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Genetic Engineering and Biotechnology Monitor

Issue No. 36 December 1991

This issue features a special article by Professor N. Weiss of the Swiss Tropical Institute, Basel, on perspectives on the diagnosis of parasitic diseases of the tropics.

This publication is distributed free of charge

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A. POLICY, NEWS AND OTHER EVENTS

UNIDO news

UNIDO convened two meetings in Vienna (March 1991) and Trieste (July 1991) with the aim of formulating an International Voluntary Code of Conduct for the release of "Genetically Modified Organisms" (GMOs) to the environment.

Some 50 experts from academia, industry, national and international regulatory authorities were involved in the drafting of the Code. The point of departure for the work of the experts was the identification and compilation of common elements in the huge array of national and international biosafety guidelines and regulations. Their work was guided by the need to protect public interest while at the same time creating an environment conducive to bringing biotechnology products to the market-place. The Code, in addition to spelling out what constitutes good practice for releasing GMOs to the environment, makes provisions for the establishment of a Biosafety Information Network and Advisory Service.

It is expected that such a service would provide an appropriate decision support i.e. a platform for national regulatory authorities involved in biotechnology risk assessment and management.

The Code of Conduct is now in its final form and has been widely disseminated. The feedback received from national regulatory authorities and the bio-industry has been most encouraging. It is intended to present the Code to the United Nations Conference on the Environment and Development in Brazil.

Expert Group Meeting on the Commercialization of Biotechnology

An Expert Group Meeting (EGM) on the Commercialization of Biotechnology was held by UNIDO during 28 October to 1 November at its Headquarters in Vienna. The meeting was attended by 34 experts from 20 countries from governments, academia and industry from North and South. Among the participants were representatives from the International Centre for Genetic Engineering and Biotechnology (ICGEB), Trieste; United States Department of Agriculture; International Development Research Centre, Canada; EEC; WHO; and Regional Biotechnology Networks.

Dr. S. Burrill of Ernst and Young gave the keynote address with an overview on the global scenario of present and future prospects of commercialization of biotechnology. This was followed by presentations from participants on the successful commercialization of products and those in the pipeline in areas of health care and food processing. The importance of human resources development in the application of biotechnology, particularly in developing countries, and the necessity for strengthening centres active in this area, such as the ICGEB, was emphasized by the participants as well as the need for the application of these novel technologies in such a manner as to promote environmentally sound industrial development, bearing in view balanced safety issues.

Presentations of case studies from different developing countries and the group discussions that followed revealed opportunities, constraints and ways for the promotion of commercializing biotechnology products.

The EGM resulted in wide-ranging recommendations that touched upon several issues including human resources; collaboration between North-South and South-South; appropriate financing mechanisms; optimal science, technology, industrial and regulatory policies; socio-cultural factors; information access; and the role of international organizations in the promotion of biotechnology for development. Among the recommendations to UNIDO were that the Organization may promote the concept of development parks to disseminate the potentials of biotechnology for industrial development; consider financing biotechnology projects in developing countries through Trust Fund schemes; and take a more active role in international cooperation for the harmonization of biosafety guidelines for biotechnology applications.

The proceedings of the meeting are expected to be published in due course.

United Nations and other organizations' news

Tough agenda for FAO Commission

The fourth session of the UN Food and Agriculture Organization (FAO) Commission on Plant Genetic Resources in Rome, Italy, 15-19 April, had an important and tough agenda. One significant agenda item was a Draft International Code of Conduct for Plant Germplasm Collecting and Transfer intended to help scientific institutes engaged in international collecting expeditions to observe a voluntary etiquette in dealing with farmers and governments. It also covers conservation and use of plant genetic resources (PGR). Voluntary though it may be, the Draft Code is absolutely thorough and demanding. Reviewed and accepted by a number of experienced practitioners it nevertheless caused considerable debate in Rome.

A second tough agenda item was a discussion paper outlining elements for a Code of Conduct for Biotechnology "as it affects conservation and use of plant genetic resources". Not a formal code, the paper still outlined a number of policy concerns related to the advance of new biotechnologies, their possible impact on PGR and their legal implications. It includes intellectual property rights versus farmers' rights; forms of compensation for communities and countries who lose markets due to biotechnology; methods for the transfer of appropriate technologies to third world countries ensuring their full participation in new opportunities; and biosafety legislation.

An additional controversial agenda item provided the discussion paper on Biodiversity and Plant Genetic Resources, which included a proposal to widen the scope of the Commission on Plant Genetic Resources to include the whole of biodiversity. Based upon a request at the

Commission's third session, the paper gave consideration to alternative scenarios that could alter both itself and the International Undertaking for Plant Genetic Resources. The undertaking was created by a resolution of the FAO Conference in 1983 in order to specify voluntary guidelines for the conservation and exchange of PGR. The objective of the recent request to the Commission on Plant Genetic Resources was to keep the Commission in line with other developments on biodiversity surrounding the UN Conference on Environment and Development (UNCED) in Rio de Janeiro, Brazil, 1-12 June 1992.

The Keystone International Dialogue on Plant Genetic Resources had recommended that the Commission take on the whole issue of biodiversity. One option could be to create a Commission on Food and Agricultural Genetic Resources. As the Commission already brings crop and forest germplasm under one roof, it is reasoned it could not be much more difficult to regroup FAO's well-regarded expertise on livestock and fisheries under the same roof. Since its last session in 1989, Australia, Canada, Japan and the USA have all become members and seven States have dropped their reservations to some aspects of the international undertaking. In total 126 countries are now either members of the Commission and/or signatories to the undertaking and even the Soviet Union, which is not yet a member of FAO, attends the sessions as an observer. (Source: African Diversity, No. 5, April 1991)

Biodiversity action programme

Calling for a decade of urgent local, national and international action to maintain, understand and manage sustainably the world's biotic wealth the World Resources Institute (WRI) has joined forces with the International Union for the Conservation of Nature and Natural Resources (IUCN) and UNEP to develop a "Biodiversity Action Programme". Set to be published in early 1992 in time to influence UNCED developments in Brazil, the Programme will evolve through a series of regional consultations that will bring together scientists, policy-makers and NGOs to sort out elements of the campaign and to discuss regional considerations. (Source: African Diversity, No. 5, April 1991)

Biodiversity convention in a jam

International efforts to establish a global legal framework instrument on biological diversity are under heavy pressure from all sides. The original hope to get a biodiversity convention or treaty ratified during UNCED in Brazil, June 1992, has been severely shaken due to disagreements over at least two issues: (1) the access to the North's new biotechnologies as a quid pro quo for access to the third world's germplasm and (2) the recognition of intellectual property rights and the rights of indigenous peoples (farmers' rights). In addition the sheer technical and logistical difficulties of wrapping up as many as 40 separate international agreements on different aspects of biodiversity into one framework convention has hampered progress.

Consensus exists, though, on the need for the Convention on biodiversity to combine mechanisms to promote conservation and sustainable utilization of biodiversity, especially at the national level, and on the need for a firm commitment on financing. Although there is formal agreement that the Convention should include an innovative mechanism for access to resources and new technolgies based on mutual agreement and reflecting sovereign rights over natural resources, the disagreement as to the rules governing access is extreme. In contrast to the letter of the International Undertaking for Plant Genetic Resources in the discussion on a biodiversity convention many third world countries oppose the concept of biological resources as the common heritage of humankind. Rather they insist on their rights to exploit and benefit from the biological resources within their borders. Industrialized countries on the other hand refuse to make commitments on technology transfer. These discrepancies are compounded and complicated by the issue of intellectual property rights over forms of life. (Further information to be found in Briefing on Biodiversity by GRAIN, see under Bioinformatics.)

Several industrialized countries, led by the USA, are unhappy to find biotechnology on the agenda of biodiversity treaty negotiations at all. Some of them propose to incorporate biotechnology under the somewhat anonymous umbrella of "appropriate technologies". Industrialized countries are still less pleased to find third world countries arguing for rights for rural innovators who have nurtured and innovated genetic resources for thousands of years.

