applying for permission to sell interferon alfa-2b as a treatment for delta hepatitis, and is conducting studies to use Intron A to treat six forms of cancer and as an AIDS treatment in conjunction with other drugs. (Extracted from *Wall Street Journal*, 14 July 1992)

Growth factor cures children with serious growth disturbance

Children who suffer from Laron's syndrome - they do not grow despite administration of growth hormone and attain a final height of only 110-130 cm - can now be treated with a human growth factor, Igef, announces Sweden's Kabi Pharmacia. Developed by the company for the treatment of Laron's syndrome, among other conditions, igef is genetically engineered IGF-1 (Insulin-like Growth Factor 1). A research study covering 30 children is now under way and highly gratifying results show that 10 out of 11 children treated for six months respond favourably to the treatment, the company says. The exception was the oldest patient, a man aged 23 years. To date, about 200 children with the syndrome, for which no treatment has been available, have been identified world wide, but this figure is likely to increase.

Kabi Pharmacia launched the first genetically engineered growth hormone, Genotropin, in 1985. It is used today for treating extremely short-statured children with a lack of growth hormone and for treating short stature linked to Turner's syndrome - an inherited chromosomal defect in girls. (Source: *SIP*, 200/92)

Phase III clinical trial begins for recombinant thyroid stimulating hormone

Results from the Phase I/II clinical study of recombinant human thyroid stimulating hormone (rhTSH) demonstrate that it is safe to expand the clinical trials to a larger patient population and to recommend a dosage regimen for the detection of thyroid cancer through radioiodine whole body scanning. The Phase III clinical trials for rhTSH have begun.

The use of rhTSH may enable patients to continue taking their thyroid hormone supplement prior to and during diagnostic testing and thus avoid the debilitating symptoms of hypothyroidism such as weakness, weight gain, constipation, mental dullness, lethargy and depression. The Phase I/II study, a safety and dose finding evaluation, involved 19 patients with well-differentiated thyroid cancer. Several doses of rhTSH, given over a period of one to three days, were tested with no major adverse effects. Whole body scans taken after rhTSH treatment were rated equal to or better than scans taken after traditional hormone withdrawal in 16 of the 19 patients, and quality of life was higher during the rhTSH treatment phase compared with that experienced during hormone withdrawal.

The Phase III study will focus on evaluating the safety and effectiveness of rhTSH administration using one dosage regimen. It will be a multi-centre study and will include 100-150 patients.

Genzyme is developing a recombinant human thyroid stimulating hormone (Thyrogen®) for use as an adjunct in procedures to diagnose, treat and monitor thyroid cancer. The company believes that the concomitant administration of Thyrogen® hormone may be more effective and result in fewer side-effects than the current approach. Genzyme has received orphan drug designation for Thyrogen®.

Further information available from Genzyme Corporation, One Kendall Square, Cambridge, MA 02139-1562, USA. (Source: *Press Release*, 24 September 1992)

Human clinical trials of treatment for severe burns

Genzyme Corporation has announced it will initiate human clinical trials for Vianain™ enzymatic debridement agent. The Phase I/II study involving safety analysis and dose ranging will take place at multi-centre sites. Genzyme received orphan drug designation and patent protection for Vianain™ in early 1992.

Vianain™ enzymatic debridement agent is a formulation of two proprietary enzymes, ananain and comosain, in a hydrophillic cream vehicle. Preclinical studies to date have indicated that Vianain™ appears to be rapid and effective in removing non-viable tissue from the burn site. The use of Vianain™ is expected to minimize the loss of blood and viable tissue, as well as reduce expenses and complications associated with traditional debridement procedures.

Further information from Genzyme Corporation, One Kendall Square, Cambridge, MA 02139-1562, USA. (Source: *News Release*, 16 July 1992)

CNTF prolongs laboratory-cultured nerve cells

Experiments conducted in Germany have shown that the protein ciliary neurotrophic factor (CNTF) can prolong the life of laboratory-cultured nerve cells. The development may be applicable to motor neurone disease, a condition in which the nerve cells connecting muscles to the brain degenerate and die. There currently is no treatment for this disease. Two companies in the United States have begun clinical trials on human patients with motor neurone disease as a result of the German research. Results from the first trial were expected by December 1992. (Extracted from *The Independent*, 17 August 1992)

Regenerating cartilage

Researchers at the University of Texas Health Science Center at San Antonio have developed a procedure that appears to regenerate cartilage in rabbits. The new technique involves surgically inserting sponge-like, biodegradable implants into joints where there is damage to cartilage - the smooth, flexible, protective covering that allows knees, elbows and other joints to bend comfortably. The implants dissolve within several weeks and release "growth factors", substances that stimulate cells to begin producing new tissue. With thousands of Americans suffering sports-related injuries each year, in many cases to cartilage - which, unlike bone or skin or other connective tissue, cannot repair itself when it is injured - these implants could become a valuable tool in treatments. In addition, the researchers believe the invention could one day provide relief to people who suffer from degenerative joint diseases such as osteoarthritis, in which cartilage breaks down over a period of time. (Source: *BioBytes*, August 1992)

Gene gel could beat blocked arteries

Gels containing molecules specially designed to block the function of genes may prolong the lives of people who have had coronary bypass surgery or treatment to widen arteries around the heart. Often, patients who have undergone such surgery have relapses because arteries become reblocked.

The developers of the gels claim that their experiments with rats are the first time such "antisense" agents have been used in animals. They cover over the genetic code of genes so that it cannot be used. Their effect is analogous to obscuring one page of a construction manual so that the instructions cannot be followed.

Robert Rosenberg and colleagues at the Massachusetts Institute of Technology smeared the gel onto the damaged surfaces of neck arteries in laboratory rats that had previously been treated with balloon angioplasty. The gel hardened, forming a translucent film on the wounds. The antisense agents appeared to prevent the smooth muscle cells forming where the gel had been applied.

Antisense agents cancel genetic instructions for making compounds such as proteins and enzymes that perform vital functions in the cells of living things. Rosenberg's antisense compound interferes with the manufacture of a protein called *c-myb* which appears to be essential in the process by which the body makes smooth muscle cells.

The antisense agent is a sequence of 18 nucleotides, the building blocks of DNA, which fits snugly onto portions of a gene which normally helps to make *c-myb*. The gene normally produces another molecule called messenger RNA which carries the instructions for making *c-myb*, but the antisense agent blocks the production of the mRNA so the gene does not function.

As a control against which to compare the performance of the gel, Rosenberg prepared another

containing strings of nucleotides that would not mask the *c-myb* gene. (Source: *New Scientist*, 10 October 1992)

Predicting the future with a drop of blood

A landmark national study may lead to the development of a genetic test that would enable doctors to predict at birth a person's risk of developing heart disease - the nation's number one killer. A molecular geneticist at Southwest Foundation for Biomedical Research in San Antonio has linked a genetic variation found in one fourth of the US population with increased risk of atherosclerosis (hardening of the arteries). The study is the first to find the effects of specific genes on atherosclerosis by looking directly at lesions on the arteries. With a genetic test, in the near future it may be possible to predict who will develop the disease from a single drop of blood, which could encourage at-risk individuals to adopt a healthier lifestyle than they might have otherwise. (Source: *BioBytes*, July 1992)

Double agent could save heart from lethal clots

A drug which homes in on blood clots and breaks them up could be used to treat heart disease without the drawbacks of present "clot-busting" drugs.

The drug, being developed by Dutch researchers, relies on a combination of two monoclonal antibodies designed to latch onto specific receptor sites. One of them attaches to a substance that breaks up clots, while the other seeks out a receptor specific to blood clots. In this way the clot-buster is ferried straight to the clot.

Present clot-busting drugs, such as streptokinase or others known as plasminogen activators, work by encouraging plasmin's precursor, plasminogen, to form plasmin. But high doses of these drugs are necessary because they are rapidly broken down in the body. And because the drugs are not specific to clots they can cause internal bleeding elsewhere in the body.

Rogier Bos and Willem Nieuwenhuizen of the Gaubius Laboratory, part of the Dutch Government's TNO Institute of Ageing and Vascular Research in Leiden, sought to overcome these problems by linking a plasminogen activator to a "bispecific" monoclonal antibody made from two monoclonal antibodies, one of which recognizes the plasminogen activator while the other recognizes fibrin. The researchers found monoclonal antibodies that recognize either of the two types of plasminogen activator: urokinase-type (uPA) or tissue-type (tPA). The antibodies bind to the activators in such a way that they do not stop them working.

The researchers have carried out *in vitro* experiments with the bispecific antibody linked to tPA. Their results showed that the combination was 20 times as effective at dissolving clots as tPA on its own. They also believe it will be harder for the liver to break down the combination because the antibody masks the receptor site on the tPA that the liver needs to identify it.

The researchers are also testing another bispecific antibody that links to uPA and fibrin which they hope will be even more successful. (Source: *New Scientist*, 25 July 1992)

Hi-tech insulin

Protein engineers from York University have produced a modified version of insulin and haemoglobin with potentially major medical applications.

Around three quarters of diabetics now use genetically engineered human insulin, which has been available since 1982. However, when it is injected, the molecules tend to cling together rather than dispersing in the body. Diabetics' blood-sugar levels can therefore be seen to fluctuate throughout the day.

Professor Guy Dogeson and his team at York have designed a new molecule with altered amino-acid side chains, which induce mutually repulsive forces in the molecules, causing them to break up and disperse in diabetics' bodies like natural insulin in non-diabetics.

In the new form, insulin might even be usable in skin patches. It is undergoing toxicological tests, and Professor Dogeson is optimistic about its long-term potential.

Another breakthrough could come with a new version of haemoglobin. Unmodified haemoglobin is unstable and cannot deliver oxygen to tissues outside red blood cells because the bond it forms with oxygen is too strong. The protein engineers have replaced an asparagine side chain with lysine, reducing the molecule's strong hold on oxygen and making it potentially suitable as a blood substitute.

The new substances are likely to have a longer shelf-life and greater biocompatibility with different blood groups than red cells from human blood. (Source: *Chemistry & Industry*, 21 September 1992)

Biosource Genetics mass produces nature's sunscreen

The small US company, Biosource Genetics Corp., has developed what it feels is a man-made answer to the man-made menace of the Antarctic ozone hole. Recognizing that dark-skinned people, who have developed a protective skin pigment, melanin, Silicon Valley venture capitalist Helen C. Leong - who had just helped to form Biosource Genetics - wondered whether the company's "geneware" could be used to mass produce this natural sun-screen? Previously, the only way to collect melanin was to extract it painstakingly from such exotic sources as cuttlefish. That made the price $95.00 a gram - or $2,995.00 an ounce. Now Biosource brews

melanin for less than $1 a gram, using fermentation vessels.

Two skin creams and a lipstick incorporating Biosource's synthetic melanin are already available in Europe. In the United States, a melanin-based sunscreen is in the final stages of FDA testing and could reach the market late in 1993.

Leong next plans to start a company that would try to plug the ozone hole by spreading thousands of pounds of fine melanin particles from high-flying aircraft every two or three years. Details from: Biosource Genetics Corp., 3333 Vaca Valley Parkway, Vacaville, CA 95688, USA. (Source: *Biotechnology Bulletin*, September 1992)

R&D yields drug advance

Researchers at Oxford GlycoSystems (OGS) and the University of Oxford say they have developed a revolutionary system that allows the systematic sequencing of oligosaccharide, molecular structures, commonly known as complex carbohydrates.

The invention introduces a technology that uses arrays of enzymes in mathematically determined mixes and relies on sophisticated software algorithms. Research into these molecules is giving new insights into diseases such as arthritis, asthma and AIDS. (Extracted from *Chemical Marketing Reporter*, 19 October 1992)

Gene therapy treatment as possibility for some forms of RP

Gene therapy may offer an effective treatment for some forms of retinitis pigmentosa (RP), according to researchers at the University of Texas Southwestern Medical Center and the Jules Stein Eye Institute, University of California, Los Angeles (UCLA). They have succeeded in correcting the disease called "retinal degeneration slow" (rds) in mice involving the same gene that causes RP in humans.

The researchers used germ-cell therapy, which is unsuitable for use in humans; however, work is ongoing to insert the normal rds gene into a modified herpes simplex virus, which can be injected directly into the retinas of affected adult mice. If the technique is effective in mice, it could lead to safe gene therapy for RP in humans.

"This study suggests that somatic gene therapy for some forms of retinitis pigmentosa may be possible", said Gabriel H. Travis, MD, a neurobiologist at the University of Texas, adding that human trials are still a long way off. Dr. Travis is lead author of a report on this work recently published in the journal *Neuron*.

Dean Bok, MD, Dolly Green professor of ophthalmology at the Jules Stein Institute noted, "This study is exciting because it is the first naturally occurring animal mutation for inherited retinal degeneration that has direct relevance to human retinitis pigmentosa." (Extracted from *Ophthalmic Times*, 1 September 1992)

Hitachi develops antiulcer drug

Hitachi Chemical Co. Ltd., Tokyo, said it is working on a novel antiulcerative drug. The drug, developed originally by Chiron Corp., consists of epithelial growth factor (EGF). The compound is produced through recombinant DNA technology. Reportedly, the drug suppresses gastric acid secretion and also promotes tissue repair. Under an agreement with Chiron, Hitachi Chemical will manufacture and market EGF in Japan. The company hopes to launch the drug in two or three years and expects to gain a sizeable share of Japan's annual antiulcerative market, which is estimated to be worth around 400 billion yen. (Source: *McGraw Hill's Biotechnology Newswatch*, 5 October 1992)

New 'flu vaccines from silkworms

Daiichi Pharmaceutical of Japan has developed a new oral influenza vaccine using silkworms. Daiichi's vaccine works by exploiting the only part of the virus, the haemagglutonin, that is necessary for inoculation. In addition, silkworms are easier and less costly to breed than chickens, whose embryos are used in current 'flu vaccines. A commercial vaccine using this method is some 10 years away, and already Daiichi is looking towards future applications for other kinds of viruses. (Extracted from *Asian Wall Street Journal*, 8 June 1992)

Experimental Lyme disease vaccine test results

Tests of an experimental Lyme disease vaccine showed protection from infection plus ridding attacking ticks of the disease-causing bacteria. Researchers at Yale University School of Medicine and Harvard University School of Public Health said the vaccine will need at least three to seven years of animal and human testing before being made available. In tests on mice, the vaccine offered a protective immune response against the spirochete bacteria carried by ticks from animals to humans. After a two-week period, none of the 30 mice inoculated with the vaccine was infected by the bacteria, but half of the 26 mice that received a placebo were infected. None of the ticks exposed to the vaccine retained the bacteria. There is still a question about the efficacy of the vaccine against the different strains of bacteria found in different parts of the United States. (Extracted from *Wall Street Journal*, 16 June 1992)

Genetically engineered liver cells to be tested on children

Genetically engineered liver cells may be used to treat children with acute liver failure. The procedure has already been tested on mice and will be tested by

researchers at Baylor College of Medicine (Houston, TX) on children whose life is threatened due to acute liver failure. The treatment could be used for phenylketonuria (PKU), which is caused by a defect in the gene that codes for phenylalanine hydroxylase (PAH). This enzyme is needed to convert phenylalanine into tyrosine. Inserting the PAH gene into mouse liver cells and injecting these into PAH-deficient mice restores PAH activity to normal levels. (Extracted from *New Scientist*, 10 October 1992)

SIBIA success with Alzheimer's diagnostic assay

The SIBIA Inc. diagnostic assay for a protein associated with Alzheimer's disease correctly identified specific gene carrier members of a family with presenile hereditary Alzheimer's disease. The data showed significant and age-dependent reductions in the levels of soluble amyloid precursor proteins (APP) in the cerebrospinal fluid (CSF) of affected family members.

The data further support the hypothesis that reductions of soluble APP are indicative of the deposition of amyloid in neuritic plaques and in cerebral blood vessel walls - as is found in Alzheimer's sufferers. Currently, the identification of these lesions at autopsy is necessary for doctors to finally confirm the diagnosis of Alzheimer's. Prior to death, diagnosis may be based on physician evaluation, neuropsychological tests and brain scans, none of which are definitive. Details from: The Salk Institute Biotechnology Industrial Associates Inc. (SIBIA), 505 Coast Boulevard South, Suite 300, La Jolla, CA 92037-4641, USA. (Source: *Biotechnology Bulletin*, September 1992)

Microbial antagonists blocking hypoxic injuries to neuronal cells

Kyowa Hakko Kogyo Co. Ltd. has discovered that a compound named ES-242 isolated from a fungus *Verticillium* sp. protects neuronal cells and that it is effective in blocking the damage after cerebral haemorrhages. The compound is an antagonist for the NMDA receptor complex to prevent hypoxic injury and is the first microbial derivative with such effect. The company plans to use this compound as a drug to prevent after-effects of conditions such as cerebral haemorrhage.

The company screened roughly 12,000 strains of micro-organisms to obtain an antagonist capable of suppressing the excessive activation of the NMDA receptor and discovered that the active substance produced in the culture broth of a fungus, *Verticillium* sp., is effective in suppressing the activity. When this active substance was isolated and purified, the company discovered that it consisted of eight kinds of analogous compounds with bioxanthracene structure.