Charged with the task of putting such a framework legal instrument in place, the UN Environment Programme (UNEP), has been immersed in technical and political uncertainties. The first negotiating session was aborted in December 1990. The first real inter-governmental examination of the issues was only held in Nairobi, Kenya, at the close of February 1991. A second negotiating round is scheduled for late June in Madrid, Spain. (Source: African Diversity, No. 5, April 1991)

UN conference backs sustainable farming

Radical changes in farming practices will be required to feed the world's growing population without destroying the environment, conferees at a United Nations conference held in the Netherlands decided in mid-April. The five-day conference organized by the UN Food and Agriculture Organization and attended by experts from 124 countries outlined a programme for sustainable agriculture in what is called the "Den Bosch Declaration". To promote sustainable agriculture and rural development, the conferees decided these changes are needed: rural people should be actively involved in the research and development of integrated farm management systems, rather than relying on "top-down" administrative mechanisms; more decision-making authority should reside at the local level; incentives to encourage the raising of crops and animals that can be produced sustainably should be provided; and training to minimize the use of chemical fertilizers and pesticides and to ensure the optimum use of on-farm inputs should be provided. (Reprinted with permission from Chemical and Engineering News, 29 April 1991, p. 12. Copyright (1991) American Chemical Society)

"Gene raiders" must pay for conservation

Biotechnology companies should pay a levy to help conserve the world's genetic resources. The global fund would be used to protect species diversity and safeguard key ecosystems. It would also finance a system of payments to countries or indigenous groups for the rights to use native species.

This radical proposal was fiercely debated in London, as negotiators prepared for talks on an international convention on biodiversity in Spain. A global treaty should be ready for signing at the UN Conference on Environment and Development in Brazil next June.

Under a royalty system, the commercial beneficiaries of every gene taken from the wild and used in biotechnology would have to be traced before fees and charges could be assessed.

Speaking at the same meeting was Vincente Sanchez, the Chilean Government's representative to the UN Environment Programme (UNEP) and chairman for the international treaty negotiations. He said that many developing countries were ill prepared for the complexities of the discussions. He also confirmed that many were highly critical of the current plan to provide money to conserve biodiversity under the auspices of the Global Environment Facility, administered partly by the World Bank.

The two-day meeting highlighted other concerns about the adequacy of the proposed treaty. Some voiced doubts about how little attention is being paid to the diversity of marine organisms. A number of speakers doubted the effectiveness of a treaty when countries that have already agreed to the Food and Agriculture Organization's Tropical Forestry Action Plans have shown little commitment to preserving their forests. (Extracted from New Scientist, 22 June 1991)

Council for Responsible Genetics communique on biological weapons

The US Council for Responsible Genetics says it was overwhelmed by public requests for information on bioweapons during the Gulf crisis.

A communique from the Council argues that the only real defence against biological weapons is a strong world-wide commitment to uphold the ban on these weapons of mass destruction. Mideast Crisis Endangers Biological Weapons Ban also notes that the Biological Weapons Convention of 1972, signed by over 100 nations, represents such a ban. As the Gulf crisis loomed, however, the more nervous observers recalled that the majority of Middle Eastern nations have not signed the Convention - among them Egypt, Iraq, Syria, the United Arab Emirates and the Yemen Arab Republic. Furthermore, Israel has neither signed nor ratified the treaty.

Future Council communiques will cover such issues as bovine growth hormone, genetic discrimination and environmental releases of genetically engineered organisms. Details from: Council for Responsible Genetics, 19 Garden Street, Cambridge, MA 02138, USA or on +1 (617) 868-0870. Fax: +1 (617) 864-5164. (Source: Biotechnology Bulletin, Vol. 10, No. 3, April 1991)

Environment protection: global companies set new endeavour

Key international companies and industrial organizations met in Rotterdam to endorse a set of principles and a charter that will commit them to environmental protection into the twenty-first century.

One hundred and fifty companies, including some major US chemical concerns, and more than 35 organizations are set to adopt the Business Charter for Sustainable Development. Underpinning this document are 16 principles developed by the Paris-based International Chamber of Commerce (ICC). These 16 principles form the basis of the charter:

- Recognize environmental management as among the highest corporate priorities;
- Integrate environmental policies and practices fully as a key element of management;
- Continue to improve business' environmental performance;
- Educate and motivate employees to carry out their activities in an environmentally sound way;
- Assess environmental impacts before starting a new project or decommissioning an old facility;
- Develop and provide products and services that do not harm the environment;
- Advise customers on the safe use, transportation, storage, and disposal of products provided;
- Develop and operate facilities and undertake activities with energy efficiency, sustainable use of renewable resources, and waste generation in mind;
- Conduct or support research on the impacts and ways to minimize the impacts of raw materials, products or processes, emissions, and wastes;
- Modify the manufacture, marketing, or use of products and services so as to prevent serious or irreversible environmental damage;
- Encourage the adoption of these principles by contractors acting on behalf of a signatory company or organization;
- Develop and maintain emergency preparedness plans in conjunction with emergency services and relevant State and local authorities;
- Contribute to the transfer of environmentally sound technology and management methods;
- Contribute to the development of public policy and government-business programmes to enhance environmental awareness and protection;

- Foster openness and dialogue with employees and the public regarding potential hazards and impacts of operations, including those of global or transboundary significance;

- Measure environmental performance through regular environmental audits and relay appropriate information to the board of directors, shareholders, employees, authorities, and the public.

According to ICC, the principles are designed to place environmental management high on corporate agendas and to encourage policies and practices for carying out operations in environmentally sound ways.

The charter and principles are being formally launched at the Second World Industry Conference on Environmental Management.

The charter and principles are expected to spawn an array of policies and programmes that eventually will form the basis for international business input to the United Nations Conference on Environment and Development in Brazil in June 1992. (Abstracted with permission from Chemical and Engineering News, 8 April 1991, p. 4, by Lois Ember. Copyright (1991) American Chemical Society)

Regulatory issues

Watery microbes fuel fresh fears over genetic release

Fresh doubts have been cast on the safety of releasing genetically engineered organisms into the environment, following the discovery by biologists in the US that microbes living in lakes, rivers and seas are capable of swapping much more genetic material than expected. The fear is that the DNA introduced into a microbe could migrate into other populations of micro-organisms.

The new findings complicate current efforts to frame legislation governing the release of genetically manipulated organisms (GMOs). A working group of the UN Conference on Environment and Development has worked out draft international guidelines on the assessment and management of risky procedures in biotechnology. If the draft is approved by the UN secretariat in August, it will go forward for ratification to a major international conference on the environment in Rio de Janeiro, Brazil, next year. It may then form the blueprint for national laws governing releases of GMOs into the environment.

Against this political backdrop, Tyler Kokjohn, of the Environmental Research Division at the Argonne National Laboratory in Illinois, and colleagues in other laboratories found that even when bacteria are at extremely low concentrations, as they would typically be in water, they are still attacked by viruses called bacteriophages. Earlier studies suggested that below a certain threshold, the bacteria are too far apart for the viruses to make the journey from one host to another.

This is a crucial finding because as bacteriophages reproduce inside the bacterial cells they can introduce DNA from previous hosts into their new host. The DNA might be in the form of a plasmid, or other stretches of genetic material. When the phages spread to new hosts, they take fragments of genetic material with them which may be incorporated into the genome of the host bacterium. (Extracted from New Scientist, 29 June 1991)

General

Plant breeders plan strategy for resilient crops

Preserving the genetic diversity of crop plants for posterity will cost hundreds of millions of dollars. But without that diversity, plant breeders will run out of the raw materials for developing new and better types of crops able to cope with a growing population and changing climate.

The Keystone Dialogue, a gathering of scientists, industrialists and campaigners, publishes its recommendations for maintaining the genetic diversity of the world's crop species. The group estimates that a global system of conservation will cost around $300 million a year. Its recommendations are intended to form the core of a convention on conserving crop diversity.

Crop species exist in numerous varieties, adapted to grow in different conditions. Faced with increasingly intractable pests and plant diseases, and the likelihood of changing climate caused by global warming, plant breeders and farmers will need to exploit the genes from as many species as possible.

But the range of crop varieties is shrinking as farmers abandon traditional strains for uniform, high-yielding varieties, and the natural habitats of wild varieties are destroyed. Experts at the UN Food and Agriculture Organization estimate that as many as 75 per cent of the varieties of some major crop species may already be extinct.

It has also become clear that the world's seed banks, where samples of seeds are kept in cold storage, simply cannot cope. The Keystone report says the existing system "remains largely inadequate ... due to a serious lack of funds and the need for improved institutional structures".