Further information is available from Kyowa Hakko Kogyo Co. Ltd., Public Relations and Advertising Dept., 1-6-1, Otemachi, Chiyoda-ku, Tokyo 100, Japan. (Source: *JETRO*, August 1992)

Animal and livestock applications

Animals as protein factories

Almost any protein the human body produces can also be made in other animals, if their genes are programmed correctly - which gives goats, pigs, cows and other mammals the potential of being turned into "bioreactors", or, in essence, drug factories.

Until now, many of the problems in creating these bioreactors have been technical, such as getting the right genes in place and getting the protein expressed at high enough levels for commercial success. Many of these problems remain, but several companies say real progress has been made and are only a few years away from testing their proteins in human clinical trials. The problems that remain have as much to do with the legal arena as with the scientific one.

Rein Strijker, Genepharming Europe BV, a Leiden, Netherlands-based subsidiary of GenPharm International, is developing transgenic cows that will produce human lactoferrin, an antimicrobial protein, in their milk. The firm's concern, like that of other players in the field, has to do with who owns key processes needed to create transgenic mammals. Pharmaceutical Proteins, in Edinburgh, Scotland, is aiming to get human alpha-1 antitrypsin (a protein that helps to keep cells elastic), made in sheep's milk, into clinical trials in 1994.

Patents are not the only issue troubling the makers of these interspecies factories. The other is uncertainty about what guidelines the Food and Drug Administration (FDA) is going to lay out for approving proteins made this way. Potential regulatory concerns may include the degree of genetic modification an organism undergoes and its potential threat to the environment, as well as the potential for impurities such as viruses or agents that could cause scrapie.

One development of interest was the possibility of getting goats to produce CFTR, the transmembrane protein that is defective in cystic fibrosis, in their milk. Scientists hope to use the bioengineered protein to replace defective CFTR in cystic fibrosis patients. Genzyme Corp. at Framingham, Massachusetts can now produce only microgram quantities of CFTR in milk - but within a decade they hope to scale up and produce

clinical quantities. (Extracted from *Science*, Vol. 257, 28 August 1992)

'Flu falls fowl of "magic" vaccine

Chickens injected with DNA from a lethal virus are still alive and healthy after having been exposed to the live virus. The DNA appears to have immunized the chickens against the virus, a lethal form of influenza called fowl plague which would normally have killed the birds within four days.

This the first time that vaccination with "naked" DNA has been shown to confer protection to a recipient, and confounds the scepticism most vaccine researchers have expressed about the approach. Rob Webster of St. Jude Children's Hospital in Memphis, Tennessee and Harriet Robinson, professor of pathology at the University of Massachusetts in Worcester, successfully protected 45 out of 88 chickens by injecting them with a whole gene from the virus. Each bird received three doses of 100 micrograms and booster doses three weeks later, then had drops of the live virus inserted into their nostrils. Only two birds out of 87 control birds survived exposure to the live virus.

Webster and Robinson have no idea how the DNA vaccine works, but suspect that the gene migrates into the chicken's cells, which then manufacture the protein spike normally made by the virus. The body recognizes the protein as foreign and this primes the body's defences for a real attack.

She and Webster stress that the approach needs extensive examination to evaluate how safe and effective it is, and how best to administer doses, before it could be considered for use in humans.

Robinson thinks that DNA vaccines have great potential because they are only parts of viruses. Many vaccines are "attenuated" or killed whole viruses which could be contaminated with live virus. Nor are DNA vaccines as difficult to produce as vaccines based on purified proteins extracted from viruses. This extraction process involves several steps which can distort the protein so that it differs from the one produced naturally. Also, Robinson believes that in DNA vaccination, the protein is produced by the cell in its natural form - as if the whole virus was there - and this causes both antibodies to form and triggers the immune system to produce protective cells called T-cells. She says that proteins only elicit an antibody response. She reported that the vaccinated chickens produced few antibodies at first, only producing more when they were exposed to the real virus.

Other groups demonstrated similar work at Cold Spring Harbor. Gary Rhodes and colleagues at Vical, a company based in San Diego, California, injected mice with gp120, a protein made by HIV. They did not expose the mice to the real virus, but report finding antibodies to gp120 and T-cells that recognized dummy cells coated with a key feature of the gp120 protein.

Margaret Liu and colleagues at the Merck Research Laboratories at West Point, Pennsylvania, injected mice with DNA from a virus which causes influenza in mice. (Source: *New Scientist*, 31 October 1992)

Converting waste into animal feed or fertilizer

The ECOBAC process is aimed at abattoirs, breweries, food processing plants, sugar refineries and other industries with a major organic waste problem. Dennis Evers has formed Rivacross Ltd. to market the process, which he says is "light years" ahead of the first ANOX system he promoted in the 1970s. It is a totally biological process, proved in three prolonged pilot study projects in Australia. Suitable wastes can be converted into commercially valuable products, including pelletized fish feeds, fortified peat or organic horticultural fertilizers. Details from: Rivacross Ltd., Unit 17J, Shrub Hill Industrial Estate, Worcester WR4 9EL, U.K. (Source: *Biotechnology Bulletin*, September 1992)

Aquaculture

World fish catches have been stuck at around 100 million tons a year for several years. This figure includes freshwater catches (about 14 million tons), and all manner of non-fish sea life - from lobsters and turtles to seaweed and worms. About 15 per cent of the total comes from fish farms, the rest from wild stocks. One ton in every 20 is now tuna, captured using huge drift and gill nets that stretch for miles across the oceans.

Despite the rapid growth in fish farming, the potential for increasing global production of fish and other aquatic food may be quite limited. This is partly because the gains in domesticated fish are likely to be offset by the decline of overfished wild stocks.

The only large untapped marine reserves are the vast numbers of krill, a kind of shrimp, in the waters around the Antarctic. Some estimates put the theoretical output of this resource at 100 million tons a year, which is equal to the entire world catch of everything else in the oceans.

Meanwhile, the output of fish farms grows by 6 to 8 per cent a year. More than half the salmon served round the world today is farmed, and a quarter of the shrimps and prawns. The future will see "very large fish cages, more akin to oil installations than fish farms, that can hold huge numbers of fish in more exposed offshore locations".

Hopefully, these offshore farms will do less ecological damage than existing aquaculture, which usurps valuable wetlands where wild fish spawn and

feed, and pollutes coastal waters with fish feed and pesticides. But the big constraint is the supply of fish feed. Most farmed fish are carnivorous and require a constant supply of wild fish from the oceans. More than a third of all the wild fish caught today is converted into meal, partly for animals such as chickens, but increasingly to feed farmed fish.

The future could lie in herbivorous fish. Step forward, the carp and the tilapia. Carp, already widely farmed in Asia and Eastern Europe, could soon be appearing on Western plates in their millions. Likewise tilapia, a large herbivorous freshwater fish from Africa, often called the "aquatic chicken". (Source: *New Scientist*, 5 September 1992)

Agricultural applications

New tomato varieties through genetic engineering

The US Department of Agriculture (USDA) has cleared Calgene's bioengineered *FlavrSavr* tomato for commercial production. The ruling allows the tomatoes to be grown and shipped anywhere in the United States without further permits or approvals.

Commenting on the ruling, Tom Churchwell of Calgene Fresh (the subsidiary established in January 1992 to grow and market the tomatoes), says it will enable Calgene to begin scaling up field production ahead of the expected launch in late summer 1993. The company is awaiting formal response from an FDA food safety review before beginning test marketing.

DNA Plant Technology (Cinnaminson, NJ) will test-market a tomato in 1993 that was developed with cloning techniques. The test is the first phase of a planned introduction of a genetically engineered tomato in the mid-1990s. DNA Plant said the new Vinesweet tomato will be firmer than current types, enabling it to hold up under shipping better. The company also claims the tomato has a better taste and a longer shelf life of seven to ten days as compared with three to four days for the typical tomato. In addition, the Vinesweet tomato will ripen naturally during transport, whereas other varieties are ripened artificially. A six-month market test will include sales of the tomatoes in stores in a yet to be chosen city.

Meanwhile, Calgene and ICI remain locked in a dispute over patents relating to one of the genes. The US patent office is continuing to review both applications, and adjudication could take two to three years. A spokesperson for Calgene says the US patent office review does not affect its commercialization programme.

Unifoods Pty. Ltd. of Australia, has recently announced its plan to test a new variety of tomato. This tomato is identical in all respects to existing tomatoes except that the fruit is able to ripen on the plant longer, giving it a better flavour and the ability to withstand damage in transport. The improvement is achieved by inhibiting the gene responsible for the softening process as fruit ripens, making use of modern biotechnology know-how.

The tomatoes produced will be processed by the CSIRO Food Research Laboratory in Sydney. This operation will be limited to trials and the fruit will not be used commercially by Unifoods. If the trials are successful, tomato plants could be ready for commercial use in 1995. The tests are part of a major feasibility study Unifoods is conducting to establish if it can use Victoria as a production base to supply the Asian markets and possibly the Northern Hemisphere (out of season), as well as the domestic market, with tomato-based products.

The tomato has been developed by ICI Seeds in the United Kingdom and has already been successfully tested in the United Kingdom and the United States. The Australian field trials have been approved for safety by the Federal Government's Genetic Manipulation Advisory Committee.

In the meantime, Unifoods will be engaged in a dialogue about the application of this technology with interested parties.

DNA Plant Technology (DNAP, Cinnaminson, NJ) has announced plans to begin test-marketing its biotechnology tomato by next year. DNAP is growing the tomatoes - which were developed using somaclonal technology to generate new plants from cells extracted from the tissues of selected plants - at several sites during 1992 and says that by October it will have completed a four-city test of the product. The tomato is designed to stand up better in distribution and have a longer shelf life than conventionally bred produce. DNAP says its joint venture with Du Pont, called Freshworld, would be a "logical" seller of the tomato. (Source: *European Chemical News*, 9 November 1992, *Wall Street Journal*, 27 August 1992, *Australasian Biotechnology*, Vol. 2, No. 5, October 1992 and *Chemical Week*, 9 September 1992)

A better potato?

Biologists at Monsanto say they have developed a potato with significantly increased starch levels and dry matter content. It is the first success, they add, in increasing a natural plant biopolymer through genetic engineering, and they are now working on other crops, including corn and tomatoes. Higher starch levels in potatoes, says Monsanto, could mean reduced cost for food processors and less oil absorbed - and fewer calories - in friend foods. The results were achieved by inserting a gene from *Escherichia coli* that codes for the enzyme responsible for starch production. Monsanto

hopes to make the line of potatoes commercially available by the end of the decade. (Source: *Chemical Week*, 16 September 1992)

New potato variety

Calgene Pacific Pty. Ltd. proposes to field-trial genetically engineered potatoes. The trial will be conducted with the fertile cultivar *Desiree*, which is widely grown in Europe and North Africa. The plants have been engineered with a kanamycin resistance gene (used during *in vitro* regeneration of plants) and a bacterial gene causing cytokinin over production. Cytokinins are naturally occurring compound(s) produced by all plants, including potato. In pot trials of transgenic potato expression of the cytokinin gene has caused an increase in tuber number and an increased yield in some lines. Potato lines showing increased yield would be extremely valuable to potato growers.

To get an accurate measure of performance, the transgenic potato must be trialled in the field. The proposed trial will occur in the summer of 1992-93, at the Field Station of the University of Melbourne (located on the western edge of metropolitan Melbourne). The plot is surrounded by grazed or cultivated land, but no potatoes are grown anywhere nearby. There is a slight risk of pollen spread from the trial site to other potatoes by insects or wind. Consequently, the trial site will be separated from land used for potato growing by a border of 500 metres in width.

For further information contact: Dr. Michael Dalling, Calgene Pacific Pty. Ltd. (Tel: (03) 419 9844; Fax: (03) 416 1761. (Source: *Australasian Biotechnology*, Vol. 2, No. 5, October 1992)

Two companies cooperate in the viral insecticides field

Biosys and Sandoz Agro Inc. have agreed to cooperate in the development of insect-specific viral insecticides that could potentially compete in a world-wide market worth over $1 billion.

Known as baculoviruses, these natural pesticides are said to be safe to humans, wildlife, water, soil and plants. If successfully commercialized, they will protect against a variety of leaf-eating pests that damage crops such as cotton, corn, soybeans and vegetables.

Sandoz and Biosys expect to complete development of the first baculovirus products by the end of 1994.

Although the insect-killing properties of baculoviruses have been known for some time, their high manufacturing costs have inhibited commercialization. The goal of the joint project is to develop cost-effective methods of mass production in an easy-to-use and stable formulation that also meets Environmental Protection Agency registration requirements.

A baculovirus, isolated from the celery looper, is being tested in the field against the cotton bollworm and the tobacco budworm. (Extracted from *Chemical Marketing Reporter*, 12 October 1992)

Genetically engineered disease resistant grapevines

Groupe Moet & Chandon is looking at genetic engineering to develop wine grapes that are resistant to disease. Currently, the wine industry uses millions of tons of expensive fungicides, herbicides and pesticides to protect grapes used to produce wine. However, years will pass before there is sufficient confidence in the quality and safety of wine produced from altered grapevines to attempt selling it. As an indication of how new the field is, only the vines exist; wine has yet to be made from them. Yet the science is making rapid progress. (Extracted from *Wall Street Journal*, 18 September 1992)

New process for drought-afflicted crops

A process that would enable corn, wheat and other crop growers to produce normal yields in times of severe drought has been discovered by Dr. Bruce Roser at the Institute for Animal Physiology, United Kingdom. While working on research into human organ transplants, Dr. Roser discovered the key to a plant's ability to withstand drought conditions. Research pointed to a sugar-like molecule called trehalose which, when added to a range of compounds, enabled them to be dried out, then resuscitated at will. The discovery could lead to the development of drought-resistant grain and has applications in the food and pharmaceutical industries as well. Japanese and US companies are now vying for the commercial production and patent franchising of the process. (Extracted from *Feedstuffs*, 18 May 1992)

Biotechnology breeds giant lily

A research group at the Okayama Prefectural Agricultural Experiment Station (OPAES) says it has used biotechnology to develop a new breed of ornamental lily. In experiments, the group crossbred two conventional lily breeds, then isolated an embryo from the pistil of a hybrid produced through the breeding.

The embryo was then cultured in a series of media to produce plantlets. Cultivation of the plantlets resulted in plants that produce upward-facing, cream-coloured flowers. With a diameter of about 20 cm, the flowers are around twice the size of conventional lily flowers. According to the research group, the new breed has a rapid growth cycle, reaching the stage of flower development within two years of scale planting.

Conventional breeds have a growth cycle of three to four years (Source: *McGraw Hill's Biotechnology Newswatch*, 3 August 1992)

New chrysanthemum variety genetically engineered

Florigene (Rijnsburg, the Netherlands) has developed a genetically engineered chrysanthemum with a transplanted gene to turn it from pink to white. The variety, designated Floriant, could become Europe's first genetically engineered plant to get marketing approval. However, environmentalists fear that genes from this and other more radically altered man-made plant varieties could spread into the environment and cause unforeseen consequences.

Robert van der Meer, Florigene's R&D manager, said "the new variety reacts almost exactly like the original one. The differences are much smaller than when mutating varieties using radiation, which is common practice in chrysanthemum breeding". Florigene ultimately aims to breed flowers that will deliver high yields while allowing farmers to comply with strict pesticide controls effective from 1995. (Source: *Technology Update*, 7 September 1992)

Fungicides from herbs

A group of British scientists has embarked on an environmentally friendly project to extract safe natural crop-protecting fungicides from herbs that are commonly used in cooking, medicine and perfumery.

Researchers at Strathclyde University, who are well known for their studies involving the use of natural compounds of tropical plant origin to treat a variety of human diseases, have joined forces with scientists from the Scottish Agricultural College to investigate the components in plant oils which give a fungicide effect and find ways in which their performance can be improved.

Natural pesticides from plant origins offer a number of desirable properties. They are far less damaging to the environment than many synthetic compounds currently in use, because they are biodegradable and therefore do not accumulate in the soil. Some pesticides of this type, among them derris, pyrethrum and nicotine, have been used for a long time against insects, but it has proved less easy to find comparable natural fungicides.

The Scottish group aims to give special attention to a wide range of crop diseases which cause serious problems to cereal growers. They also expect major benefits for human and animal health to result from the research. Some of the compounds they are studying are active in controlling fungi which produce cotoxins in foods - very harmful substances which can accumulate in the body.

Further information available from Professor Peter Waterman or Dr. Sandy Gray, Pharmacy Department, University of Strathclyde, Glasgow, Scotland G1 1XQ, UK. (Source: *Tech Monitor*, March/April 1992)

CSB-RRLJ collaborative project for mulberry silk industry

The World Bank is emphasizing the development of mulberry sericulture in India for which the Central Silk Board (Ministry of Textiles, Government of India) has initiated the National Sericulture Project. The Regional Research Laboratory at Jorhat is receiving financial assistance from the Central Silk Board under the World Bank Fund for a research project on the pathological problems of the mulberry in North-East India - survey and identification of diseases, studies on their biology and management.