The countries of the world have so far failed to agree on a way to halt the loss of genes. Poor tropical nations, which are home to most of the varieties, want recompense for their contributions, while rich countries have been reluctant to pay.

The Keystone Dialogue was set up in 1988 to provide a private forum for antagonists in the debate to try to reach agreement. The group included representatives from seed companies, activists who say seed companies are part of the problem, and scientists from both rich and poor countries and from international agricultural institutes. It held its final meeting in Oslo in June.

Pat Mooney, a Canadian activist in the group, says the closed discussions allowed opposing factions to reach consensus in areas where none had been possible before. In particular, all

eventually agreed that much more money would have to be spent, especially for work in developing countries and on their behalf. Keystone also approved the idea that farmers should be paid to keep growing traditional varieties instead of switching to higher-yielding ones.

The group recommends that $303 million should eventually be spent each year in addition to existing programmes. The plan is to spend $50 per year for each of the four million samples preserved in seed banks, to ensure that they stay viable; $20 million a year to conserve crops in the field which cannot be stored in seed banks; $20 million to conserve crops on the farm, to provide a hedge against losses in seed banks; $67 million for international coordination, public education and training; and $50 million for research, especially for characterizing plant varieties and improving conservation in the field. This is some four times what is spent now to conserve crops. But the report points out that the cost is just 0.6 per cent of the total annual market value of seeds, and only 0.002 per cent of the annual value of agricultural production.

The Keystone group suggests that all countries should contribute to a trust fund that would be managed by the World Bank. It recommends that an intergovernmental council should decide on work programmes and budgets; an executive board supported by a committee of independent scientists would implement the programmes.

Jaap Hardon, head of the Dutch seed bank, and a member of the Keystone group, says the recommendations will be passed to the organizers of the UN conference in Rio de Janeiro next year, as a proposed part of a convention on biodiversity.

The biodiversity convention was discussed in Madrid at a meeting organized by the UN Environment Programme. The Keystone plan, which has already been approved by most of the players in the crops debate, could form a quick, effective international agreement, Hardon says. (Source: New Scientist, 6 July 1991)

Tropical Forest Medical Resources and the Conservation of Biodiversity - 24-25 January 1992

The Periwinkle Project of the Rainforest Alliance, in conjunction with the New York Botanical Garden's Institute for Economic Botany, is organizing a two-day symposium at the Rockefeller University for approximately 400 health professionals, scientists and conservationists. The symposium, scheduled for January 1992, is designed to carefully examine the role of medicinal plant research in the conservation of tropical forests.

The symposium will bring together people from the diverse professions affected by medicinal plant research, including pharmacologists, ethnobotanists, conservationists, medical doctors, research scientists and others. It will provide an opportunity for those involved in the many stages of natural products drug development to interact and explore the issues and opportunities raised by their research. The sessions will be geared primarily to the scientific and conservation communities, but will not be limited to one field or area of expertise.

Symposium sessions will offer lectures on ethnopharmacology, natural products research and the economic and conservation potential of the utilization of tropical medicinal plants. For further information contact Rainforest Alliance, 270 Lafayette Street, Suite 512, New York, NY 10012. Tel. (212) 941-1900. Fax (212) 941-4986.

Standards for biotechnology

The Comité Européen de Normalisation (CEN), involved in the development of European-wide standards for EC and EFTA countries, decided to initiate a new Technical Committee on Biotechnology (TC233). Sub-groups were set up to assess requirements in the areas of the biotechnology research laboratory, industrial production, agricultural and environmental applications, and equipment. Details from Chairman B. Ager, CEFIC, tel. (00322) 640-2095, or Secretary A. Cayla, AFNOR, tel. (00331) 4511-3740. (Source: Biotechnica Journal '91)

Participants needed to help develop standards for polymerase chain reaction (PCR) and human immunodeficiency virus (HIV)

A new standards development activity on characterization and identification of viruses has been developed by E48.02 on Characterization and Identification of Biological Systems, a sub-committee of ASTM standards-writing Committee E-48 on Biotechnology.

The group plans to develop a general standard for the detection of micro-organisms by polymerase chain reaction (PCR) and a specific standard for detection of the human immunodeficiency virus (HIV) by PCR. These standards will be beneficial to biotechnology laboratories initiating PCR work and will aid in the comparison of PCR results from laboratory to laboratory.

Interested persons concerned with PCR and the HIV virus are encouraged to participate in the development of these standards. The next meeting of Committee E-48 is 29-30 October 1991 at the Holiday Inn Crown Plaza, Rockville, Maryland. For more information contact Larry E. Bockstahler, Food and Drug Administration, HFZ-113, Rockville, MD 20857, (301) 443-7287 or John Vowell, ASTM, 1916 Race St., Philadelphia, PA 19103, (215) 299-5496. (Source: ASTM News Release, 13 June 1991)

First International Symposium on the Biology of Adventitious Root Formation

The First International Symposium on the Biology of Adventitious Root Formation will be held at the Texas A&M University Research and Extension Center in Dallas, 19-22 April 1993. The symposium will be composed of several sessions dealing with various aspects of the biology of adventitious root formation and development in conventional cuttings, tissue cultures, or whole plants. Each oral session will be composed of related presentations from invited speakers. Planned oral session themes include: predisposition to rooting (stock plant characteristics), root primordium initiation, root primordium development, root system establishment and development. Possible levels of discussion include molecular, cellular, biochemical,

physiological, and whole plant. Each invited presentation will be published as a full-length paper in the proceedings of the symposium. Contributed papers will be presented in poster sessions and published as abstracts. For more information on the symposium contact: Edith Franson, Executive Secretary - Rooting Symposium, USDA Forestry Sciences Laboratory, Box 898, Rhinelander, WI 54501 USA. Tel. (715) 362-1112; Fax: (715) 362-7816. Executive Committee: Bruce E. Haissig (USDA Forest Service, Rhinelander), Tim D. Davis (Texas A&M University, Dallas), R. Daniel Lineberger (Texas A&M University, College Station), Stanley L. Krugman (USDA Forest Service, Washington, D.C.), Narendra Sankhla (University of Jodhpur, India).

European Biotech Partnering Event, 1991 The Netherlands

The NIAB, a foundation of the Netherlands Industrial and Agricultural Biotechnology Association (NIABA), supported by the European Community (EC) and the Dutch Government, has announced the first European Biotech Partnering Event (EBPE), to be held in The Hague from 16 to 18 October 1991.

This exclusive event will give the directors of biotechnology companies an opportunity to establish contacts with high-level management of large internationally operating companies active or interested in the application of biotechnology in Europe, the US and Japan.

In parallel sessions, the EBPE will bring together companies in the following sectors: agro-plant breeding - food; health care, human and animal; environment.

In each sector carefully screened and promising small European biotech companies will give short presentations on advanced technologies and/or specific products. The selection of presenting companies will be based on the relevance of the issue being presented to potential partners.

Partnering: participating companies will be asked to indicate potential partner companies with whom they wish to meet, after receiving the book of strategic profiles of all participants. Bilateral contacts will be planned before the start of the EBPE. Additional arrangements can be made during the course of the meeting through the EBPE officials at the EBPE desk, or through own initiative. For more information, please contact the Secretariat of EBPE Organizing Committee, c/o Moret, Ernst & Young, Wassenaarseweg 80, 2596 CZ 's-Gravenhage, the Netherlands. Tel.: +31-(0)70-328-6666; Fax: +31-(0)70-324-2075.

US-EC cooperation in biotechnology

EC Vice-President Pandolfi and Dr. Bromley, Assistant to the US President for Science and Technology, recently signed an agreement setting up a "Task Force on Biotechnology Research" as a mechanism of exchange. It will review R&D programmes, facilitate communication and collaboration in biotechnology research, and define research needs. It will report to the US Biotechnology Science Coordinating Committee (BSCC) and to the EC Biotechnology Research Development and Demonstration Committee (BRDDC). (Source: Biotechnica Journal'91)

Agriculture: Latin America weighs pros and cons of biotechnology

Latin American nations are debating whether to spend more money on biotechnology research to enhance agriculture or boost harvests by more traditional means.

Biotechnology has improved production in many Latin American countries, but some experts doubt if it would be the answer to the urgent food needs of Latin America and fear it may make the region more dependent on high technology from the industrialized world.

There are also doubts about its possible effect on Latin America's entry into the international market, if the region tries to open its economy to the world.

"In vitro" fertilization of plants in test tubes could be done just as well in a laboratory in the fertile lands of the Peruvian mountains as on the twentieth floor of a skyscraper in New York.

This could mean losing the main advantage of Latin American farm products: the richness of its soils, according to Peruvian expert Jurgen Schuldt during a recent seminar in San Jose (Costa Rica) on economic options.

Despite certain doubts, this technique is used in many laboratories in Latin America. Costa Rica has at least 15 biotechnology laboratories, a few commercial ones and others connected with the Government or international organizations.

Central American countries have also sought the help of the international community in creating a biotechnology network to improve the production of farm exports.

This project is included in the special cooperation plan for Central America (PEC), formulated by Governments in the area to channel international support for peace and economic integration efforts of the region.

Although biotechnology helps improve farm production and protect plants from diseases, agronomist Roberto Valverde said Costa Rica could run up huge debts to cover the cost of putting up laboratories. Valverde heads a project on plant tissue cultivation at the Centre for Agricultural Research of the University of Costa Rica. The centre has increased the number of choice plant varieties such as pejivalle and dioscoreas, and develops species of onaceas that are free from viruses.

The pejivalle palm is grown from Honduras to the north of Brazil and Peru, and is known as pixibae in Panama, chontadura in Colombia, pijuayo in Peru and pupuntra in Brazil.

The plant offers great trade possibilities - the fruit is edible and is used to make flour, the

palm heart is very much in demand in the world market, and its trunk can be used as wood.

Although tissue reproduction is considered advantageous, Valverde said the proliferation of laboratories in Costa Rica prevents the country from concentrating its efforts and resources, thus hampering the development of the new technique. (Source: IPS, 2 May 1991)

AIDS threatens Asia

New data reported by experts at the seventh International AIDS Conference in Florence indicated that developing countries are now facing an even worse AIDS emergency than previously believed.

The latest epidemiological studies performed by the World Health Organization (WHO) show that even though the incidence of AIDS is still low and is just beginning to be reported in many developing countries such as India, the disease is beginning to spread at an alarming speed. Although earlier data had shown Africa to be seriously endangered by the spread of HIV, the virus that causes AIDS, the new data reveal an alarming rate of increase in both Asia and Latin America as well.

By the year 2000, more than 90 per cent of HIV infections in the world will probably be found in the developing world, reports James Chin, a WHO epidemiologist in Geneva. At the same time, the number of new infections in industrialized countries will begin to level off or even to decline because of changes in behaviour.

The new data show that HIV has spread in India far beyond its initial entry points of the port cities of Madras and Bombay and is beginning to threaten rural populations, which are virtually defenceless against the virus because of a lack of information and condoms. One Indian official, Vulimiri Ramalingaswami of the All India Institute of Medical Sciences in New Delhi, said that India is "sitting on top of a volcano".

In Thailand, HIV has begun to race through the population with a remarkable speed. The prime minister of Thailand recently told WHO that the estimated number of people infected with HIV increased from 200,000 to 400,000 in just the six months between June and December 1990. The prevalence of HIV among male military recruits had jumped from 2 per cent to 6 per cent during the same period.

Accordingly, WHO raised its estimate for the present number of HIV infections in South Asia from 500,000 to 1,000,000, Chin said. While he stressed a basic uncertainty about the figures (which other epidemiologists said could be off by as much as 95 per cent), he also said that it is more likely that the WHO estimates will be revised upward rather than downward as more data become available.

At the same time, there is little money available in many developing countries to combat AIDS. In Uganda, for example, President Yoweri Kaguta Museveni said that per capita health spending amounts to just $3.50 a year - not nearly enough to treat people with AIDS, let alone try to prevent infection.

By the year 2000, about 90 per cent of the transmissions of the virus are expected to occur through heterosexual intercourse, despite the fact that this is one of the least efficient methods of transmission. Therefore, William Haseltine of Harvard University said it is time that AIDS, originally thought of as primarily a homosexual disease, should be recognized as being a "lethal venereal disease" that can be transmitted from fully healthy men to fully healthy women through mucous membranes. (Source: Nature, Vol. 351, 27 June 1991)

Human genome project

The Human Genome Organization (HUGO) is negotiating to affiliate its American office in Bethesda, Maryland with Johns Hopkins University in Baltimore. Such a move would allow the office to receive grants from federal agencies, ending its reliance on charitable funding.

HUGO's Bethesda office is now funded through a four-year, $1-million grant from the Howard Hughes Medical Institute. But if HUGO is to fulfil its intended role of coordinating the international effort to map and sequence the human genome, some support from governments is essential.

Any large university could serve as an umbrella organization for the HUGO office, but Johns Hopkins is particularly appropriate. Apart from its proximity to Bethesda, Hopkins also houses the Genome Database, the main repository for human gene mapping data.

Since HUGO was conceived in 1988 as an organization of genome researchers to provide "bottom-up" coordination between the various national genome initiatives, one goal has been to win government funding. But HUGO's regional offices have so far had to depend on charitable support.

The European office in London has got off the ground with help from the Wellcome Trust and the Imperial Cancer Research Fund, and there are hopes that European governments will also provide money. The Pacific office in Osaka has been paralyzed by a lack of funds. No government agency has shown any interest in providing money for HUGO and the Japanese office is finding it difficult to raise money from private sources because of government red tape that inhibits the establishment of tax-free foundations.

Ironically, HUGO's newest venture - a local office in Moscow that opened this week - is the first to get official government backing, with the Soviet authorities pledging financial support. (Source: Nature, Vol. 352, 4 July 1991)

Combio Group pools bio-talents for 1992

1992 is already spurring a restructuring of some parts of Europe's biotechnology industry. In the build-up to the Single European Market, five independent biotechnology companies recently set up a cooperative structure that does not affect their individual ownership or shareholdings, but instead aims to find ways in which they can work together across Europe.

The five - Biotech Instruments in the UK, Dalton of the Netherlands, Cytolab in France,

Dunn Labortechnik from Germany and Swiss Bio Cell Consulting - continue to trade as independent entities, but now call themselves the Combio Group. Apart from sharing know-how, they are also offering each other first option on new developments. (Source: Biotechnology Bulletin, Vol. 10, No. 5, April 1991)

International Bioindustry Forum founded

The International Bioindustry Forum (IBF), an organization conceived by the Japan Bioindustry Association (JBA), was inaugurated officially in July. Participants in IBF will consist of JBA, as well as US, Canadian and European bioindustry associations. Australian, New Zealand and Eastern European biotechnology associations are also expected to join in the near future. Details of management and organization will be decided at its first meeting in London. IBF will address global issues, including regulations and intellectual property rights.

JBA also announced that it will support the Industrial Science and Technology arm of the Organization for Economic Cooperation and Development in biotechnology in Europe. JBA will supply ¥ 72 million over two years and send a Japanese expert from Sumitomo Chemical Co. Ltd., Osaka, to act as a specialized OECD staff member. (Source: McGraw-Hill's Biotechnology Newswatch, 17 June 1991)

People's poll shows confusion over biotechnology

Just what do people think about biotechnology? The European Commission has asked 12,800 people across Europe how they feel about it. Those who said they knew most about biotechnology also said they thought it was risky. All of those surveyed said they had far more confidence in what environmental and consumers' groups had to say about biotechnology than in what they were told by governments or industry.

Thirteen questions on biotechnology were included in the first of the twice-yearly Eurobarometer surveys. The survey results will be published later.

Only half of the people questioned thought biotechnology would improve life. Solar energy, computers, telecommunications and new materials all scored higher; only space exploration scored lower. A tenth of all respondents, and 20 per cent in Holland and Denmark, thought biotechnology would make things worse.

The Germans, Danes and Dutch scored themselves highest in their understanding of biotechnology. They also perceived the most risk. Britain was the exception: it scored fourth highest in understanding biotechnology, and third lowest in perceiving risks, just above Spain and Portugal.