It is expected that identification of pathological problems of the mulberry in the north-eastern region of India and development of a management technology will be a significant impact on the survival and growth of the mulberry silk industry of the region in particular, and the country in general. Although scattered reports on the occurrence of diseases of the mulberry are available, systematic investigations have not yet been taken up for survey and identification of such diseases, their occurrence and assessment of disease incidence, particularly on a local and regional basis. Losses in terms of quality and quantity are yet to be assessed for many of the diseases recorded so far. Such information will be helpful for the development of appropriate measures of disease control. Varieties resistant to a number of races and/or species of pathogens are to be developed. (Source: *RRL News*, August/September 1991)

Bacterial mediated termite control

Eradication of termites on live plants including tea (*Camelia sinensis* (L) *O. Kuntze*) has been found to be possible by spraying the fermented liquor of a strain of *Arthrobacter* RRL J3, on the mud runs built by termites on live plants. Termite activity inside the treated mud runs disappeared within 24 hours and the mud runs gradually disintegrated over a period of 7-14 days and fell off the plants by themselves. The Tea Research Association at Jorhat also undertook field trials by spraying the liquid on the ground around plants infested with termites. This product is now under trial to control termites in buildings in collaboration with CBRI Roorkee. Experiments with termite-susceptible mango wood have been set up by CBRI Roorkee by introducing

blocks treated with various concentrations of the produc' inside termite mounds. While controls were attacked by termites within three days, the treated blocks were intact over 30 days. Further work is in progress. (Source: *RRL News*, August/September 1991)

Carnation plants

Calgene Pacific Pty. Ltd. of Australia has a proposal for the small-scale release of genetically engineered carnation plants. The plants will be propagated and grown to flowering at a commercial carnation-growing facility, located in the outer suburbs of Melbourne. The genetically engineered carnations contain an "anti-sense" version of a carnation gene, critical to the ability of the plant to produce the growth regulator, ethylene. Normally, cutting a flower induces production of ethylene, triggering petal senescence and flower deterioration. In the genetically engineered plants, the "anti-sense" gene prevents the cut flower making ethylene, with the result that the carnation flowers have a much longer vase life. As consumers consider vase life important, this adds value to the engineered plants. In addition, flower quality can be extended without the need to use chemical preservatives. Such preservatives are usually carelessly discarded, but contain potential pollutants such as silver.

The genetically engineered plants bear no different biological, chemical or ecological risks to unmodified carnation. Carnations do not interbreed without the aid of manual or insect-pollination and, in any event, there are no weeds in Australia with which carnations could hybridize. More importantly, the carnation is grown by vegetative propagation and flowers are never able to set seed before or after sale. There is, therefore, no obvious route by which the introduced gene could "escape" to other plants.

For further information contact: Dr. Michael Dalling, Calgene Pacific Pty. Ltd. (Tel: (03) 419 9844; Fax: (03) 416 1761). (Source: *Australasian Biotechnology*, Vol. 2, No. 5, October 1992)

Tropical treatment for sweeter salad

Sweeter-tasting lettuce, potatoes and tomatoes could soon be available. American researchers at the University of California, Berkeley, have successfully transferred a gene into tomatoes and lettuce which manufactures a sweet-tasting compound called monellin.

Researchers in Belgium, meanwhile, have inserted an anti-sense gene into chicory, a major source of fructans. Fructans are soluble forms of fibre and are used in a range of foods from pizza to mousse.

The problem with harvesting chicory is that enzymes rapidly break down the fructans to fructose as soon as the chicory is picked. The anti-sense gene inserted by the Belgian researchers blocks the enzyme that performs the breakdown step. (Source: *New Scientist*, 5 September 1992)

Where there's dust, there's dollars

For the past 1,000 years, Asian coconut farmers have been dumping coir dust, the worthless debris that remains when a coconut has been stripped of its edible flesh and the fibre used to weave coconut matting. Coir dust is 30 per cent of the coconut by weight, but it absorbs too much water to be burnt and has never seemed useful for anything else. Its antibiotic properties stop it from rotting. So coir just accumulates. Sri Lanka has more than 40 million tons lying around and India is adding 2,000 tons a day to the 80,000 coir hillocks on its southern tip.

Now, a new company called Dutch Plantin has begun buying and processing coir dust in Sri Lanka. In 1990 the firm started to sell coir dust to commercial and amateur gardeners in Europe, South Africa, Japan, Australia and the Middle East. Its sales, though modest, are sprouting like a prize bloom. In 1992 it expected to supply 3,750 tons of coir dust, worth $1.5 million, double what it sold the year before and ten times sales in 1990.

The very properties that have made coir dust a nuisance for generations of Asians recommend it to modern European gardeners. Because of its sponginess, coir holds ten times its own weight in water; and its alkalinity means that it can hold and gradually release nutrients to plant roots. As a mulch, it survives in soil longer than other additives such as peat. About half the coir Dutch Plantin sells is put into growbags for sale at garden centres. The other half is sold to commercial greenhouses.

In countries such as Britain, where peat must be imported, coir is cheap enough to compete, even after being shipped all the way from Sri Lanka. But in North America and Germany, where there are large supplies of peat, only green laws like those in force in Holland could give coir the edge. At current rates of consumption the world has 2,000 years of peat left, but environmentalists are worried about the destruction of bogs near big horticultural markets and are keen to curb the use of peat. (Source: *The Economist*, 29 August 1992)

New and cheap rice harvester

A cheap and simple rice harvester that cuts the work of harvesting by at least two thirds, has been developed by researchers in the Philippines. They believe it could enable rice cultivation to continue in areas where it might otherwise cease because there are too few people to bring in the crop.

The machine strips the rice grains from the plants, leaving the stems standing. The "stripper" was developed

at the International Rice Research Institute (IRRI) in the Philippines, using funds from Britain's Overseas Development Administration.

It is economical and can be built by local craftspeople out of readily available materials. It is also small and light enough to be manoeuvred over the low, water-retaining levees which surround most rice fields.

Boru Douthwaite, of the Institute of Engineering Research at Silsoe run by Britain's agriculture ministry, and Graeme Quick of the IRRI, who has been working on the machine with Douthwaite, point out that in places like North-East Thailand, the labour shortage is becoming acute as many young people have left to work in Bangkok and in the industrial sector. The stripper could be the only way to continue cultivating rice in the region's small fields, which prevent the use of the full-size combine harvesters used elsewhere in the country. The IRRI has adapted the stripper for peasant farmers, the comb can be made from a steel strip and old car tyres, and is developing one with a built-in thresher, which will further speed up harvesting. The stripper is powered by a petrol engine, which can be removed and used in other equipment, such as water pumps. The machine presently costs $1,200 and should pay for itself after being used to harvest 50 hectares. The combined stripper-harvester will cost $1,700. The IRRI has given the design to a rural workshop in the Philippines to see how easy it is for them to make. Machines have also been sent to Thailand, Malaysia and China for testing. (Extracted from *New Scientist*, 22 August 1992)

Food and food processing applications

The perfect food

Genetic engineering holds the promise of a brave new world in which foods can be tailored into "nutriceuticals" that provide not only a better overall nutritional profile, but address specific medical conditions in both preventative and therapeutic capacities. "Biotechnology will be used to manufacture a variety of nutriceuticals", says Kiyoshi Nara, director of the Vitamin & Food Research Laboratories at Takeda Chemical Industries (Osaka). Indeed, a host of Japanese companies are pursuing nutriceutical research, including Suntory (Osaka) and Hayashibara (Okayama).

For its part, food modification by traditional processing methods is already well established. Witness low-fat milk with added protein and calcium.

One of Japan's first commercial nutriceuticals is a low-calorie sweetener, erythritol, made from glucose by *Aureobasidium* yeast. At 0.3 Kcal/gm, erythritol has less than one tenth the caloric value of glucose and fructose, has no bitter aftertaste and can be used in cooking since it is stable at high temperatures. It is already being manufactured, sold and included in various sweets and chocolates in Japan, though US sales await approval by the Food and Drug Administration. The next step will be to work with cellulase made by *Clostridium gilvus* to derive even lower-calorie cello-oligosaccharides and hemicello-oligosaccharides from cellulose and hemicellulose, respectively.

A number of nutriceutical researchers are focusing on soybeans and rice, long the nation's staples. Kyuya Harada, head of the Molecular Biology Laboratory at MAFF's National Institute of Agrobiological Resources (Tsukuba), is using genetic engineering and selective breeding to increase the methionine level of soybean protein to make it more appropriate for people and livestock. Harada is also working to improve soy protein's gelling characteristics. At Kyoto University's Research Institute for Food Science, Shigeru Utsumi and Makoto Kito are attempting to improve the amino acid complements of both soybeans and rice, which is deficient in lysine, through genetic modification. (Source: *Bio/Technology*, Vol. 10, September 1992)

In search of a better French fry

David Stark, a chemist at Monsanto Co. in St. Louis, and co-workers have inserted a starch-producing gene from the common intestinal bacterium *E. coli* into potatoes, creating tubers that have up to 20 per cent more starch than the best potatoes now on the market.

The increase in dry matter makes a difference when the potatoes go into the frying pan. Frying replaces the water in the potatoes with oil, so less water content means less oil, resulting in fried potatoes that are more nutritious and take less energy to cook (since much of the energy needed to fry potatoes actually goes into removing the water). Potato chips, for instance, are usually about 36 per cent oil, Stark said, but if made from his new improved potatoes they would contain only about 30 per cent oil. The improvement is big enough - at least in terms of p.r., if not nutrition - that he expects potato chip manufacturers and fast food companies that serve French fries to switch over.

The potatoes have already been grown in field tests under commercial conditions with no problems. If Monsanto can get federal approval for these genetically engineered potatoes to be used in food products, they may be commercialized by the late 1990s. (Source: *Science*, Vol. 257, 11 September 1992)

Industrial microbiology

Prawn waste derivative for industrial and biomedical applications

Waste prawn shells are being used by Northern Ireland scientists in world-leading research for which they claim far-reaching success in applications for industry. The work is being carried out in the

Department of Chemical Engineering at Queen's University in Belfast.

In the new process, the limestone and residual protein are removed from the waste shells and are left with a compound called chitin from which a material known as "chitosan" is derived.

Although prawn shells form the basic material, other crustacea such as lobster or crab could also be used.

Chitosan has many commercial applications. Among the applications presently being tested is one said to allow fruit to be preserved for longer than six months - a considerable increase on normal life-spans. In this case, a chitosan-based solution is sprayed onto the fruit, which acquires a very fine protective film. This can be washed off before the fruit is presented for market. Another use for the material has been found in the cosmetics industry, where it can be used as a thickener in soaps, detergents and shampoos. One of the most important benefits, however, is in the treatment of toxic waste material.

In other tests, the team have successfully clarified wine and fermented beverages, and have produced a teat dip for cattle to combat mastitis. In the treatment of wounds, chitosan is said to accelerate the healing process and form a tough protective coating.

Contact: Professor Gordon McKay, Process Engineering Design Centre, Department of Chemical Engineering, Queen's University, Belfast, Northern Ireland. (Source: *Tech Monitor*, March/April 1992)

Ciba and Genencor team up in enzymes for paper

A new partnership is underscoring the potential for biotechnology in markets other than human health-care and agriculture. Ciba-Geigy (Basel) and Genencor International (Rochester, NY) have agreed to develop, manufacture and market enzymes for the pulp and paper industry.

Genencor will pursue R&D activities and manufacture the enzyme products, and Ciba-Geigy will market the products world-wide. The partners estimate that demand for such enzyme products will approach $100 million by the end of the decade.

Genencor has already conducted full-scale plant trials of enzymes in bleaching and dewatering, and several mills are converting to enzyme usage, says Genencor. The company cites the use of xylanase enzymes in reducing chlorine consumption and cellulases in enhancing water removal during the production of specialty paper. Other applications of enzyme technologies under development include pitch control, microbial growth control, newsprint de-inking, and effluent treatment. (Extracted from *Chemical Week*, 10 June 1992)

Technology for preparation of substituted amino acids

Data published in the *Journal of Organic Chemistry* describes a discovery by Genzyme Corporation which could be useful in simplifying the preparation of certain pharmaceuticals that will make them purer and possibly more potent. This work describes technology based on the use of biocatalysis for separating pairs of substituted amino acids whose molecular structure have a mirror relationship to each other.

Many drugs and chemicals on the market contain a mixture of two molecules that appear in two forms that are mirror images of each other called stereoisomers. These include several agricultural chemicals, ibuprofen, and the no-calorie sweetener aspartame. Often the mirror image of the biologically active stereoisomer produces side-effects or is inactive, thus opening the opportunity to find less costly and more reliable methods for separating the stereoisomers. (Source: *News Release*, 25 June 1992)

Three-stage waste water purification system using micro-organisms

Oji Paper Co. Ltd. has introduced a novel three-stage waste water purification system in its Kasugai Plant that uses micro-organisms.

The new treatment facility uses a micro-organism film, so comparatively fine organic substances can be decomposed for easier removal. This facility will be installed as a facility to support the present aeration facility that supplies air to micro-organisms in the water to decompose comparatively large organic particles and the coagulating sedimentation facility that coagulates and settles organic substances by chemical means.

About 8,000 tons of waste water are generated at the plant, and a facility with a capacity for treating 1,600 tons will be installed as the first stage, with the remaining 80 per cent installed sequentially.

The Kasugai Plant, together with the Tomakomai Plant, is recycling used newspaper for conservation of natural resources. The use of recycled newspaper for producing printing paper generates waste water in the de-inking process, while the recovery of lignin contained in the raw material in the paper-making process for use as a fuel is difficult, so the waste water generally contains about double the quantity of organic substances compared with the chemical pulp process.

The Ise Bay region where the Kasugai Plant is situated has rigid water quality preservation standards. Therefore, the new facility was introduced as such measures are indispensable to enable the increased recycling of used newspaper in the future.

Further information is available from Oji Paper Co. Ltd., Public Relations Office, 4-7-5, Ginza, Chuo-ku, Tokyo 104, Japan. (Source: *JETRO*, August 1992)

Fats and oils-rich waste-water treatment technique using yeast

Yamazaki Baking Co. Ltd., Nisshin Oil Mills Ltd. and Nishihara Environmental Sanitation Research Corp. have jointly discovered three yeasts which decompose fats and oils which can treat water containing soybean oil, which is four times thicker than the fats and oils contained in confectionery plant waste water.

These yeasts were screened from the waste water of confectionery plants containing 0.56 per cent of oils and fats. Simply adding to waste water enables up to about 90 per cent of oils and fats to be decomposed, so no massive facility is required for waste-water treatment, while the proliferated yeast can be used for producing feeds and fertilizers.

Today, waste water containing oils and fats in high concentrations is generally treated by the dissolved air floatation method of blasting high-pressure air into the waste water to float the fat and oil content, then using the activated sludge process for treating the oil and fat. However, with controls becoming ever stricter even for small businesses such as hotels and restaurants, a waste-water treatment system which can be installed at a low capital investment cost is needed.

The research team screened the three yeasts by shifting fats and oils decomposing micro-organisms to the higher-concentration fats and oils waste water one after another, then separating those with excellent fat and oil decomposition functions. Three species of yeast such as the *Hansenula* and *Candida* sp. were isolated. These yeasts were mixed, added to water containing 2 per cent of soybean oil, and the oil decomposition checked after a week. Seventy per cent of the soybean oil was decomposed completely into carbon dioxide and water, and 20 per cent into fatty acid, so about 90 per cent of the oil can be treated.

Waste-water treatment using micro-organisms is called the activated sludge process, but proliferated bacteria disposal is a serious problem. Burial or incinerated as industrial waste is costly and causes environmental disruption. Yeasts have a fivefold processing capacity that allows a smaller system facility and a reduction in surplus yeast, and since they contain nutrients such as vitamins and proteins, can be used effectively for producing feeds and fertilizers. The research team plans to use about a dozen or more yeasts in combination to improve the system efficiency further.

This research project was advanced as a link of a water treatment technology development project using micro-organisms called the Clean Eco-System implemented by Japan's Ministry of Agriculture, Forestry and Fisheries.

Further information available from Yamazaki Baking Co. Ltd., Office of the President, 3-2-4, Iwamoto-cho, Chiyoda-ku, Tokyo 101, Japan. (Source: *JETRO*, August 1992)

Energy and environmental applications

Microbial reactor to mop up wool industry waste

Environmentally harmful wastes from the wool industry will soon be disarmed by a special blend of microbes housed in on-site reactors. Research that will lead to the establishment of the first such reactor in the United Kingdom within the next 18 months is being carried out by Professor Richard Burns from Kent University at Canterbury in south-east England. His microbiological and biochemical work is backed by a group of wool scouring companies and financial support from the UK Government.