Not everyone was sure what biotechnology was, however. A sample of people who were asked about "genetic engineering" perceived greater risks and fewer benefits than those asked about "biotechnology". (Extracted from New Scientist, 13 July 1991)

B. COUNTRY NEWS

Australia

ANUTECH moves into syndicated R&D

ANUTECH Pty Ltd., the marketing arm of the Australian National University (ANU), has won two syndicated research and development contracts to fund research on a portfolio of seven projects in the biotechnology area. Under these contracts, a syndicate of investors will fund a scheme, which incorporates research funding of projects that have a high probability of generating commercially viable products.

The scheme has a contract value of $60 million, with a research component of $17 million over three years. The framework for such a scheme was offered by the federal Government under its taxation concession legislation, as an attractive incentive to business investment in R&D. ANUTECH has spent several months on negotiations involving the Tax Department and Department of Industry, Technology and Commerce.

All seven projects are being conducted at the ANU, three at the John Curtin School of Medical Research (JCSMR), two in the Research School of Biological Sciences, one in the Faculties and one a cooperative project between the Faculties and JCSMR. The seven projects are:

- Bioactive natural products. The research carried out in this project aims to build on the basic knowledge of host parasite interrelationships in livestock to identify vulnerable points in parasites. The projected outcome of the research is the development of a new veterinary product in the form of a drench for use in eradicating parasites in sheep, cattle, goats and horses.

- Kit for dieback diagnosis. Dieback of native Australian plants due to the fungus Phytophthora cinnamomi has caused extensive losses both to eucalyptus forests and commercial crops. Efforts to control the spread of dieback fungus have been hampered by the difficulty of diagnosing the disease and screening soils in areas before planting susceptible crops. This project aims to develop a quick and easy field diagnostic kit to detect and identify the dieback fungus.

- Resistance genes in plants. Research carried out in this project aims to clone and characterize resistance genes in agricultural plants. The research uses a fungal toxin as a "fishing hook" to extract the gene of interest. If successful, the project will have significant commercial applications in developing crops resistant to disease.

- Anti-tumour agents. Certain sulphated polysaccharides have been shown to have anti-cancer properties. These compounds, which are long-chain relatives of ordinary sugar, are non-toxic and highly specific, and appear to inhibit tumour growth by

inhibiting the development of new blood vessels. They have also shown an ability to prevent cancer cells moving out of the bloodstream through blood vessel walls to colonize other organs. The project aims to identify the most potent of these sulphated polysaccharides for use as anti-cancer drugs.

- Graft pretreatment against rejection. This project investigates the use of a fungal toxin, gliotoxin, in pretreatment of tissue before transplantation to inhibit rejection of the tissue. It has been demonstrated that treating bone marrow cells with gliotoxin allows for successful transplants without the use of immunosuppressive drugs. The aim of the project is to extend the studies from the mouse model to human cells; to synthesize and identify the effective "gliotoxin-like" molecules; and to extend their use for the treatment of larger organs.

- Sheep vaccine. In this project a research team will investigate the use of glutathione transferases from the parasite Fasciola hepatica as a vaccinating antigen against the parasite in sheep. This parasite, which is becoming increasingly resistant to current drug treatments, is conservatively estimated to cost Australian primary producers $20-30 million annually. The project aims to develop an effective vaccine for sheep and to extend the studies to cattle, as calves are especially vulnerable to fascioliasis.

- Assessment of coronary heart disease risk. At present the main methods of profiling coronary heart disease risk are the measurement of the concentration of total cholesterol, low density lipoprotein (LDL) cholesterol and high density lipoprotein (HDL) cholesterol in the blood. However, since coronary atherosclerosis frequently occurs in individuals with normal cholesterol concentrations, a more specific screen is desirable. Research has identified the formation of atherosclerotic plaques. This project aims at providing a number of tests to identify those at risk of coronary heart disease by measuring the levels of oxidized LDL and oxidized HDL and developing an imaging technique for localizing atherosclerotic plaques.

Further information can be obtained from ANUTECH. (Contact: Julie Burke (Tel.: 06(249 5864)). (Source: ABA Bulletin, Vol. 6, No. 3, June 1991)

Brazil

Reaforestation

Brazil's Klabin is stepping up its research work on the genetic improvement of its forests, especially of pine trees. Its research laboratory, located at Monte Alegre, Parana, is focusing on reaforestation through cloning, with minute fragments of the best pine trees to obtain top quality seedlings. Research is being supported by the University of North Carolina. (Source: Genetic Engineering News, May 1991)

European Community

EUREKA and biotechnology: national project coordinators and EC liaison

The EUREKA project portfolio on medical and biotechnology projects was updated in April 1991 by Olaf Meyer, head of the EUREKA Brussels-based secretariat. This was one of several informative documents tabled at the meeting in Amsterdam on 9-10 April of the National Project Coordinators (NPCs), who were holding one of their "X-ray sessions", studying in depth the sector "Medical and Biotechnology".

The 64 projects, 17 per cent of the total, form less than 7 per cent by value, because their average value is only 8 million ECU as against 20 million ECU for EUREKA in general. Two hundred and thirty-two organizations are involved, 143 of them industrial, including 48 SMEs, 53 research institutions, 33 universities and 3 government bodies.

The first impact of biotechnology has been in the area of human health. The EUREKA project portfolio reflects this reality. Of the total of 64 projects in this area, 29 are directly linked to medical or pharmaceutical technology.

There is, however, a great deal more to biotechnology than the health-care sector. As a set of technologies it also offers benefits to a number of other industrial sectors and areas of research which are also reflected in the EUREKA project portfolio: agrobiotechnology and genetic engineering of plants (14 projects), biotechnological production processes (14 projects) and animal breeding (7 projects).

Seven projects can also be classified as "bio-informatics" projects, a very important field of research for the future.

For details of EUREKA activities, interested companies (or other organizations) should in the first instance contact the National Project Coordinator in their country; if you do not know who is your NPC, contact O. Meyer, Director of the EUREKA central secretariat in Brussels (Tel.: (32) 2 217 00 30, Fax: (32) 2 218 79 06, address: Avenue des Arts, 19H, Box 3, 1040 Brussels).

The meeting of NCPs emphasized the need for greater EC liaison, and the importance for industrial projects in biotechnology of "supportive measures", such as the general legal framework, and specific aspects such as intellectual property law. It is the intention of Commission staff in programmes such as VALUE and VENTURE CONSORT to collaborate with EUREKA, and the Commission has appointed a "EUREKA Coordinator", Mr. N.K. Newman (Tel.: (32) 2 235 59 76), Fax: (32) 2 236 33 08), who covers all EUREKA technological domains apart from telecommunications and information technology, which are covered by Mr. G.C. Grata. (Source: EBIS, No. 3, May 1991)

BRIDGE programme: the "Immunoclone Database" project

The medical, industrial and other applications of monoclonal antibodies ("mabs") are amongst the largest current and future

applications of modern biotechnology. Kohler and Milstein received the Nobel Prize for demonstrating how the pure mabs could be produced by "hybridomas", cells created by fusion of lymphocytes (producing antibodies) and tumour cells ("immortal" in culture).

The Commission has co-financed the launching of an international "Hybridoma Data Bank" by supporting from 1987 to 1989 its European node, from which developed CERDIC. More general than "hybridoma", the term "IMMUNOCLONE" is defined as any permanent cell line (obtained by hybridization, virus transfection, DNA transfer, etc.) producing (secretion, cell surface expression, etc.) homogeneous substances of immunological interest (monoclonal antibodies, T-cell receptors, interleukins, macrophage factors, etc.).

The new "ICDB" project launched under the BRIDGE programme coordinates the activities of seven leading European centres and aims at building up the complete database of all immunoclones and their related products.

It is expected that 2,000 new records per month will be collected, via:

- Computerized screening of the scientific literature (covering more than 1,500 journals);
- Patent applications at the European Patent Office;
- Industrial and commercial catalogues of biotechnology firms;
- Descriptions sent by public or private research laboratories. The procedures used will allow most sources to be included within three months of publication date. More than 25,000 descriptions are currently included.

The network of laboratories will enable rapid utilization of European immunoclone resources, which will serve as a model for the management of similar products in the face of strong international competition.

Details: CERDIC (Centre Européen de Recherches Documentaires sur les Immunoclones) Centre International de Communication Avancée, 2229 route des Crêtes, Sophia-Antipolis, F-06560 Valbonne, France. Tel.: (33) 9294 22 88, Fax: (33) 9365 30 58. (Source: EBIS, No. 3, May 1991)

BRIDGE programme - progress with biosafety proposals

The final call for proposals within the BRIDGE programme (deadline September 1990) attracted 41 transnational proposals, for projects on biosafety involving 185 research laboratories.

The proposals were evaluated independently by scientific experts and selected on the basis of their relevance to the specific areas of the programme as laid down in the Council decision and information package of 1990.

Based on the above procedure and with the advice of representatives of the Member States, 16 projects have been proposed for financing, involving 78 research groups, total value more than 8 million ECU.

The projects address issues of biosafety relating to the release of transgenic plants, genetically modified microbes and viruses, and the development of automated methods for microbial identification. The last of these is the object of a large, so-called "targetted" T-project, involving 16 laboratories (10 on cost-sharing contracts, 6 under "concerted action").

Details of these projects will be disclosed after the signature of the contracts with the Commission. Details: I. Economidis. Fax: (32) 2 235 63 65. (Source: EBIS, No. 3, May 1991)

SAGB calls for clarity in Community biotechnology policy

"Promoting the competitive environment for the industrial activities based on biotechnology within the Community".

The Senior Advisory Group on Biotechnology (SAGB) recently reaffirmed its support for efforts to create a coherent European Community policy for Biotechnology and called for greater clarity following the European Commission's Communication to Council (adopted 17 April).

Biotechnologies promise new opportunity for economic growth, new job creation, industrial renewal, environmental management and revitalized strength in the agricultural marketplace. Future European competitiveness on a par with the US and Japan in the many industries, which will depend on biotechnology, must therefore become the principle objective of Community policy.

The Commission's Communication is an important first step towards a coherent Community policy. In particular the SAGB welcomes the Commission's commitment to:

- The assessment of biotechnology products based on scientific criteria and the assurance that it is not the intention to add a further regulatory assessment procedure;
- A coherent regulatory approach;
- The setting up of an advisory structure on ethical issues at Community level.

The SAGB emphasizes, however, that much work remains to be done to clarify the Commission's thinking on specific policy issues - notably the future European regulatory framework and economic and social policy responses.

An effective regulatory framework must be adaptable, non-discriminatory and avoid unnecessary duplication and overlap. It is unclear how the Commission's ideas will satisfy these objectives. Where social and economic policy responses are concerned, the Community faces clear political choices. The Community has

proven policies for positive social and economic adjustment to new technologies, and must avoid political controls on technology itself. The SAGB applauds the Commission's call for open procedures and consultative mechanisms for resolving ethical concerns as they arise.

In summary, the SAGB believes that the Commission's Communication provides a good opportunity for bringing clarity and coherence to Community policy for biotechnology, which will in future create the necessary conditions for social, economic and industrial strength. (Source: ABA Bulletin, Vol. 6, No. 3, June 1991)

Programme on agro-industrial materials

The EC Commission has prepared a regulation to start an agro-industrial demonstration programme in the non-food sector. A total of ECU 226.5 million for the period 1991-1994 (about ECU 45/year) is planned for demonstration projects in agriculture to produce raw materials for industry. The programme should assist the restructuring of agriculture to reduce surplus production in the food sector. The regulation updates a previous regulation (797/85) adopted to improve efficiency of the agricultural structure. (Source: Biotechnica Journal '91)

Boost for EC industry

The EC Commission has outlined a new strategy for biotechnology in a recent communication to the Council of Ministers.

The Commission notes the promise of biotechnology, for both the industrialized and developing nations. The sector is also gaining significant economic importance, and world-wide sales could climb to as much as ECU 41,000 million by the year 2000. By this date, EC biotechnology could provide 17 million jobs. But the European industry suffers from insufficient patent protection, a fragmented European market and a bad public image, the Commission says.

On one front, the Commission hopes to make the EC more attractive to foreign investors. The communication points out that in 1987 European firms invested nearly ECU 2,000 million in US biotechnology, while American firms reciprocated with a European investment of only ECU 12 million.

In order to boost the competitiveness of EC biotechnology, the Commission plans to improve patent protection, and streamline the regulatory process. However, industry is unhappy that the prospect of a "fourth hurdle", or the evaluation of a product's social, environmental and economic impact, remains. Finally, the Commission would like to set up a system of Community advisory groups to consider related ethical issues. (Source: Chemistry and Industry, 6 May 1991)

Europe battles over biotechnology

Tension is mounting between European biotechnology companies and the environmental authorities who must approve their work. The stresses were revealed when the European Commission presented a policy document to Community ministers that contradicts directives governing biotechnology that have already been adopted by the Community.

The paper states Commission policy on promoting the biotechnology industry in the Community. It was signed by the commissioners for industry, agriculture and research, but not by the environment commissioner. It was written largely by the staff of industry commissioner Martin Bangemann, say Brussels officials.

The document says products of genetic engineering should be regulated under existing laws, according to the sector in which the product is to be used, without extra environmental approvals designed to monitor genetically modified organisms (GMOs). This supports the view taken by CEFIC, the European chemicals industry federation. Brian Ager of CEFIC says a GMO released to control pests, for example, should be approved for sale under existing procedures for chemical pesticides.

The Community passed two directives last year, which must become law in member States by 1992, regulating the contained use and deliberate release of GMOs. They require installations using GMOs to produce an environmental impact statement before work begins and before GMOs are released into the environment. A majority of States can block the marketing of a GMO.

Ager calls it "crazy" to set up a separate system for authorizing products that discriminates on the basis of how they were produced. It is as yet unclear how the matter will be resolved. (Source: New Scientist, 4 May 1991)

EC sets up framework and ethics council for biotechnology

The European Commission has made further moves on clearing up the current legislatory confusion on biotechnology. It has adopted a communication designed to provide a precise regulatory framework to encourage competitive growth within the Community and outside investment.

The EC has also announced that it is to set up an ethical council to advise the Commission on the merits of genetic engineering projects. The EC communication comes weeks after it set up an inter-directorate Biotechnology Coordination Committee (ECN, 8 April).

The Commission highlights three problem areas:

- Higher R&D costs due to fragmentation of financial aid and regulatory procedures, for example, market authorizations for pharmaceuticals;
- Insufficient patent protection, which deters investors;
- Growing public antagonism towards genetic engineering.

CEFIC's Scientific Advisory Group on Biotechnology (SAGB) said it welcomed the Commission's commitment but that much work remains to be done. In a statement, the SAGB also drew attention to the social and economic considerations on the use of biotechnology. The Commission states in the communication that it has decided against this "fourth hurdle" system, but then goes on to say that the Commission will

normally act on scientific advice but reserves the right to make exceptions. The SAGB said it is looking for clarification of the added statements.

The SAGB said: "The Community has proven policies for positive social and economic adjustment to new technologies and must avoid political controls on technology itself". It welcomed the creation of an ethical committee.

The Commission calculates that the growth in sales of products derived from biotechnology (not including food and drinks) would increase from ECU 7.5 billion in 1985 to ECU 26-41 billion in the year 2000. But it said that while European companies often work with Japanese and US firms there is a reluctance for these countries to invest in Europe.

It emphasized that the main responsibility for growth lies with companies, but that it was crucial for public authorities to fix conditions for these activities that would be acceptable to the public and that would establish international policy strategies and enable the protection of intellectual rights.

In drawing up international policies, the Commission said it recognized that member States must be able to keep the freedom of laying down stricter standards as long as this does not hinder the free movement of biotechnological products. (Source: European Chemical News, 29 April 1991)

New EC policy group

The European Commission has created a high-level interservices group "to develop a well-balanced Community policy in biotechnology". It will extend to all Commission activities in biotechnology, which currently are distributed among at least a half-dozen Directorates General.

The new group will examine all new Commission initiatives in biotechnology, create a forum for the involvement of industry and other parties in Commission developments, and will evaluate existing EC policy.

The move has been welcomed by the European industrial lobby, SAGB. (Source: Bio/Technology, Vol. 9, May 1991)

Other Euro-regulatory news

The technical committee of European standardization organization, CEN (Paris), has formally agreed to develop norms in a number of biotechnology areas including the classification of micro-organisms, laboratory equipment, and large-scale practice and procedures. It is expected that financial support will be shortly forthcoming. (Source: Bio/Technology, Vol. 9, April 1991)

Positive EC verdict for BST

Monsanto is preparing to target the UK and France as early markets for its bovine somatotropin (BST) hormone, Somatech, following the positive conclusions of a three-and-a-half year investigation of the product by a Europe-wide committee of regulators.