The wood industry's waste products are mainly the pesticides used in sheep dips and, under a £1 million clean-up project, Professor Burns and his colleagues are isolating microbes from various UK wool industry sites. Many of the microbes have been found to be unassociated with the industry but thrive where extensive contamination by pesticides over many years has left the land barren.

Once the bugs best able to degrade the wastes have been identified and their ideal growth conditions refined in the Kent University laboratories, the aim is to reproduce these conditions in a reactor that can be set up on the site to treat waste pumped direct into it from wool scouring plants. The reactors will be scaled-up versions of Professor Burns's laboratory experiments and will be built by the March Consulting Group, whose environmental research laboratories are located within Kent University's chemical laboratory. Also involved in the design of the reactors is the University of Manchester Institute of Science and Technology from north-west England.

Although the first reactors will be used to treat wool industry waste, it may be possible to extend the technique to treat wastes from the wool dye industry, with additional implications for the carpet industry.

Further information available from Professor Richard Burns, University of Kent, Tanglewood, Giles Lane, Canterbury, Kent CT2 7LX, UK. (Source: *Tech Monitor*, March/April 1992)

Waste wood to fuel oil

The Forest Research Institute of Malaysia (FRIM) has developed a process for recovering liquid fuel and

charcoal from waste wood. It uses heat treatment to break down organic compounds into their constituent molecules. The US Department of Energy's Solar Energy Research Institute in the state of Colorado pioneered the technology. Now FRIM has adapted it to Malaysian wood, particularly rubber wood.

The process resembles charcoal-making. Scrap wood is heated in an airtight oven called a retort. US wood pyrolyses at temperatures in the range 500 to 800° C, but FRIM found that the moist, dense rubber wood requires a temperature of up to 900° C. The high temperature breaks down the wood into charcoal, gases and liquids, whose proportions depend on the rate of heating and the final temperature. One metric ton of rubber wood pyrolysed by the FRIM system can yield 360 kg of charcoal, 80 kg of tar, 15 kg of wood alcohol and 200 kg of gas. The liquid products are of primary interest because they pack a lot of power; they are potential substitutes for diesel and gasoline.

Further information available from Director-General, Forest Research Institute of Malaysia (FRIM), Karung Berkunci 201, JLN. FRI, Kepong 52109 Kuala Lumpur, Malaysia. (Source: *Tech Monitor*, March/April 1992)

A novel method for waste composting

A Finnish firm, Ideachip Oy, has developed a method for the treatment of organic waste that reduces composting time by 70 to 90 per cent.

The method - named Allu - can be used for composting sewage sludge, bio sludge, organic industrial waste, household waste, contaminated soil, etc.

The process starts with the crushing of large pieces into small particles, which are then composted with a mixing machine in 3 x 6 metre windows. Regular mixing of the material increases oxygen content and accelerates the composting process. In a large, well-mixed window, the proportion of nitrogen and carbon is correct, and moisture level adequate. Nitrogen or other substances can be added when necessary.

The compost is turned every second week, five times altogether. During this time, the volume shrinks to one third of the original. Compared to the traditional composting method, the Allu method has the advantage of maintaining a temperature of 55-65° C around the year, which speeds up composting from two-three years to three months.

The Allu 36 model has a processing capacity of about 3,000 m^3 per hour, which makes it suitable for big communities. A tractor-mounted version Allu 24 is suitable for smaller municipalities and individual companies.

Further information available from Ideachip Oy, POB 62, SF-15870, Hollola, Finland. (Source: *Tech Monitor*, March/April 1992)

Natural materials

Natural materials such as straw and seaweed could form the basis of filters to remove brightly coloured organic chemicals from the wastes that companies discharge into rivers.

These natural materials would provide cheap and flexible alternatives to activated carbon and other methods of removing bright colours from waste streams, says Dr. Robert Edyvean of Leeds University's chemical engineering department.

The UK Government's Environmental Technology Innovation Scheme (ETIS) is putting up half the cost of a project to develop the technology over the next three years. Leeds University is collaborating in the three-year project with Yorkshire Water Services and specialist chemicals company Hickson and Welch of Castleford.

Although the discharges of azo dye compounds and other organics may not be particularly toxic, no one likes their bright colours. Edyvean says industrial companies also face more stringent discharge limits. "The National Rivers Authority is looking into developing standards for colour quality of waterways", he says.

The ETIS project has developed from research at Leeds to create straw textiles to remove metal ion pollutants from waste discharges. This project is supported by the Science and Engineering Research Council and Yorkshire Water. The project will identify suitable dead biomass from straw waste and the residues from citric acid production and seaweed processing.

The biomass removes the colour by adsorption as colour compounds become attached to the filter material. Edyvean says the project is looking at ways of regenerating the system by washing off the compounds, using designs such as cartridge filters. Recovered material could be recycled, he says. (Extracted from *Engineering*, 14 May 1992)

Bioprocessing

A cluster of genes that causes micro-organisms to float could increase savings to the beverage industry and improve cleanup of oil spills. An extra gene added to yeast cells can result in a tenfold increase in protein production for recombinant pharmaceuticals.

Research Corporation Technologies (RCT) is looking for strategic partners to help develop these and

other new bioprocessing technologies for future industrial use.

Bioprocessing, the use of biological systems for industrial processes, is used increasingly to produce therapeutics, specialty chemicals and in bioremediation.

Floating cells are created by introducing novel DNA-encoding proteins to produce gas vesicles in cells. This system can be used in any process where cell removal would enhance production. The invention could be used in brewing and wine-making, reducing the need for centrifugation or filtration.

Likewise, this technology can increase the efficiency of oil-spill-eating bacteria by increasing their interaction with oil at the water's surface. The cell floatation system was developed at the University of Massachusetts.

The yeast protein secretion system invented at the University of Illinois at Urbana-Champaign could provide a means to manufacture recombinant proteins for therapeutics cheaply and more efficiently.

Yeast cells are used to make a variety of recombinant pharmaceuticals currently on the market. But this process is inefficient, the inventors say, due to the lack of a "protein chaperon" that helps newly synthesized proteins pass from a cell to the growth medium. By transferring an extra gene for the chaperon into yeast, the improved yeast strain produced 10 times more erythropoietin than conventional yeast strains. (Source: *Chemical Marketing Reporter*, 19 October 1992)

Microbial mats may mop up oil

Blue-green microbial mats have spread across the oil layers around the Saudi Arabian research station on the coast of Jubail. The cyanobacterial mats only appear where there is oil, and the mats with the strongly adhering oil layers become torn and dissected into irregular scales, researchers from Kuwait and Germany report.

The higher forms of life that usually feed on the cyanobacteria have been adversely affected by the oil, leaving the cyanobacteria to flourish. The growth of microbial mats is thought to be the first sign that the polluted region is cleaning itself up.

Microcoleus sp. is found to be the predominant micro-organism. Research is continuing into whether the organisms can degrade the oil. So far one million cells per gram of fresh mat of organotrophic bacteria have been found embedded in the mucilage, and these are capable of utilizing crude oil and individual *n*-alkanes as sole sources of carbon and energy. (Source: *Nature*, 10 September 1992)

Decomposition of trichloroethylene in soil by aerobic micro-organism

Japan's National Institute for Environmental Study has confirmed that trichloroethylene (TCE) in the soil can be decomposed by an aerobic micro-organism. Almost 100 per cent TCE at a concentration of 100 ppb can be decomposed in three days. The technique may lead to commercialization.

TCE is widely used as an IC detergent and the groundwater contamination by TCE is presently a serious problem. TCE is a cause of cancer. TCE is difficult to decompose, so the research was conducted to establish an effective method for treating TCE.

The TCE-decomposing micro-organism was the methane-utilizing bacteria, *Methylocystis* sp. M-strain from a farm soil in the northern part of Ibaraki Prefecture. Previously, laboratory experiments confirmed that TCE in water was decomposed by this bacterium.

TCE-contaminated water-soil environment in a cylindrical glass was prepared. Then, the M-strain bacterium was added and the decrease of TCE was measured periodically with a gas chromatograph. Fifty per cent of the 0.1 mg/l TCE was decomposed in three days when 1 million/ml M-strain bacteria were added. When 10 million/ml M-strain bacteria were added, TCE was completely decomposed in three days.

Further information is available from National Institute for Environmental Studies, Japan Environment Agency, Water and Soil Environment Division, 16-2, Onogawa, Tsukuba-City, Ibaraki Pref. 305, Japan. (Source: *JETRO*, August 1992)

Flower power

A fuel derived from oilseed rape, rape methyl ester, is becoming increasingly popular in Europe for buses, taxis and tractors. Reading Transport is the first British bus company to try this alternative to diesel.

Although RME is slightly more expensive than diesel, it produces almost no sulphur dioxide and less carbon dioxide and carbon particles making it particularly suitable for buses and taxis in urban areas. It also does not make a net contribution to carbon dioxide in the atmosphere because the carbon it contains was only recently extracted from the air by the yellow flowers of the rape plants.

Oil is extracted from rape simply by crushing, with 3 tons of rape yielding 1 ton of oil. Most diesel engines will run without modification on unblended rape oil but they become clogged after several days. To prevent this, glycerine must be removed from the oil.

Each ton of oil is mixed with 110 kilograms of methanol in the presence of a nitrogen hydroxide catalyst and heated to between 40° C and 50° C. The glycerine settles out leaving a clear, thin liquid, which is RME.

Engines do suffer from a slight loss of power when using RME, but the Italian tractor maker Same estimates that the average power loss is less than 2 per cent compared with conventional diesel.

Austria leads the rest of Europe in using the fuel. It is on sale in at least 100 petrol stations and almost a fifth of the 50,000 hectares of rape grown in Austria last year was used to make RME. Companies in France, Germany, Italy and Spain are also building factories to make RME and environmentalists have estimated that production could be more than 600,000 tons a year within five years.

There is disagreement over how much more expensive RME is compared with normal diesel. British RME makers say it may be as much as 15 per cent more expensive, but Austrian producers claim they can make it for the same price as diesel. RME producers are lobbying for it to be exempt from the taxes levied on mineral oils and for changes to Europe's new Common Agricultural Policy so that oilseed rape can be grown specifically for fuel on land that has been set aside from food production. (Extracted from *New Scientist*, 3 October 1992)

E. PATENTS AND INTELLECTUAL PROPERTY RIGHTS

Biotech patent issues clearly explained

The UK Chartered Institute of Patent Agents is worried by the controversy over patenting of life forms. In an effort to "set the record straight" and to "establish a more realistic perspective", it has produced Briefing Papers on the following:

- Patentability and EC Proposals on Plant Varieties;
- Patentability of Animals;
- The Patenting of Living Organisms;
- The European Commission Proposal for a Council Directive on the Legal Protection of Biotechnological Inventions.

These are clear, short and factual, such comments as they include being favourable to the usual aims of the patenting system; while acknowledging its limits.

Obtainable from CIPA, Staple Inn Buildings, High Holborn, London WC1V 7PZ. Fax: +44 (71) 4300471. (Source: *EBIS*, Vol. 2, No. 4, 1992)

European Patent Office rejects bid to revoke first plant patent

The European Patent Office (EPO) rejected an appeal by industrialists, environmentalists and farmers in June 1992 against its decision three years ago to grant the first European plant patent.

The patent, held by the US-based Lubrizol Corporation, covers any transgenic plant originally derived from a plant cell that has been transfected with a plant gene under the control of a plant promoter, using the agrobacterium T-DNA as the gene-transfer system. An appeals board within the EPO rejected claims that the technical advance made by Lubrizol was insufficiently novel, and said that it has never been a generally accepted principle in Europe that patents may not be granted for plants. It also dismissed a range of moral objections which, it said, are outside its authority.

Opponents of the Lubrizol patent argue that patent laws that worked happily when the biological arena was confined to microbiological products do not fully come to terms with the complex possibilities offered by biotechnology. They also claim that the EPO's decision gives an unfair market advantage to the patent owner, whose innovative contribution they allege to be minimal. In addition, political interest groups are challenging the basic assumption that the EPO has the right to issue patents on any life form.

All of the interest groups intended to appeal further against the patent. Unlike the US system, where the issued patent is final, European laws allow appeals to be heard after every decision in the process, provided that objections are lodged within nine months. (Extracted from *Nature*, Vol. 357, 18 June 1992)

Novo settles Mycogen suit

Following resolution of patent suits with Mycogen Corporation, Novo Nordisk's Entotech Inc. unit has become the sole owner world wide of all basic patent rights covering a class of biopesticides used against beetles.

Entotech says products made with the technology, used to protect corn, potatoes and cereal crops against beetles, compete in a world-wide crop chemical market worth $500 million to $700 million.

Biopesticides claim less than 1 per cent of that market today, but Novo expects their share to increase on the basis of technological advances and the trend towards integrated pest management systems that put less strain on the environment.

Under the patent suit settlement, Mycogen acknowledges that Entotech scientists discovered a strain of *Bacillus thuringiensis tenebrionis* - that is toxic to beetles. In addition to use in biopesticides that replace chemical insecticides, Entotech says its technology is the only one for developing transgenic plants that are beetle-resistant and the only one for managing those beetles for which chemical products are not available. (Extracted from *Chemical Marketing Reporter*, 31 August 1992)

NIH cDNA patent rejected; backers want to amend law

The US Patent Office has rejected a controversial application by the National Institutes of Health (NIH) for patents on more than 2,000 cDNA sequences. Although NIH is expected to appeal against the decision, the interim ruling could set a precedent that would ban patents on genes that share even tiny sections with already published sequences.

The ruling on 20 August 1992 finds the NIH sequences unpatentable on the grounds that they are "obvious": many of the sequences contain small fragments that the patent office was able to find in other, already published, sequences. Once part of a sequence has been published, according to the patent office, it is a trivial matter to get a larger sequence or the entire gene.

Both NIH and Congress are expected to attack that decision on the grounds that, if allowed to stand, it would make impossible a patent for any gene containing sequences already patented. The NIH application, for example, covers fragments of human genes, several hundred bases long, whose function is unknown. Even if the patent office were eventually to grant that application, the ruling would deny a patent to those who had sequenced the full genes and found their function. That would effectively discourage many biotechnology companies from trying to find base products on those genes.

The patent office also ruled that the claimed sequences lack legal novelty because they were derived from publicly available cDNA libraries.

At the same hearing, former NIH geneticist Craig Venter proposed a legislative solution to the dilemma posed by the patent office decision. Venter, who discovered the sequences last year but has since left NIH to start a new private research institute to pursue cDNA sequencing, suggests amending US patent laws to allow patents on sequences containing previously patented or published fragments.

Venter says that his change would not affect the status of his NIH application but would apply to subsequent filings. Changes to the patent code are not retroactive. (Extracted from *Nature*, Vol. 359, 24 September 1992)

Large grant to university promised

A subsidiary of the world's largest drug company has pledged US$ 12 million for Canada's first molecular medicine and therapeutics centre if the parliament approves legislation to extend patent protection for new drugs. The legislation, expected to be passed by the end of 1992, is the Government's reward to the pharmaceutical industry for more than doubling its research and development spending since the last extension in patent law was granted in 1987; the grant from Merck Frosst Canada Inc. is the biggest single investment by industry in university-based biomedical research in Canada.

The centre, to be located at the University of British Columbia (UBC), is seen as the first step in creating a fully-fledged pharmaceutical industry on the country's western shore. Its director will be Michael Hayden, professor of medical genetics at UBC, who will investigate the way in which genes confer susceptibility to disease as well as trying to develop new treatments. The new centre will have major programmes in molecular genetics, in creating animal models for human genetic disease through gene targeting and transgenics and in gene therapy. Although the centre will be independent, its scientists will interact with Merck researchers world wide and some will hold joint appointments at UBC. (Extracted from *Nature*, Vol. 359, 1 October 1992)

Could copyright safeguard the secrets of the genome?

Copyright law might provide researchers in the human genome project with an acceptable way to protect commercial applications of DNA sequences without obstructing the flow of data between academics, says Dai Rees, the secretary of Britain's Medical Research Council.

After a debate in London on "Who owns DNA?", Rees said that copyright is one of a number of options which could help to resolve an international dispute between genome researchers who are attempting to map the human genetic blueprint. The dispute began last year when the National Institutes of Health in the United States decided to apply for patents on fragments of DNA for which there was no known use. Since then, the MRC has applied for similar patents in Britain and the United States.

In September 1992, the US Patent Office rejected the NIH's applications, but the NIH is appealing against the decision.

Academics fear that patents will restrict access to crucial data containing the sequence of molecular units that make up human DNA. Rees says that copyrighting might be a fairer way of sharing the data.

Researchers automatically receive copyright protection as soon as they publish a sequence of DNA in the scientific literature. If they wanted to, they could claim royalties from research groups or companies that had used the data for commercial gain.

Thus the data would be more readily available than if it was covered by a patent. In this case, someone wishing to use the sequence published as part of the patent would have to negotiate some form of licence to recompense the owner of the patent.

David Owen, the industrial liaison officer at the MRC, said that the problem with copyrighting is that it places the onus on the owner of the copyright to prove that someone has violated copyright. A scientist could claim to have discovered a DNA sequence independently of the copyright owner, but would have to produce notebooks and other evidence to prove it.