BST is a genetically engineered hormone designed to boost milk yield in dairy cows. The product increases milk production efficiency in the range of 2.7 to 5.7 kg/day/cow.

The European Commission's Committee for Veterinary Medicinal Products (CVMP) concluded that Monsanto has demonstrated "its ability to produce a homogeneous stable product, with a shelf life of 18 months ... using a well-controlled biotechnological process".

It also found that the company had shown that residues of Somatech do not present any risk to the health of consumers of meat or milk obtained from treated animals.

The majority of the committee, which consists of 12 representatives from each State's regulatory authorities, also decided that administration of the hormone to dairy cattle does not pose undue risk to their health or welfare.

However, the Irish, Italian and UK delegations called for further studies of the incidence of mastitis in a large number of treated animals. The CVMP concluded that such information should be gathered under practical condition of use after authorization of BST. The delegations also expressed concern about hygiene at the tailhead site of injection at certain times of the year and the possibility the animals could suffer infection.

The committee recommended that "authorization to place Somatech on the market should be subject to a condition requiring the company to collect and evaluate all reported suspected adverse reactions to the product throughout the Community and to prepare an annual safety report for the five years following authorization".

If the EC gives marketing authorization, Monsanto can then apply to each member State for a marketing licence. In the meantime, the EC has placed a moratorium forbidding widespread use of BST in any member State until the end of this year, while the EC assesses the socio-economic impact of a number of biotechnology products, including BST.

Monsanto's BST product has been approved for use in the Soviet Union, Bulgaria, Czechoslovakia, Mexico, Brazil, South Africa and Namibia. In the US, the FDA is still reviewing a large amount of technical information on the product and is expected to reach a decision in the next few months. (Source: European Chemical News, 8 April 1991)

France

French food research programme

The French ministries for agriculture/forestry and research/technology have started a food research programme called AGROBIO which will extend activities run under two previous programmes. The new programme covers research upstream and downstream of agriculture: genetic improvement, environmental and economic issues, quality control and toxicology, biotechnology and food transformation, and nonfood uses for agricultural products. (Source: Biotechnica Journal '91)

French bioethics

The French Government is to put a bioethics bill before parliament in the first half of 1992. It will be based on a report published in June that recommends outlawing surrogate motherhood and trade in human organs.

The 400-page report by Noëlle Lenoir, who is a member of the French Council of State, also recommends restricting genetic fingerprinting to individual cases that have been ordered by magistrates at authorized centres. (Source: New Scientist, 22 June 1991)

Insect cell technology

The Institut National de la Recherche Scientifique and Institut National de la Recherche Agronomique have started an enterprise called Protéine Performance to promote proteins produced from modified insect cells.

The technology involves the use of insect virus cells in applications such as vaccines, antibodies, pharmaceutical blood proteins, cosmetics, fine chemicals and agro-chemical industries. The cells can synthesize human proteins with greater efficiency than bacteria, yeast or rodent cells.

Protéine Performance will have funds of FF 1.8 million provided by venture capital companies and will go through a probation period before launching on an industrial level. (Source: European Chemical News, 29 April 1991)

French training for Romanian laboratory

The French Institut Pasteur has renewed its relationship with Romania's Cantacuzene Institute after a 30-year break. The move means the Romanian organization will be given help in training researchers, acquiring international scientific literature and setting up laboratories.

Institut Pasteur has undertaken to train Romanian researchers in modern molecular biology and virology technologies and will provide the institute with scientific periodicals dating back a decade.

One specific project at the Cantacuzene Institute is the design of a high-security laboratory for research into the detection of the human immunodeficiency virus (HIV).

Extra financial help will also be given by the French Ministry of Research and Technology which will provide funds for Romanian researchers to visit the Institut Pasteur, for the Cantacuzene library to be reorganized and for the installation of the AIDS laboratory. (Source: European Chemical News, 29 April 1991)

Germany

"Biotechnologie 2000"

The Federal Ministry for Research and Technology has published the new national plan "Biotechnologie 2000" which outlines the governmental research policy objectives in biotechnology, the priorities for the promotion of research, and the instruments and infrastructure available. The financial envelope for governmental support of biotechnological R&D amounts to DM 1.7 billion for the six-year period 1989 to 1994. The Ministry's budget for 1991 earmarks DM 263 million for biotechnology. Copies available from: Dr. Warmuth,
Tel.: 0049.228.59-3145.
(Source: Biotech '91 Journal No. 2)

Research grants

Germany's Ministry for Research and Technology is to provide DM 100 million ($56 million) in grants over the next five years to biotechnology firms with less than DM 1 million turnover.

Companies not linked to larger industrial groups will be eligible for project funding up to 40 per cent of costs, to a maximum of DM 600,000. This ceiling can be raised to DM 1 million if two companies and at least one research institute are involved.

Research minister Heinz Riesenhuber says the Ministry is particularly interested in sponsoring several projects to develop equipment for biotechnological production; biotechnological environmental protection processes; enzymatic processes; biotechnological methods of plant culture, as well as use of agricultural raw materials for non-food production. Gene-splicing projects are also interesting to the Ministry, he added. (Source: European Chemical News, 24 June 1991)

German genome rules on cards

The German Government is planning to introduce a bill regulating the use of genome analysis in medical diagnostics.

Two recent studies conducted for the Ministry suggest that Europe will need to increase its efforts in genome research to close the gap between it and the US. The US currently spends some $150 million on genome research while Europe spends only $50 million.

German legislation will set down "clear regulations" for prenatal diagnostics as well as testing of potential employees for job suitability. (Source: European Chemical News, 15 April 1991)

Biotechnology and Law Centre seeks international collaborators

A research centre for biotechnology and law has been established at the Universities of Lüneburg and Hannover. The centre has a data bank covering German biotechnology laws (recommendations, decisions, comments, literature). They are now seeking partners in universities, firms or other organizations in the EC member States who would be interested in establishing an international data bank. The objective is to provide a Europe-wide on-line source of information for consultation, communication and research that might aid in standardizing the law throughout the member States.

Details: Prof. Dr. J. Simon,
Forschungszentrum Biotechnologie und Recht an den Universitäten Hannover und Lüneburg.

Hanomagstrasse 8, D-3000 Hannover 91. Tel.: (49)511 449 81 67; Fax: (49)511 83 03 37; ECHO EUROMAIL NOMOS R 457 22 19 32 02. (Source: EBIS, No. 4, July 1991)

Japan

Japanese Government genome projects: 1990/91

The Japanese Government is finally launching its programmes for the human genome project, with research to begin in 1991.

The Ministry of Education is requesting an FY 1991 budget of ¥720 million from its science research funds for its two human genome projects. It has also submitted a request to fund a human genome analysis centre to manage the massive data to be gathered by the projects. The centre would be built at the Tokyo University Medical Science Research Institute. The Ministry of Health and Welfare has also requested a budget of Y200-300 million for human genome analysis.

Each of these projects will study genes related to human diseases, including chronic diseases such as diabetes. Last June, the Ministry for International Trade and Industry organized a genome analysis group within its Industrial Technology Promotion Council. The group includes such corporations as Toyota affiliate Aishin Precision and Hitachi (Tokyo).

- The Ministry of Agriculture, Forestry, and Fisheries (MAFF) is strongly promoting its rice-genome project as a new project to be funded in FY 1991. It hopes to invest Y600 million in the first year, and Y30 billion overall during an ambitious seven-year plan.

- Some local Japanese government entities are responding to the genome challenge as well. Chiba Prefecture (just above Tokyo) is planning to open its Kazusa DNA Research Institute some time in 1993.

In addition, a Japanese office for the international human genome organization, HUGO, is being established and will open some time in late 1990 or early 1991. (Source: Bio/Technology, Vol. 9, May 1991)

Malaysia

Guinness not good for fruit-flies

After years of research, the Malaysian Agricultural Research and Development Institute, working with the Australian Centre for International Agricultural Research (ACIAR), has found a better way of controlling the fruit-fly. Rather than blanketing crops with chemical sprays, which are not terribly effective, they have developed a bait partly derived from beer by-products that attracts and poisons the pests.