Owen says that the MRC hopes to press ahead with a plan to make its human genome database, stored in Northwick Park, London, freely available to academics who would receive a "key" to gain access to the data. (Source: *New Scientist*, 10 October 1992)

Biogen wins EPO patent approval

The European Patent Office's board of appeal has upheld the claims made by Biogen in its patent application for genetically engineered alpha-interferons. The decision, which is final and binding, completes the legal process in the EPO and "reaffirms Biogen's fundamental patent position in alpha-interferon", the company said.

In supporting the patent the EPO dismissed an appeal by Böehringer Ingelheim Pharma, Böehringer Mannheim and Bender that had sought to overturn a 1990 ruling that the claims by Biogen were patentable in all aspects, thereby giving Biogen complete patent approval. (Source: *European Chemical News*, 16 November 1992)

Genome patents "a waste of time"

Anyone trying to patent sequences of DNA emerging from the human genome project will soon be wasting their time, according to Tony Vickers of Britain's Medical Research Council, who argues that the flood of published reports of human DNA sequences will stymie attempts to patent the human genome.

An international row began two years ago when the US National Institutes of Health applied for patents on more than 1,000 sequences of human DNA worked out by its genome researchers. Since then, the NIH has applied for patents on several thousand more, and the MRC has done the same in order to protect its own interests. During last summer, the US Patent and Trademark Office rejected the NIH's patent application. The NIH is to appeal against the decision but critics doubt whether the sequences are patentable because they have no recognizable function.

Vickers argued last week that the patents issue is likely to burn out because of the avalanche of sequences published in the scientific literature.

Vickers reckons researchers have published the sequences of fragments from at least 20,000 genes. He expects fragments from another 20,000 genes to be sequenced and published over the next year. (Source: *New Scientist*, 5 December 1992)

F. BIOINFORMATICS

Bio Link - new quarterly newsletter

The United States Agency for International Development (USAID) has sponsored a new quarterly newsletter that is prepared and produced by Michigan State University. Bio Link is actually the newsletter of the Agricultural Biotechnology for Sustainable Productivity project, described earlier on in this issue of the Monitor. The newsletter, which is free of charge, aims at functioning on the basis of service to readers, in a format of open exchange. Further information is available from Bruce Bedford, Editor, Bio Link, Michigan State University, 412 Plant and Soil Sciences Building, East Lansing, MI 48824-1325, USA.

Diversity

Since 1982, scientists, development workers, policy-makers, and opinion leaders in more than 100 nations have relied upon *Diversity* as their link to the international genetic resources community. Each quarterly issue offers readers news they can use, analysis and interpretation from some of the best informed sources - the kind of information you can find nowhere else.

Further information available from *Diversity*, 727 8th Street SE, Washington, DC 20003, USA. Tel.: (202) 543-6843; Fax: (202) 544-2521.

Biotechnology World wide

COBIOTECH, a committee of the International Council of Scientific Union, has produced a directory of national and international biotechnology programmes: objectives, structures, legal frameworks and work under way. Over 50 national programmes are reviewed from all continents and a wide range of regional and

UN initiatives. A handy guidebook for policy researchers and development workers by Jim Coombs and Peter Campbell (editors) of CPL Press (June 1991, 335 pp., ISBN 1-872691-30-7). Available from CPL Press, Science House, Winchcombe Road, Newbury, Berkshire RG14 5QX, United Kingdom. Tel.: +44 (635) 52-40-64; Fax: +44 (635) 52-93-22.

Emerging therapeutic R&D companies in Europe

Synthetic small molecule chemistry is the major technology specialization of newly established therapeutic companies in Europe, according to a new CONNECT Pharma Ltd. report "Emerging Therapeutic Biotechnology and Pharmaceutical Companies in Europe".

Of the over 70 emerging therapeutic R&D companies surveyed, half were involved in anti-cancer drug R&D, with 42 per cent active in immunology and 33 per cent in the anti-infective area. Surprisingly, nearly half of the companies surveyed were involved in synthetic small molecule chemistry and only 4 per cent were involved in gene therapy, antisense or transgenic-based drug R&D.

In terms of partnering interests, collaborative R&D and licensing-out represented the most sought-after business arrangements with joint ventures being of the least interest.

In terms of the development status of drugs being researched by emerging European companies, 39 per cent were in clinical trials, 35 per cent in preclinical with 16 per cent of companies surveyed having products already on the market.

Emerging European companies detailed in the report include such organizations as British Biotechnology, Celltech, Innogenetics, etc., and more recently formed companies such as Bioxytech, Canag Research, Neurosearch, etc.

CONNECT's Emerging Therapeutic R&D Report was compiled from information supplied directly by the companies themselves and provides hitherto undisclosed information on each company's partnering interests; therapeutic focus; technology specialization; development status of the most advanced drug and contact details including named persons.

For further information on the report, please contact: Sandie Roddie, CONNECT Pharma Ltd., The Magdalen Centre, Robert Robinson Avenue, Oxford Science Park, Oxford OX4 4GA, UK.

ATCC biological culture catalogue on diskette

The American Type Culture Collection (ATCC) has released a computer diskette version of their culture catalogues including all information in the current printed catalogues *Bacteria & Bacteriophages, Cell Lines and Hybridomas, Filamentous Fungi, Protists (Algae Protozoa, ATCC Recombinant DNA Materials, ATCC NIH Repository of Human & Mouse DNA Probes and Libraries, Animal Viruses and Antisera, Plant Viruses and Antisera and Yeasts*. The diskette contains eight sections, which can be purchased individually or in any combination. The price per section is $20.00 or $25.00, depending on the section purchased. Basic computer requirements are: IBM compatibility; 512 K RAM; DOS 3.0, or higher; hard disk; and high density floppy disk drive (3.5" or 5.25"). Details from: ATCC Marketing, 12301 Parklawn Drive, Rockville Drive, Rockville, Maryland 20852-1776, USA or on +1 (301) 881-2600. (Source: *Biotechnology Bulletin*, September 1992)

Biodiversity information network

Within the context of the UNCED Biodiversity Convention and Agenda 21, an international group has established a Biodiversity Information Network to solve the problem of managing global biological diversity information.

The new network was initiated at a workshop held at the Tropical Data Base (Base de Datos Tropical), Campinas, Brazil on 26-31 July. The workshop was sponsored by the International Union of Biological Sciences, the International Union of Microbiological Societies and the World Federation of Culture Collections. The sustainable management of the environment and conservation of the biodiversity of plants, animals, micro-organisms and other living things depends on reliable and readily accessible information.

Without information on the names, location, activity and interactions of organisms in particular ecosystems, conservation and sustainable development strategies are unlikely to succeed. The network will be primarily electronic, linking databases and providing a communications system. Details from: Barbara Kirsop, Microbial Strain Data Network, 307 Huntingdon Road, Cambridge CB3 0JX or on 0223 276622. Alternatively, use BT Gold 75:DBI0710 or Email:msdn@egnet.com. (Source: *Biotechnology Bulletin*, September 1992)

Network on global environmental change

Global warming data is to be put onto a single information network under a GB720 000 research contract from the Economic and Social Research Council (ESRC) to Loughborough University.

Loughborough aims to create a user-friendly system to provide easy access to information on global environmental change. The network, called Global Environmental Network for Environmental Change (GENIE) will be based on remote data centres located throughout the world.

Run on various hardware systems, it will tell users about data availability, location, currency and quality, and offer links to other international data directories.

Oxford University's Environmental Change Unit, the British Geological Survey, the British Oceanographic Datacentre and the Institute of Terrestrial Ecology have already expressed interest in the network. GENIE could be up and running by the end of 1993.

The ESRC funding is part of the Government's contribution to the International Geosphere Biosphere Programme, a Stockholm-based independent body funded by national Governments which monitors the global environment.

Software house Genasys and Nottingham and Leicester universities will assist in the project. (Source: *Technology Update*, 9 June 1992)

Theta Market Report No. 360: current and new vaccines market

This report is a comprehensive review and analysis of the changing vaccine market. World-wide quantitative analysis is given for the six largest industrial economies: USA, Germany, UK, France, Italy and Japan. The report segments the market by types of vaccine, vaccines in development, paediatric, travellers and adult vaccines.

Over a dozen biotechnology and pharmaceutical companies are competing to develop vaccines to diseases such as malaria, AIDS, hepatitis, chicken-pox and herpes. Estimates of the market size and projected growth for current and new vaccines in development are supplied through 1996.

Because the vaccine for HIV will be the largest market for any new vaccine and there are so many companies developing an HIV vaccine, the report devotes an entire section to the HIV vaccine market and development. Theta estimates an AIDS vaccine could represent 25-33 per cent of all revenue from vaccine products.

Findings from the report reveal that:

- The US vaccine market was $663.54 million in 1991, or 54 per cent of the world market;
- Real growth will come out of new vaccines now in development;
- Paediatric vaccine segment represents 64.4 per cent of the world-wide vaccine market; and that
- Work on a six-disease (mega shot) combination paediatric vaccine continues.

The report investigates 20 competitors, discussing products, R&D, clinical trials, marketing strategies, licensing agreements and distribution rights. Regulatory demands are reviewed as they impact marketing.

Theta believes the explosion of new products, many out of biotechnology, will revitalize the entire vaccine market.

Information used to prepare the report was obtained from US government data, industry surveys, interviews with marketing managers, annual reports and 10K's, trade publications, information collected at trade shows, product literature and Theta's databases. Price: $795.00. (Source: *News Release*, September 1992)

Animal biotechnology

Animal biotechnology is not just the development of transgenic farm animals and the consequent possibilities of bio-pharming (producing human pharmaceuticals in transgenic farm animals). These aspects, along with long dragged-out controversy over the registration of bovine somatotrophin (bST) in Europe and the USA, tend to dominate our view of the potential impact of the biotechnologies on the animal industries.

The animal biotechnologies also include embryo transfer, techniques of sex determination, nuclear transfer, production of genetically engineered vaccines, new diagnostic techniques for animal diseases and pesticide contaminants, and modification of gut micro-organisms.

Whilst research groups in Australia in Adelaide and Sydney have been to the forefront in the production of transgenic pigs and sheep respectively, the main commercial action with transgenic animals is occurring in companies such as Gene Pharming Europe (Leiden, Netherlands), Pharmaceutical Proteins (Edinburgh, UK), Genzyme (Framington, USA) and DNX (Princeton, USA). Further information on these activities can be found in recent issues (May and August 1992) of the journal *Bio/Technology*. The same journal also summarized the bST issue in its February issue in an article by Dr. Henry Miller (FDA in the USA) and another by William Vandaele (Federation Europeenne de la Santé Animale, Belgium).

In the special feature section of *Australasian Biotechnology*, Vol. 2, No. 4, August 1992, are mini-profiles from five Australian companies active in animal biotechnology, an extensive review from New Zealand on *in vitro* production of domestic animal embryos, an

article from South Australia summarizing Australian research on the genetic modification of rumen micro-organisms, and an article on the development of new animal diagnostics from Victoria. Not covered is Australian and New Zealand work on transgenic animals. (Source: *Australasian Biotechnology*, Vol. 2, No. 4, August 1992)

Biopolicy International

The African Centre for Technology Studies (ACTS), in conjunction with the World Resources Institute (WRI), has launched *Biopolicy International*, a special policy research series on biotechnology and biological diversity. *Biopolicy International* covers country studies, new technological developments, impact assessments, conservation activities, policy reforms, and analyses of national as well as corporate biotechnology strategies. The series is based on current research and is widely consulted by scholars, policy makers and university students in relevant fields.

Those interested in submitting papers should forward abstracts or papers for consideration to Mohamed Khalil (ACTS); Norman Clark (Science Policy Research Unit, University of Sussex, Falmer, Brighton BN1 9RF, UK) or John Mugabe (ACTS Biopolicy Institute). Information for subscribers is provided below: ACTS Press, African Centre for Technology Studies, P.O. Box 45917, Nairobi, Kenya. Tel.: (254-2) 744047; 744095; Fax: 743995. ACTS Biopolicy Institute, Witmakersstraat 10, 6211 JB Maastricht, Netherlands. Tel.: +31 (43) 258499; Fax: 258433.

Regulation and discussion on genetic modification of animals - the situation in the European Community, the Netherlands, the United Kingdom, Germany, Denmark, France and the United States
by René Custers and Lydi Stemenberg

The Netherlands Organization for Technology Assessment (NOTA) has produced a most useful review of attitudes towards, and legislation controlling, the genetic engineering of animals and their use in the Economic Community and the United States. The report reveals that there are clear differences of opinion in the different countries on the perception of risks, economic significance, animal welfare and ethical considerations. The issue of animal patenting is fuelling much of the discussion in the European Parliament on the desirability of transgenic animals.

The genetic modification of animals to produce more or better food appears generally to be less acceptable than their modification for the production of vital medicines.

The report in English may be ordered from: Distributiecentrum Overheidspublicaties (D.O.P), P.O. Box 20014, 2500 EA The Hague, Netherlands. Price Dfl 25 quoting ISBN 9034628116. (Source: *EBIS, Biotechnology in Europe*, Vol. 2, No. 3, 1992)

Biosafety: The safe application of biotechnology in agriculture and the environment
by G. J. Persley, L. V. Giddings, and C. Juma (1992)

This document is a useful introduction for non-experts to the guidelines and procedures that have been developed to ensure the environmentally safe application of modern biotechnology. Its purpose is to provide a practical guide for policy makers and research managers with limited time and restricted access to the extensive documentation that is accumulating on biosafety. On the basis of the recommendations from authoritative studies of organizations such as the Organization for Economic Cooperation and Development (OECD) and the US National Research Council (NRC), the authors present a possible series of steps that might be taken to establish a national biosafety system. Such a system should consist of a National Biosafety Committee and Institutional Biosafety Committees with Biological Safety Officers. The authors recommend that a national biosafety system should be established within the existing regulatory framework and draw on existing institutions, personnel, and current legislation to the greatest extent possible. This recommendation follows from the presumption that the risks, associated with the introduction of genetically modified organisms, are similar to those assessed when an exotic plant, animal, or micro-organism is to be introduced into any area. Consequently, the authors argue that biosafety regulations need not be too stringent: "It wouldbe unfortunate if concerns over the potential impact of planned introductions of genetically engineered organisms, which may be safer than the competing chemical technologies they could displace, lead to such a stringent and expensive regulatory approach that economics force continued reliance on older, less safe technologies, such as the widespread use of chemical pesticides in the environment". Appendices include a list of experts for additional information and a bibliography.

Available from: International Service for National Agricultural Research, P.O. Box 93375, 2509 AJ The Hague, Netherlands; 39 pages, ISBN 92-9118-005-X.

"Ecological Effects of Genetically Modified Organisms"
edited by Jaap Weverling (of Mondiaal Alternatief) and Piet Schenkelaars (European Coordination, Friends of the Earth)

This report presents nine papers by qualified specialists writing for a general audience, the proceedings of a national symposium organized by the Netherlands Ecological Society in cooperation with the Provisional Committee on Genetic Modification, Amsterdam, September 1991.

The papers range from scientific topics (the ecology of invasions, horizontal plasmid transfer), mainly covering micro-organisms, plants and insects, via risk assessment to risk management and regulatory policy for field release. Finally a list of knowledge gaps or research requirements is provided.

The report may be obtained from Netherlands Ecological Society, Drenthesingel 11, 6835 HG Arnhem, Netherlands. Price: Dfl 27.50. (Source: *EBIS, Biotechnology in Europe*, Vol. 2, No. 3, 1992)

Books in the BIOTOL series

In the last issue of the Monitor, we described the BIOTOL open learning scheme, a joint project initiated by the Open Universiteit of the Netherlands and Thames Polytechnic (UK) to develop advanced level flexible training material, including books, computer-based and video training programmes for biotechnology. In addition, a network of collaborating colleges and universities will provide tutorial support, making training available as and when it is required. BIOTOL will be of particular value to employees in providing cost-effective flexible industrial training.

BIOTOL books have been designed for all those who wish to know and use the principles and techniques of modern biotechnology, whether they are technicians needing further education, graduates wishing to extend their knowledge base and potential mature workers faced with changing work or a new career, managers unfamiliar with the new technology or those returning to work after a career break. The books are divided between three levels: fundamentals, methodologies and business applications. Each title costs £19.95 and may be ordered from Catriona Burns, Butterworth Heinemann (Publishers), Linacre House, Jordan Hill, Oxford OX2 8DP, UK. Inspection copies are available for 30 days at no cost. At the end of this time they can be returned, purchased or retained if the book is adopted. The following is a list of titles in the three levels:

Level One - Fundamentals

The Molecular Fabric of Cells
Infrastructure and Activities of Cells
Principles of Cell Energetics
Energy Sources for Cells
Biosynthesis and Integration of Cellular Metabolism
Techniques Used in Bioproduct Analysis
Analysis of Amino Acids, Proteins and Nucleic Acids
Bioprocess Technology: Modelling and Transport Phenomena
Operational Modes of Bioreactors

Level Two - Methodologies

Bioreactor Design and Product Yield
Product Recovery in Bioprocess Technology
In-Vitro Cultivation of Micro-Organisms

Level Three - Business Applications

Biotechnological Innovations in Health Care
Biotechnological Innovations in Food Processing
Biotechnological Innovations in Crop Improvement
Biotechnological Innovations in Animal Productivity

ECOSCRIPTS - Publication series from the Foundation for Ecodevelopment (Stichting Mondiaal Alternatief) (MA)

In issue No. 40 of the Monitor (December 1992) we briefly described the activities of the Foundation for Ecodevelopment and mentioned its publication series, ECOSCRIPTS. The following titles could interest readers and may be obtained from the following address: Stichting Mondiaal Alternatief, PO Box 26047, 1002 GA Amsterdam, Netherlands.

ECOSCRIPT No. 36 - Ecology of Hope (Biomass conservation in tropical agro-forestry systems - alternatives to the destruction of tropical rain forests) by Bob Baars. Price: Dfl. 15.

ECOSCRIPT No. 37 - Export of Biotechnological Experiments and Production Units (concerns relocation of experiments from developed to developing countries) by Marie-Jose Smits. Price: Dfl. 4.

ECOSCRIPT No. 38 - Environment-driven Biotechnologies (concerns relocation of biotechnology production plants to a less regulatory environment) by Harold H. Lee. Price: Dfl. 3.50.

ECOSCRIPT No. 39 - Biotechnology and the Third World: The unmasking of a new promise (in preparation) by Guido Ruivenkamp, in cooperation with Henk Hobbelink). Price: Dfl. 6.50.

ECOSCRIPT No. 40 - Modern Genetic Engineering as a Political Issue of the Risk-fraught Society (in preparation) by Bernhard Claussen. Price: Dfl. 5.

ECOSCRIPT No. 41 - The Impact of Biotechnology on the Food Chain (in preparation) by Guido Ruivenkamp. Price: Dfl. 9.

ECOSCRIPT No. 42 - Biotechnology and Environmental Concerns in Mexico: Arguments for a research proposal by Rosalba Casas. Price: Dfl. 4.

ECOSCRIPT No. 43 - Ethical and Political Problems in Third World Biotechnology by Daniel J. Goldstein. Price: Dfl. 9.

ECOSCRIPT No. 44 - Latin American Pseudo Biotechnology - a pathway to underdevelopment, misery and more trade deficit by Daniel J. Goldstein. Price: Dfl. 9.

ECOSCRIPT No. 48 - The Risks of Ecological Effects of Genetically Modified Organisms (in preparation) by Piet Schenkelaars and Jaap Weverling. Price: Dfl. 9.

ECOSCRIPT No. 49 - Changes in Valued Capacities of Soils and Sediments as Indicators of Nonlinear and Time-Delayed Environmental Effects (in preparation) by William M. Stigliani.

ECOSCRIPT No. 50 - Chemical Time Bombs: Definition, concepts and examples (in preparation) by William M. Stigliani. Price: Dfl. 7.50.

ECOSCRIPT No. 51 - Plant-derived Pesticides in Developing Countries: Possibilities and research needs (in preparation) by Ronald Gerrits and Ed van Latum. Price: Dfl. 12.50.

G. SPECIAL ARTICLE

MUSHROOMS: TRENDS IN PRODUCTION AND TECHNOLOGICAL DEVELOPMENT

S.T. Chang and P.G. Miles *

1. Introduction

Almost certainly prehistoric man used mushrooms as food. There is ample evidence that the great early civilizations of the Greeks, Egyptians, Romans, Chinese and Mexicans prized mushrooms as a delicacy, for purported values of a therapeutic nature and, in some cases, in religious rites. Throughout recorded history there is repeated reference to the use of mushrooms as food and for medicinal purposes, and it is not surprising that the intentional cultivation of mushrooms had a very early beginning. We now know that this occurred in China around 600 A.D. with the cultivation of *Auricularia auricula* on wood logs (Chang and Miles, 1987). Other wood-rotting mushrooms such as *Flammulina* and *Lentinus* were later cultivated in a similar manner, but the biggest advance in mushroom cultivation occurred in France around 1600 A.D. when *Agaricus* was cultivated upon a composted substrate. In the Western world *Agaricus* (champignon or button mushroom) has remained up to the present time the mushroom that is produced in the greatest amounts, but now mushrooms long popular in Asia (e.g. *Lentinus*), and produced there in large numbers are making inroads into Western markets, but in the United States in 1990-91 the production of *Agaricus* still exceeded 99 per cent of total US mushroom production (NASS, 1991). In the years since World War II, there has been a consistent increase in mushroom production, which greatly accelerated in the period from 1986 to 1989-90, with an increase of 74.4 per cent and a total world production of 3.79 metric tons valued at about US$ 7.5 billion dollars (Chang and Miles, in press).

Although mushrooms were long appreciated because of their flavour and texture, and some for medicinal or tonic attributes, the recognition that they are nutritionally a very good food is much more recent. It is now known that mushrooms have a high protein content (19-35 per cent on a dry weight basis) of good quality (all essential amino acids for man including lysine and methionine, which are present in plants in only small amounts). Furthermore, mushrooms have a high proportion of unsaturated fatty acids, are a good source of several vitamins, fibre and minerals, and they are low in calories, sodium, fat and cholesterol. In addition, their nucleic acid content is not high enough to limit their daily use as a vegetable (Li and Chang, 1982a).

Mushrooms are a special group of fungi. Fungi lack chlorophyll and consequently cannot use solar energy to manufacture their own food as do green plants. However, mushrooms do produce a wide range of enzymes that degrade complex substrates, following which they absorb the soluble substances so formed for their own nutrition (Wood and Fermor, 1982; Wood, 1984). This absorptive nutrition is a characteristic of mushrooms. These complex substrates, which are generated annually in huge quantities, are agricultural, industrial and forest waste products. Examples are: cereal straws, coconut and coffee waste products, sugar cane bagasse, sawdust and cotton wastes, etc. (Chang and Miles, 1989). Much of these materials are either burned, shredded or used as landfill or for improvement of soil quality, even though these wastes constitute a potentially valuable resource for the production of edible food for man. Although physical and chemical technologies may, in some cases, play important associated roles, biotechnical approaches are essential for the emergence of practical conversion processes which can be applied to situations in developing countries throughout the world where large-scale capital intensive operations are inappropriate.

One of the most economically viable processes for the bioconversion of lignocellulosic wastes is the cultivation of edible mushrooms. The nutritional value and desirable gastronomic properties of mushrooms are

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now widely recognized. Of particular significance, especially to regions with populations whose diet is commonly deficient in protein, is the protein content of mushrooms. As previously mentioned, this is relatively high (19-35 per cent on a dry weight basis) as compared with 7.3 per cent in rice, 13.2 per cent in wheat, 39.1 per cent in soybean and 25.2 per cent in milk. Therefore, although mushrooms rank below most animal meats in crude protein content, they compare very favourably with most other foods (Crisan and Sands, 1978; Li and Chang, 1982b). With respect to essential amino acid indices, amino acid scores and nutritional indices, the overall nutritive value of high grade mushrooms almost equals that of milk. Furthermore, the proteins of commonly cultivated mushrooms contain all the essential amino acids and are especially rich in lysine and leucine, which are lacking in most staple cereal foods (Chang, 1980). It is also claimed that mushrooms contain other beneficial health promoting substances (Chang and Miles, 1989; Breene, 1990; Jong and Birmingham, 1990). In addition, the material remaining after the mushroom crop has been harvested can often be used as a valuable additive to the soil, thus increasing its potential for the production of other agricultural and horticultural crops, or possibly being used directly as a source of animal feed.

Many people have been attracted to mushroom cultivation because mushrooms can be grown on waste substrates and do not make the demands upon land space as is the case with most agricultural crops. This certainly is an attractive aspect of mushroom cultivation and, in an environmentally conscious society, the bioconversion of potential poilutants to a food for human consumption is not to be dismissed lightly. As we shall point out, however, mushroom cultivation requires an understanding of certain scientific principles and practical experience in mushroom technology for the successful achievement of a profitable mushroom farm. There is no doubt that if mushroom cultivation technology is properly promoted and developed, mushroom cottage industries will make important contributions to the nutrition and economic welfare of the people in many countries, particularly in developing countries.

The purpose of this article is to describe recent trends in mushroom production and the technological developments for research and cultivation of mushrooms. It should be noted that, in the long term, successful mushoom production must be supported by a background of sound scientific knowledge and technology.

2. Mushrooms and mushroom biology

The word mushroom may mean different things to different people in various countries. In this article, mushroom refers to the definition given by Chang and Miles (in press). In a broad sense "the mushroom is a macrofungus with a distinctive fruiting body which can be either epigeous or hypogeous and large enough to be seen with the naked eye and to be picked by hand. Thus, mushrooms need not be Basidiomycetes, nor aerial, nor fleshy, nor edible. Mushrooms can be Ascomycetes, grow underground, have a non-fleshy texture and need not be edible." In this context, mushrooms can be roughly divided into four categories: (1) those that are fleshy and edible fall into the edible mushroom category, e.g., *Agaricus bisporus*; (2) those mushrooms that are considered to have medicinal applications are referred to as medicinal mushrooms, e.g., *Ganoderma lucidum*; (3) those that are proven to be, or suspected of being, poisonous are called poisonous mushrooms, e.g., *Amanita phalloides*; and (4) a miscellaneous category that includes a large number of mushrooms whose properties remain less well defined and which may tentatively be grouped together as "other mushrooms". Certainly, this form of classifying mushrooms is not absolute. Many kinds of mushrooms are not only edible, but also possess tonic and medicinal qualities.

It has been estimated that in nature there are approximately 1.5 million species of fungi of which only approximately 5 per cent or 69,000 species, have been described (Hawksworth, 1991). Out of these described species of fungi, there are about 10,000 species of fleshy macrofungi and only a handful of these are lethal (Kendrick, 1985). There are no simple ways to distinguish between edible and poisonous mushrooms. Mushrooms should be eaten only if they have been identified with precision and the history as to edibility of that species is known. About 2,000 species from more than 30 genera are regarded as prime edible mushrooms, but only about 80 of them are grown experimentally, 40 cultivated economically, around 20 cultivated commercially, and only 5 to 6 are produced on an industrial scale (Chang, 1990a). In general, the oriental countries, China, Japan, and Korea grow and consume more varieties of mushrooms than the Western countries. However, in recent years, the production of what are referred to as "specialty or alternative mushrooms", mainly *Lentinus edodes* and *Pleurotus* spp., has increased rapidly in Western countries (Chang and Miles, 1991).

When knowledge increases and areas of specialization develop within a discipline, it is convenient to indicate that area of specialization with a self explanatory name. We have suggested that the term "mushroom biology" be used for the discipline concerned with the scientific study of mushrooms (Chang and Miles, in press). The term mushroom science has been defined as the discipline that is concerned with the principles and practices of mushroom cultivation, and thus dealing solely with cultivation, mushroom science is only one aspect of mushroom biology, the subdiscipline of mycology dealing with mushrooms. That is, mushroom biology includes not only cultivation, but it deals with any aspect of mushrooms, such as: taxonomy, development, nutrition, physiology, genetics, pathology, medicinal and tonic attributes, edibility, toxicity, etc.

3. Trends in production

Although various mushrooms have been highly valued as food, as a tonic, and in some cases as medicine for a long period of time, the use of mushrooms has become even more widespread in recent years, as can be witnessed by the increased demands for higher production volumes (figure 1). Their popularity is derived from three highly desirable characteristics as food: (1) they have remarkable taste and flavour; (2) they are nutritious; (3) they can be easily processed, dried, pickled and canned to permit them to be stored and transported from the place of production to the consumer.

In addition to these unique characteristics, many edible mushrooms have been traditionally used in China and Japan for their medicinal and tonic properties. The pharmaceuticals developed from mushrooms in Japan (table 1) and their pharmaceutical components (table 2) have been compiled recently by Pai *et al.* (1990). Cosmetic products and some healthful beverages have also been produced in China from mushrooms of *Ganoderma*. A variety of proprietary products including health drinks and foods, have also become available on the market and the demand for these is expected to increase.

With technical advances during the past few decades, cultivation of edible mushrooms has spread all over the world. Since cultivated mushrooms can be grown under different climatic conditions and on agricultural and industrial wastes, they can be used as an aid in solving many problems of global importance, including protein shortage, resource recovery and re-use and environmental management.

In an overall view, the world production of cultivated edible mushrooms was 2,176 thousand metric tons and 3,794 thousand metric tons in 1986 and 1989/90, respectively (table 3). In those three years, mushroom production increased by 74.4 per cent and an annual increase of 24.5 per cent (Chang and Miles, 1991). A comparison of production between 1986 and 1989/90 reveals that all cultivated mushroom species increased during that period, ranging from 19 per cent for *Agaricus* up to 43 per cent for *Pleurotus*. The next big increase was 23.6 per cent for *Auricularia*. However, the percentage of the total world production of edible mushrooms for *Agaricus* and for *Lentinus* mushrooms decreased as a consequence of the increase in production of the other cultivated edible mushroom species, in particular *Pleurotus* species (figure 2).

A comparison of the mushrooms in 1986 and 1989/90 cultivated in China is given in table 4. The increase in growth rate for all 12 cultivated mushrooms in China was 175 per cent. *Pleurotus* became the number one cultivated mushroom in China with an increase of 700 per cent during the three years from 1986 to 1989/90. Second in total production was *Auricularia*. These two mushrooms are used mainly for domestic consumption with a small proportion for export to Japan and Hong Kong. In 1989 the percentage of the production of individual species exported was 76 per cent for *Agaricus*,, 20 per cent for *Lentinus*, 4.4 per cent for Pleurotus and 4 per cent for *Auricularia*. For the first time, China grew over 50 per cent of the cultivated mushrooms produced in the world (1915 MT/3794 MT).

In the three-year period from 1986 to 1989/90, the production of edible mushrooms in Japan (table 5) is most notable for the increase in production of two species, *Hypsizigus marmoreus* and *Grifola frondosa*. The increase was 94.5 per cent and 175 per cent, respectively. This increase in production was partially offset by decreases in production of *Lentinus edodes* by 9.6 per cent and of *Auricularia auricula-judae* by 25.4 per cent, but with steady increases in production of *Flammulina velutipes* and *Pleurotus* spp., there was still an increase of total mushroom production in Japan of 4.4 per cent during this period.

It can be seen from table 6 that mushroom consumption in Japan increased significantly in the period from 1986 to 1989/90, since exports decreased and imports increased by 39.6 per cent from 17,403 to 24,286 metric tons. In amount, the greatest increase was of *Auricularia auricula-judae*, of which 19,875 metric tons were imported (mainly from China) in 1989/90, compared to 16,299 metric tons in 1986. The highly prized *Tricholoma matsutake*, which is farmed by semi-cultivation techniques, was imported into Japan in the amount of 2,210 MT in 1989/90, an increase of 125.5 per cent over the 980 MT imported in 1986. It is also interesting to note that the import of dried *Lentinus edodes* (*shiitake*) into Japan increased greatly from 124 MT in 1986 to 2,201 MT in 1989/90 (an increase of 1,675 per cent!), while exports of dried *Lentinus edodes* decreased from 3,538 to 1,439 MT. In general, the *shiitake* imported into Japan were of lower quality mushrooms to be sold to lower income people who could not afford the expensive high quality mushrooms, which have traditionally been a good export item from Japan but which can now be sold more readily in Japan because of the thriving economy of that country.

Total mushroom production in South Korea increased by 37 per cent during the period from 1986 to 1989/90 (table 7). The greatest amount of this increase was due to *Pleurotus* spp. of which 11,570 MT more were produced in 1989/90 than in 1986, an increase of 44.8 per cent. As was true in China, the mushroom produced in greatest amount was *Pleurotus* spp. Second in production was *Agaricus bisporus*, whose production was 12,025 MT in 1989/90, with little change since 1986. Production of *Lentinus* in Korea increased by 48 per cent to 10,710 MT in 1989/90. It is readily seen that there was considerable change in the amounts of the various species being produced in South Korea during this period, with the most dramatic being the

656 per cent increase in *Flammulina velutipes*, but the amounts are still relatively small - 16 MT in 1986 and 121 MT in 1989/90. *Flammulina velutipes* is grown primarily for export to Japan, as is *Tricholoma matsutake*. In 1989/90 Japan paid a higher price for the *Tricholoma* from South Korea than that from any other country, and Japan bought 84 per cent of Korea's *Tricholoma*. It should be noted that 1986 was an unusual year in *Tricholoma* production in Korea, since it amounted to only 311 MT, a drop from 1,313 MT the previous year. The percentage increase in production of *Tricholoma* between 1986 and 1989/90 shown in table 7 is misleading, since production has not yet reached the 1985 amount. Another item of interest in table 7 is the increase in production of the medicinal mushroom *Ganoderma lucidum* of approximately 307 per cent between 1986 and 1989/90.

4. Trends in technological developments

Mushroom cultivation is a complicated business. It involves a number of different operations including the selection of an acceptable fruiting culture of the mushroom, preparation of spawn and compost, inoculation of the compost, crop care, harvesting, preservation of the mushroom and marketing. Each of these operations consists of many sequential steps, which are equally crucial and important if success is to be achieved in the mushroom business (Miles and Chang, 1986).

While there is available a solid background of scientific information for these various operations with a number of cultivated species, in many aspects mushroom cultivation is also an art, just as wine making is both a science and an art. Consequently, in order to maintain a reasonably high and stable yield of mushrooms, both fundamental knowledge of mushroom science and the accumulative information of practical experience are required.

In Western countries cultivation of *Agaricus* - the most popular edible mushroom, which is variously known as the white mushroom, button mushroom, champignon, or simply the common cultivated mushroom - has developed over the past 50 years from a beginning as a risky venture to a largely predictable and controllable industrial process, e.g., 50 years ago the yield was less than 5 kg per square metre in more than 12 picking weeks. The picking was done by hand. Today, the yield can be 50 kg per square metre in four picking weeks and the harvesting can be done by cutting machines. The deep-trough method of cultivation, developed in the UK and adopted in Czechoslavakia with technical refinements, now achieves average yields of 60 kg per square metre (Noble, 1989).

Agaricus in nature is a temperate climate mushroom. It is produced in Western countries where the production involves the most advanced and highly mechanized technology in the mushroom industry. In 1965 Taiwan, with a subtropical and tropical climate, emerged as the third leading producer of *Agaricus*, although currently it only ranks tenth. This production in Taiwan was possible because it was found that *Agaricus* could be grown profitably on a seasonal basis in the period from September through March. Since then, *Agaricus* has also been grown successfully in countries with similar climatic conditions, either seasonally or in cooler mountainous regions. The growth in Taiwan was also notable because *Agaricus* was cultivated on a synthetic compost having rice straw as the main component because there was an absence of a plentiful supply of horse manure. In contrast to *Agaricus* cultivation in Western countries, Taiwan did not use a highly mechanized technology on a relatively few large mushroom farms, but developed the industry as a cottage-type enterprise on thousands of farms in which the mushroom houses were constructed of bamboo frames and banana leaves and/or straw and plastic for the roof and siding (Chang and Miles, 1989).

Among the South-East Asian nations Taiwan consistently led in the production of *Agaricus* until recently. Indonesia has now developed the industry, using mechanized methods and with the farms located on cooler mountainside areas. South Korea has also produced large amounts for export. By 1983 China became the third leading producer of *Agaricus* in the world, and by 1986 it was second only to the USA in total production, but then China slipped to third in 1989/90. This was undoubtedly influenced by the ban of canned mushrooms from China to the United States as a consequence of problems with faulty canning procedures. Much of the production of *Agaricus* in Asia reaches foreign markets as canned mushrooms. This is because of the lower cost of production in Asian countries so that these canned mushrooms can be sold at a lower price than the canned mushrooms produced by the mechanized growers in Western countries. This also had the effect of a larger share of the *Agaricus* mushrooms produced by Western countries being sold fresh. In no small measure this remarkable achievement in modern mushroom industrial development can be attributed to contributions resulting from the vigorous research activities conducted at various academic institutions as well as mushroom research stations. This history of *Agaricus* production technology has shown the way for cultivation of other mushrooms.

Lentinus edodes has for many years been grown on wood logs. It usually takes at least 8-12 months for the first flush to occur with the biological efficiency not exceeding 15 per cent. Since the early 1970s, a method using "plastic bags", sometimes known as "synthetic logs", was introduced. This method utilizes a sawdust-based substrate prepared in autoclavable plastic bags, has a shorter production cycle and gives higher yields. The cultivation also usually takes place in a controlled environment, which facilitates a consistent year-round production. This method of production involves the expense of higher energy costs compared with other

growing procedures (Chang and Miles, 1989; Cho and Nair, 1987). Since the introduction of the "plastic bag" method, various patents have been filed on variations of this method. While technical information is difficult to obtain without paying substantial technology fees for detailed production protocols, it would appear that they either differ in the formulation of the substrates (although still using sawdust as the main carbon source) or in the methods of manipulation of the environmental factors, which are important in triggering fruit body formation.

One of the main drawbacks of the existing "plastic bag" method is that the quality of the mushrooms obtained is considered by many to be inferior to the mushrooms cultivated by the log method. The method of inoculating individual bags using either grain or sawdust-based spawn is also laborious, and thorough spawning is not always easily accomplished by shaking after inoculation or by the use of a "spawning channel". Research work jointly carried out by the University of Sydney and The Chinese University of Hong Kong has resulted in the development of a novel method for the cultivation of *shiitake*, which overcomes such shortcomings. The use of a new type of substrate without sawdust and the right formulation results in a substrate preparation, which not only is nutritionally suited for fruiting, but also provides better conditions for aeration, which is also very important. The introduction of a liquid spawn instead of solid spawn and an improved method of dispensing the spawn, reduces labour costs and facilitates thorough spawning. The amount of spawn introduced far exceeds that when sawdust or grain spawn is used. The latter two contain at most less than 1 per cent mycelium based on the dry weight of the carrier. Heavy spawning results in a shorter spawn run period (usually about six weeks). The use of synthetic medium also results in the reduction of contamination since the medium is not nutritionally rich for other competing microorganisms. The use of strains adapted for growth on the new substrate also helps to produce good quality *shiitake*. Finally, supplements are introduced, usually after the first cropping, which significantly increases yield of subsequent flushes. The average biological efficiency is about 60-80 per cent over a period of six months. With an extended cropping period, 100 per cent is not unusual.

Vegetative growth of the straw mushroom, *Volvariella volvacea*, occurs efficiently at 32-34° C and is consequently referred to as a "warm mushroom". A related outstanding feature of *Volvariella volvacea* is its rapid growth - only 8-10 days being required from spawning to harvesting. This can be accomplished by the straw mushroom under favourable conditions, and it is a shorter period from planting to the table than any other vegetable or cultivated mushroom. Since the ability of the mycelium to become colonized with its substrate is weak, the mycelial network is easily broken and disconnected if the compost is disturbed. Thus, mismanagement or improper care during any phase of production of *Volvariella volvacea* will drastically decrease the yield. This species has the ability to use cellulosic materials more effectively than other cultivated mushrooms; e.g., during the mycelial running stage the optimum C:N ratio for *V. volvacea* is about 40 to 60, for *Agaricus bisporus* it is 16 to 18, and for *Lentinus edodes* it is 20 to 25. It grows quickly and easily on substrates of high cellulosic content including such waste organic materials as paddy straw and cotton wastes. The primordium of the mushroom can be formed 4-5 days after spawning under conditions of favourable environmental conditions and a suitable growth medium. For the reasons just stated, *V. volvacea* has been considered to be one of the easiest mushrooms to cultivate, but even under appropriate conditions the biological efficiency is lower than that of most other cultivated mushrooms.

The use of cotton wastes from the textile mills was first used in 1971 as a substrate for growing the straw mushroom under controlled conditions (Chang, 1972; Yau and Chang, 1972). This use of cotton wastes completely replaced paddy straw in Hong Kong in 1973 for the cultivation of the mushroom in indoor conditions (Chang, 1974). This marked a turning point in straw mushroom cultivation since it was found that cotton waste compost gave a higher and more stable yield (30-45 per cent), earlier fructification and harvesting than under the same conditions with straw as the substrate. With the composted waste cotton substrate, pinheads appeared in four days and the first harvest was ready nine days after spawning. These good characteristics of cotton waste compost have led to the cultivation of the straw mushroom being semi-industrialized in Hong Kong, Taiwan and Indonesia, as well as in Thailand.

The fact that the oyster mushroom (*Pleurotus* spp.) jumped to second position in total production with 909,000 MT produced in 1989/90 is partially due to new techniques resulting from research into bag culture methods. It is anticipated that continued research will result in increased production of more species, of improved cultivars of such species by breeding techniques, of an extension of the geographic limits imposed by climate to cultivation of certain species, and the development of composting methods for the wood-rotting mushrooms, which will reduce requirements for energy. While research may make many things possible, the successful operation and expansion of any enterprise requires trained personnel. Thus, in addition to scientific research, the advancement of the mushroom industry requires centres for training

personnel in principles and practices of mushroom cultivation.

5. Requirements to help reach the potential

A. Basic and applied research in all aspects of mushroom biology

Mushroom scientists are working to increase mushroom production by four main pathways. The first is to find better cultivation methods that will increase mushroom production in places where it is already cultivated. The second pathway is to expand growing areas to places such as subtropical or tropical climates where *Agaricus bisporus* has not been grown previously. The third is to preserve the production strains that have already been obtained by promoting sustainable mushroom cultivation systems. The fourth pathway is to use advanced research techniques such as biotechnology to design and breed new strains of mushrooms that will give higher yield and better quality.

At each pathway mentioned above, there are many potential ways in which biotechnology can be applied to improve mushroom yield and quality. As we know, genetics, biochemistry and fermentation technology are three of the most important areas of modern biotechnology. Our present understanding of the developmental genetics of mushroom species is based almost entirely on studies of mutant strains. We know most about the genetics of fruiting body development and least about the genetics of spore formation, maturation and germination. The discovery of sporeless mutants in *Pleurotus* spp. (Yu and Chang, 1989) will have important economic and health benefits and will also help to further our understanding of sporulation. On the biochemical front, recent research reports have indicated that there are great changes in levels of extracellular enzymatic activity in mushroom mycelium and in the compost, and that these changes are associated with the formation of fruiting bodies and the production of flushes of mushrooms (Claydon, *et al.*, 1990; Wood, 1980; Wood and Goodenough, 1977; Wood and Leatham, 1983). To be able to control the mushroom flushes is one of the goals of mushroom scientists.

Progress in scientific research and in the application of biotechnology to the culture of mushrooms has resulted in the use of specifically fermented liquid nutrients absorbed on inert physical supports such as vermiculite (Miles and Chang, 1987; Tautorus and Townsley, 1987). This kind of "hydroponic mushroom cultivation" has the potential of enabling a grower to conduct a completely controlled fermentation of the substrate with the use of pre-selected thermophilic microorganisms (i.e., thermophiles which would prevent disease or contamination and stimulate mushroom growth and yield). Eventually, this could become a continuous culture technique, in which fresh liquid nutrients could be pumped into the culture tank to obtain high yields in successive flushes (Cho and Nair, 1987; Wood, 1989).

Other potential applications of biotechnology to the mushroom industry include: (1) strain improvement (Miles and Chang, 1986; Peberdy, 1989) (e.g., faster growing strains and strains suitable to different environmental circumstances); (2) selection of thermophilic *Bacillus* and *Humicola* spp. to inhibit mushroom pathogens and promote mushroom growth; and (3) development of techniques to increase the biological efficiency for conversion of agricultural and industrial waste materials.

B. Mushroom gene bank

The basic requirement in breeding for higher yielding and better quality strains of a mushroom species is to have available as large an amount of genetic material as possible so as to increase the amount of variation in the progeny for selection purposes. Hybrid progeny can be generated by conventional breeding methods involving crosses between selected strains within a species by protoplast fusion techniques, where the two parental cells may come from normally non-mating strains, or by the transfer of genes from one kind of organism to another using recombinant DNA technology. However, since the organism is the only source of the exchanged genomes or the transferred genes, the loss of an individual strain or species can mean the loss of tens or even hundreds of thousands of individual genes. A loss of germplasm from the loss of genes, strains or species will reduce the amount of variation that can occur within the species, thus lessening the capacity for genetic selection and improvement.

The methods of establishing mushroom gene banks can consist of *in situ* and *ex situ* conservation activities. The former describes the maintenance of mushrooms, including wild representatives, in natural preserves and will result from the conservation of ecosystems. The latter case, where spores or tissue cultures are preserved outside their area of growth, is the conservation of germplasm. Therefore, in the context of this paper, mushroom gene bank means *ex situ* conservation of mushroom germplasm in the form of culture collections of the mushroom species. Mushroom germplasm collections are assemblages of genotypes representing wild fruiting bodies, or commercial stocks that are the product of scientific breeding, and their derivatives (e.g., spores, tissues). All this genetic capacity of a particular mushroom [illegible] uding both cultivated and wild relatives, [illegible] gene pool of the mushroom, assuming th[illegible] ources can contribute genes to progeny by crossing, fusing or by other methods of gene transfer. Conserving the world's biological diversity has emerged as a matter of international concern (Abelson, 1991). Characterization of individual cultures, which have been collected and preserved, is of fundamental importance in establishing

the collection of the germplasm of a mushroom. Information on the genetical, morphological, physiological and biochemical characteristics of the strains is stored in computers to construct a database. The process is called "gene bank accession". The function of this database is expected to provide valuable and rapidly accessible information for future breeding and academic research in mushroom biology.

C. Regional workshops for bringing current information and techniques pertinent to the mushroom species to be grown in the region

During the past decade there has been a great increase in popularity and production of mushrooms in South-East Asia. This has been due in part to an awareness that mushrooms possess great nutritive properties (apart from their use as a delicacy) and that they can serve as a cheap protein source. An important contributing factor has been the financial and moral assistance received from United Nations agencies such as UNESCO, UNEP, ICRO, and UNU, which have conducted training courses and workshops in Asian countries on mushroom production (Chang, 1990b). It is hoped that this trend will continue not only by these agencies, but also by other agencies and foundations.

D. International Mushroom Research Centre

Mushroom science, derived from the principles of microbiology, environmental engineering and fermentation technology, has developed in modern times both as the basis for new cottage-type industries and for highly developed industrial mushroom growing complexes. Thus, the activities stemming from mushroom studies have achieved global dimensions and there are many long term world-wide implications. One such activity is the conservation of mushroom germplasm as a part of the conservation of the world's biological diversity. Conservation of germplasm has emerged as a matter of very serious internationai concern. The cultivation of mushrooms is a biotechnology that does not require extensive mechanization and produces results within a short time, bringing direct benefits to developing countries. However, progress in mushroom cultivation and the development of the industry are dependent upon the collective efforts of scientists from the industrialized and developing countries. To achieve effective collaboration of scientists and mushroom biologists throughout the world on mushroom research and production, an international centre for mushroom studies and training should be established.

6. Conclusion

In spite of the many conceptual and technical problems in their cultivation, we foresee a more important role for mushrooms as a source of protein in tropical and subtropical regions, where the shortage of protein in the human diet is more marked. We also see no reason why both rural and urban areas cannot share in this new possibility and prospect, especially in view of the 7-fold increase in total world production of mushrooms in the past two decades. The introduction of technology to breed new strains that are adapted to more varieties of climates, and to maximize mushroom production per unit area at minimum cost for the purpose of providing a cheap source of food protein from those agricultural and industrial organic wastes that are abundant in tropical and subtropical regions, is a continuing challenge. Already over 50 per cent of total mushroom production takes place in developing countries, where *Lentinus, Volvariella, Pleurotus, Auricularia, Tremella, Pholiota* and *Hericium* are cultivated in greater amounts than they are in the developed nations.

The term mushroom biology refers to the discipline that is concerned with the scientific study of mushrooms (macrofungi with distinctive fruiting bodies). It includes all of the activities of mushroom cultivation as well as the various biological subdisciplines, such as genetics, taxonomy, physiology, etc. It is believed that the term mushroom biology will bring together many diverse studies, thus facilitating the dissemination of knowledge about mushrooms and a greater recognition of this field of science, which is increasingly affecting peoples' lives for their betterment.

7. References

Abelson, P.H. (1991). Resources of plant germplasm. **Science,** 253:833.

Breene, W.M. (1990). Nutritional and medicinal value of specialty mushrooms. **J. of Food Production,** 53:833-894.

Chang, S.T. (1972). The Chinese Mushroom (*Volvariella volvacea*) - Morphology, Cytology, Genetics, Nutrition and Cultivation. The Chinese University Press, Hong Kong. 99 pp.

Chang, S.T. (1974). Production of the straw mushroom (*Volvariella volvacea*) from cotton wastes. **The Mushroom J.**, 21:348-354.

Chang, S.T. (1980). Mushrooms as human food. **Bioscience**, 30:399-401.

Chang, S.T. (1990a). Future trends in cultivation of alternative mushrooms. **The Mushroom J.**, 215:422-423.

Chang, S.T. (1990b). Biotechnology for mushroom cultivation in developing countries. In: Flegel, T.W., Gunter Tharven and Yongyuth Yuthavong (eds.) Biotechnology for Small Industries in Developing Countries, pp. 92-97. Text and Journal Corporation, Bangkok, Thailand. 260 pp.

Chang, S.T. and P.G. Miles (1987). Historical record of the early cultivation of *Lentinus* in China. **Mushroom J. for the Tropics**, 7:31-37.

Chang, S.T. and P.G. Miles (1989). Edible Mushrooms and Their Cultivation. CRC Press, Boca, Raton, Florida, USA. 345 pp.

Chang, S.T. and P.G. Miles (1991). Recent trends in world production of cultivated mushrooms. **The Mushroom J.**, 503:15-18.

Chang, S.T. and P.G. Miles (in press) Mushroom biology - a new discipline. **The Mycologist** (UK).

Cho, K.Y. and N.G. Nair (1987). Advances in the biotechnology of mushroom cultivation. **Aust. J. Biotechnology**, 1:53-57.

Claydon, N., M. Allan and D.A. Wood (1990). Fruit bodies biomass regulated production of extracellular endocellulase during periodic fruiting by *Agaricus bisporus*. **The Mushroom J.**, 206:53-55.

Crisan, E.V. and A. Sands (1978). Nutritional value. In "The Biology and Cultivation of Edible Mushrooms", edited by Chang, S.T. and W.A. Hayes. pp. 137-165. Acad. Press, New York, USA. 819 pp.

Hawksworth, D.L. (1991). The fungal dimension of biodiversity: magnitude, significance, and conservation. **Mycol. Res.**, 95:641-655.

Jong, S.C. and J.M. Birmingham (1990). The medicinal value of the mushroom *Grifola*. **World J. Micro. & Biotechnology**, 6:227-235.

Li, G.S.F. and S.T. Chang (1982a). The nucleic acid content of some edible mushrooms. **European J. Appl. Microb. Biotechnol.**, 15:237-240.

Li, G.S.F. and S.T. Chang (1982b). Nutritive value of *Volvariella volvacea*. In "Tropical Mushrooms - Biological Nature and Cultivation Methods", edited by Chang, S.T. and T.H. Quimio. pp. 199-219. Chinese Univ. Press, Hong Kong. 492 pp.

Kendrick, B. (1985). The Fifth Kingdom. Waterloo. Mycologue Publication. 364 pp.

Miles, P.G. and S.T. Chang (1986). Application of biotechnology in strain selection and development of edible mushrooms. **Asean Food J.**, 2:3-10.

Miles, P.G. and S.T. Chang (1987). Fruiting of *Lentinus edodes (Shiitake)* in liquid media. **MICREN J.**, 3:103-112.

National Agricultural Statistics Service. (1991). Mushrooms. United States Department of Agriculture, Washington, D.C., USA.

Noble, R. (1989). Growing deep in Czechoslovakia. **The Mushroom J.** 203:352-353.

Pai, S.H., S.C. Jong and D.W. Lo (1990). Usages of mushrooms. **Bioindustry** 1:126-131.

Peberdy, J.F. (1989). Fungi without coats - protoplasts as tools for mycological research. **Mycol. Res.**, 93:1-20.

Tautorus, T.E. and Townsley (1987). Biotechnology in commercial mushroom fermentation. **Bio/Technology** 2:696-701.

Wood, D.A. (1980). Inactivation of extracellular laccase during fruiting of *Agaricus bisporus*. **J. General Microbiology** 117:339-345.

Wood, D.A. (1984). Microbial processes in mushroom cultivation: a large scale solid substrate fermentation. **J. Chem. Technol. Biotechnol.** 34B:232-246.

Wood, D.A. (1989). Mushroom Biotechnology. **Intl. Indust. Biotechnology** 9:5-8.

Wood, D.A. and T.R. Fermor (1982). Nutrition of *Agaricus bisporus* in compost. **The Mushroom J.** 114:194-197.

Wood, D.A. and P.W. Goodenough (1977). Fruiting of *Agaricus bisporus*. Changes in extracellular enzyme activities during growth and fruiting. **Archives of Microbiology** 114:161-165.

Wood, D.A. and G.F. Leatham (1983). Lignocellulose degradation during the life cycle of *Agaricus bisporus*. **FEMS Microbiology Letters** 20:421-424.

Yau, C.K. and S.T. Chang (1972). Cotton waste for indoor cultivation of straw mushroom. **World Crops** 24:303-304.

Yu, M. and S.T. Chang (1989). Mutants of *Pleurotus florida* deficient in sporulation. **MIRCEN J. Applied Microbiol. Biotechnol.** 5:487-492.

Table 1. Pharmaceuticals developed from mushrooms in Japan

Name	Krestin	Lentinan	Schizophyllan
Abbreviation	PSK/PSP		
Date for sale	May 1977	December 1985	April 1986
Mushrooms species	*Coriolus versicolor* (mycelium)	*Lentinus edodes* (fruiting body)	*Schizophyllum commune*
Polysaccharide	Beta-1,6 branch; Beta-1,3; Beta-1,4 mainchain	Beta-1,6 branch; Beta-1,3 mainchain	Beta-1,6 branch; Beta-1,3 mainchain
Molecular weight	ca. 100,000	ca. 500,000	ca. 450,000
$[alpha]_D$	-	+ 14~22°C (NaOH)	+ 18~24°C (H_2O)
Products	1g/package	1mg/vial	1g/2ml bottle
Administration	Oral	Injection	Injection
Indication	Cancer of digestive system, breast cancer, pulmonary cancer	Gastric cancer	Cervical cancer
1985 sale value	556 M$	85 M$	128 M$

Source: Pai *et al.* 1990

Table 2. Pharmaceutical components of mushroom species

Pharmacodynamic	Component	Species
1. Antibacterial effect	Hirsutic acid	Many species
2. Antibiotic	E-beta-methoxyacrylate	*Oudemanxiella radicata*
3. Antiviral effect	Protein, Polysaccharide	*Lentinus edodes* and *Polyporaceae*
4. Cardiac tonic	Volvatoxin, Flammutoxin	*Volvariella*
5. Decrease cholesterol	Eritadenine	*Collybia velutipes*
6. Decrease level of blood glycogen	Peptide glucan, Ganoderan	*Ganoderma lucidum*
7. Decrease blood pressure	Triterpene	*Ganoderma lucidum*
8. Antithrombus	5'-AMP, 5'-GMP	*Psalliota hortensis*
9. Inhibition of PHA	r-GHP	*Psallliota hortensis, Lentinus edodes*
10. Antitumor	Beta-glucan RNA complex	Many species, *Hypsizygus marmoreus (Lyophyllum shimeji)*
11. Increase secretion of bile	Armillarisia A	*Armillariella tabescens*
12. Analgesic, Sedative effect	Marasmic acid	*Marasmius androsaceus*

Source: Pai *et al.* 1990

Table 3. Comparison of 1986 and 1989/90 world production of cultivated edible mushrooms

Unit: (metric ton x 1000)

Species	Common Name	1986		1989/90		% increase
		Fresh wt.	%	Fresh wt.	%	
Agaricus bisporus bitorquis	Button mushroom	1,215	55.8	1,446	38.1	19.0
Lentinus edodes	Shiitake or oak mushroom	320	14.7	402	10.6	25.6
Volvariella volvacea	Straw mushroom or Chinese mushroom	178	8.2	207	5.5	16.3
Pleurotus spp.	Oyster mushrooms	169	7.8	909	24.0	437.9
Auricularia spp.	Wood-ear	119	5.5	400	10.5	236.1
Flammulina velutipes	Winter mushroom	100	4.6	143	3.8	43.0
Tremella fuciformis	White Jelly fungus/ or "Silver Ear"	40	1.8	105	2.8	162.5
Pholiota nameko	"Nameko" or Viscid mushroom	25	1.1	53	1.4	112.0
Hericium erinaceus	Monkey head mushroom or Hedgehog fungus	-	-	90	2.4	
Hypsizigus marmoreus	Shimeji	-	-	22	0.6	
Grifola frondosus	Sitting-hen mushroom or Limuo, Maitaka	-	-	7	0.2	
Others		10	0.5	10	0.3	
Total		2,176	100.0	3,794	100.2	74.4

Source: Chang & Miles (1991).

Table 4. Comparison of 1986 and 1989/90 production of cultivated edible mushrooms in China

(unit: x 1000 tons)

	1986		1989/90		% increase
	Fresh wt.	%	Fresh wt.	%	
Agaricus bisporus	185	26.6	170	8.9	-2.7
Lentinus edodes	120	17.2	210	11.0	75.0
Volvarilla volvacea	100	14.4	110	5.7	10.0
Pleurotus spp.	100	14.4	800	41.2	700.0
Auricularia spp.	80	11.5	360	18.8	350.0
Tremella fuciformis	50	7.2	100	5.2	100.0
Hericium erinaceus	50	7.2	90	4.7	80.0
Flammulina velutipes	10	1.4	40	2.1	300.0
Pholiota nameko	0.8	0.1	32	1.7	3,900.0
Tremella aurantia	-		3.50	0.2	
Grifola frondosus	-		0.20	0.01	
Dictyophora indusiata	-		0.04	0.002	
Total	695.8	100.0	1,915.74	99.412	175.3

Table 5. Comparison of 1986 and 1989/90 production of cultivated edible mushrooms in Japan

(unit: tons)

Species	1986		1989/90		% increase
	Fresh wt.	%	Fresh wt.	%	
Lentinus edodes	176,800	56.0	159,857	48.5	-9.6
Pholiota nameko	20,079	6.4	21,125	6.4	5.2
Flammulina velutipes	74,378	23.6	83,200	25.3	11.9
Pleurotus spp.	30,050	9.5	36,095	11.0	20.1
Hypsijigus marmoreus	11,493	3.6	22,349	6.8	94.5
Grifola frondosus	2,203	0.7	6,167	1.8	178.0
Auricularia auricula-jadae	205	0.06	153	0.05	-25.4
Tricholoma matsutake	199	0.06	457	0.15	129.6
Total	315,407	99.9	329,403	100.0	4.4

Table 6. Comparison of 1986 and 1989/90 import and export of edible mushrooms in Japan

(unit: tons)

Species	1986		1989/90		% increase	
	Import	Export	Import	Export	Import	Export
Lentinus edodes	124	3,538	2,201	1,439	1,675	-59.3
Auricularia auricula	16,299	-	19,875	-	22.0	-
Tricholoma matsutake	980	-	2,210	-	125.5	-
Total	17,400	3,538	24,286	1,439	39.6	-59.3

Table 7. Comparison of 1986 and 1989/90 production of cultivated edible mushrooms in South Korea

(unit: tons)

Species	1986		1989/90		% increase
	Fresh wt.	%	Fresh wt.	%	
Agaricus bisporus	11,860	26.0	12,025	19.3	1.4
Pleurotus spp.	25,850	56.8	37,420	60.1	44.8
Lentinus edodes	7,238	15.9	10,710	17.2	48.0
Flammulina velutipes	16	0.04	121	0.2	656.2
*Tricholoma matsutake**	311	0.7	954	1.5	206.8
*Ganoderma lucidum***	256	0.6	1,028	1.7	301.6
Total	45,531	100.04	62,258	100.0	36.7

* Semi-cultivated
** Medicinal mushroom

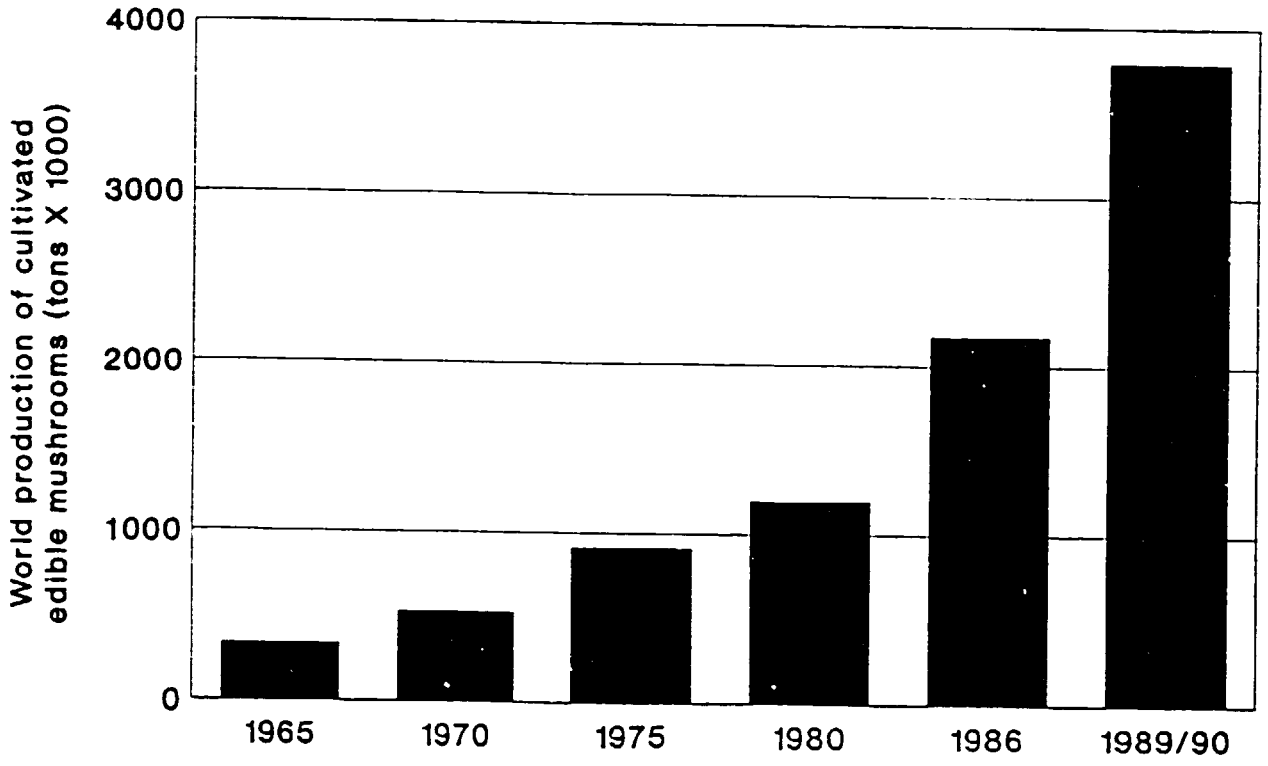

Fig. 1. Annual world production of cultivated edible mushrooms

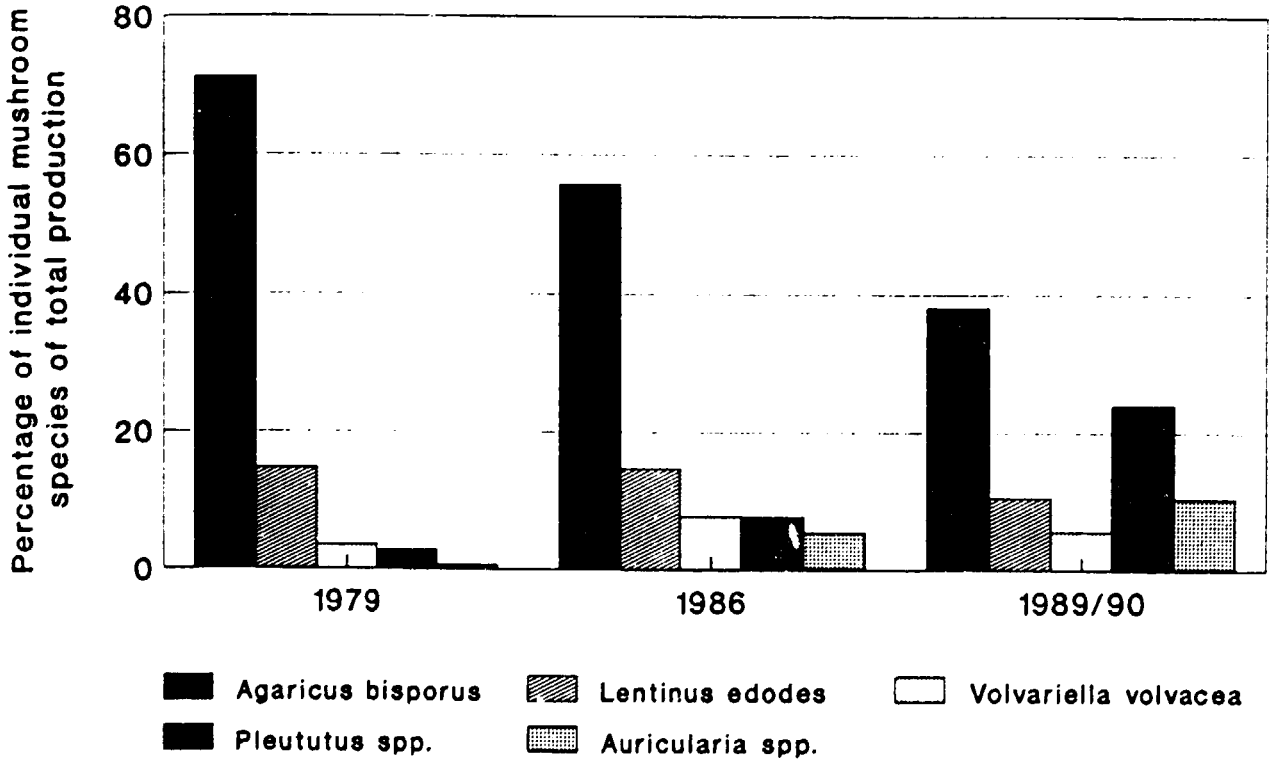

Fig. 2. Percentage of world production of five major mushrooms in 1979, 1986 and 1989/90