The fruit-fly, a world-wide problem for farmers, lays its eggs on fruits like mangoes, peaches and apples as they begin to ripen. The larvae eat their way into the fruit, until they pupate and become fruitflies to continue the cycle. The damage they do to fruits invites diseases and fungi to take hold, making the fruits unmarketable.

The technique the researchers have used is to make a bait of hydrolyzed protein, which fruit-flies find particularly attractive and other insects do not. There is something about the odour of hydrolyzed protein that very strongly draws the fruit-flies, but not other insects, to it.

The hydrolyzed protein is a by-product of the Guinness beer brewery at Petaling Jaya, in Malaysia. Apparently, there is something special about the stout-brewing process that produces this very potent attractant.

The attractant is then mixed with a poison chemical to produce a bait. This is then spread around the orchard, in small dollops, on leaves. Putting the bait out in this way means beneficial insects like bees and natural enemies are not harmed by spraying. Fruit-flies are attracted to the bait and are killed on contact with it.

The bait spraying was tried initially in starfruit orchards in Malaysia, because starfruits are a very important crop, both for consumption in Malaysia and for export. The starfruit farmers found that they got many more starfruits when bait sprays were applied, as compared to cover spraying with insecticide of the whole orchard. The fruit-flies were very effectively controlled, but the other pests in the orchard seemed to be fewer as well, probably because the natural enemies were coming in and controlling them.

The farmers also found that better fruits were forming, because there was better pollination as bees were coming back into the orchard, whereas previously they had been killed by the cover sprays.

The Malaysian Agricultural Research and Development Institute has now prepared the bait commercially and is marketing it in Malaysia and in Thailand under the name of Proma. For more information regarding this project, contact Australian Centre for International Agricultural Research (ACIAR), GPO 1571, Canberra ACT 2601, Australia. (Source: Development Forum, July/August 1991)

The Netherlands

New third world agriculture effort

Companies and research institutions in industrialized countries plan to make available proprietary technology to research institutes in the developing world.

A new venture to promote the application of agricultural biotechnology in developing countries was announced at a recent conference on Biotechnology and Farmers' Rights held at the Free University of Amsterdam in April. Details of the project - the International Biotechnology Coordination Programme - were given by Jasper Veldhuyzen van Zanten of the Sandoz Seeds subsidiary, Zaadunie (Enkhuizen, the Netherlands). The programme is funded by the Hitachi Foundation (Tokyo) and the Resources Development Foundation (RDF, Washington, DC).

The institutes will apply the technology locally, avoiding crops and markets in which the companies have commerical interests. Non-governmental organizations, which often have important networks in developing countries, may also be involved.

The prime mover behind the programme is Clive James, a former deputy director-general of the

International Maize and Wheat Improvement Centre in Mexico. During the past year he has been canvassing support from international development agencies, companies and research institutions. James' "honest brokering" has drawn in organizations such as Monsanto, Plant Genetic Systems (PGS, Ghent, Belgium), Zaadunie, the John Innes Institute (Norwich, UK) and the Max-Planck Institute (Cologne, Germany). Monsanto's technology for coat protein-mediated resistance, for instance, is being applied in Mexico against virus X and Y disease in local potato varieties and against virus diseases of peppers. PGS is involved with a project sponsored in Thailand on bioinsecticides to combat malaria-transmitting mosquitoes. Other projects include diagnostics for bacterial diseases in cabbage (Taiwan) and virus resistance in tomatoes (Egypt).

One main criticism of the programme is that it does not address the problems of subsistence farmers. The countries targeted by RDF for support - Malaysia, Indonesia, Thailand, the Philippines, Brazil, Mexico, Costa Rica, Egypt, Zimbabwe and Kenya - are among the most developed. The farmers most likely to benefit will be cash croppers, a group for whom there is significant economic, infrastructural and political support.

But it was another, less privileged group, the resource-poor small-scale farmers of developing countries, that was the main focus of the Amsterdam conference. The Netherlands' Minister for Development Cooperation, J. Pronk, announced that his ministry would be using a new project assessment method, the "Interactive Bottom-up Approach" (IBUA) developed at the Free University of Amsterdam, in deciding how to allocate its development funds in biotechnology. In IBUA, technical and social scientists mobilize both high technology and the know-how of indigenous small-scale farmers. Importantly, IBUA considers the prevailing social, political and economic conditions of resource-poor farmers in implementing innovation. (Source: Bio/Technology, Vol. 9, June 1991)

Nordic countries

Nordic environmental biotechnology R&D

The Nordic countries have started a programme of R&D on biotechnology for detoxification and regeneration of waste water and industrial waste. The programme is supported by the Nordic Fund for Technology and Industrial Development at Oslo and covers four project areas:

- Detoxification of waste water from the pulp and paper industry;
- Degradation of priority pollutants in waste water and industrial waste;
- Biological removal of heavy metals from mine drainage, industrial waste water, waste and biological sludge;
- Anaerobic processes for treatment of solid waste.

A total of 18 industrial companies from the Nordic countries are participating in the programme. (Source: Biotechnica Journal '91)

Philippines

ICLARM

The International Center for Living Aquatic Resources Management (ICLARM) was established to conduct and stimulate research on all aspects of fisheries and other living aquatic resources. It is an autonomous, non-profit, international scientific and technical centre.

The origin of ICLARM was the Rockefeller Foundation's concern for the development of aquatic resources for food and income in tropical developing countries. The Foundation was the main force in establishing ICLARM in the Philippines in 1977. The research policy of ICLARM is to assist the development and sustainability of aquatic resources. It focuses on small-scale fishermen and traditional fish farmers. This is done through four basic programmes:

1. Aquaculture;
2. Coastal area management;
3. Capture fisheries management;
4. Information services.

The programmes are supported by a number of private foundations and by governments. Specific programme-related newsletters (Fishbyte and Aquabyte) supplement the general magazine Naga, the ICLARM quarterly. ICLARM currently employs about 60 scientific and support staff. Its 1989 budget totalled $US 3.8 million. For more information contact ICLARM, MC P.O. Box 1501, Makati, Metro Manila 1299, the Philippines. Tel.: (*63-2) 818-0466; Fax: (*63-2) 816-3183. (Source: Biotechnology and Development Monitor, No. 7, June 1991)

Seaweed processing in the Philippines

In the Philippines, the cultivation of seaweeds contributes to the national economy as a source of foreign exchange.

In 1989, 268,701 tons of fresh seaweeds were produced in the Philippines, from an estimated area of 5,700 hectares under cultivation. Only 1 per cent of total production was consumed locally as food, while the bulk was absorbed by local processors and export traders. Exports of seaweeds totalled about 31,000 tons in the same year, valued at more than $US 37 million.

The major cultivated seaweed is Eucheuma. More than 50 per cent of its harvests are utilized by a growing local processing industry in the manufacture of carrageenan. Carrageenan exports tripled from about 260 tons in 1987 to almost 900 tons in 1989. The Philippines are now the leading producer of raw Eucheuma and semi-refined carrageenan, contributing about 70 per cent of the world's supply. Seaweed and seaweed products rank third among Philippine marine exports, surpassed only by shrimp and tuna.

The growing importance of seaweed production and processing has stimulated modest research and technological development activities. The University of the Philippines Marine Science Institute (UPMSI) has undertaken genetics research activities on several commercially important

seaweed species, leading for instance to the establishment of an Eucheuma seedling bank. UPMSI has also set up a Seaweed Information Center (SICEN), through funding of the International Development Research Council (IDRC). The Aquaculture Department of the South-East Asian Fisheries Development Center (SEAFDEC) and the Bureau of Fisheries and Aquatic Resources (BFAR) have ongoing research projects on the assessment of stocks, culture and processing of seaweeds. (Source: INFOFISH International, No. 1, 1991. "Production and utilization of seaweeds in the Philippines" by E.J. Llana, (1991))

Singapore

Biotech master plan calls for strategic alliances with MNCs

Development of strategic alliances with international companies is among the comprehensive package of initiatives - supported by a budget totalling $60 million over three to five years - in the Biotechnology Master Plan recently adopted by the Singapore Government.

Drafted by the National Biotechnology Committee (NBC) and managed by the EDB under its National Biotechnology Programme (NBP), the Master Plan is made up of initiatives for the development of four key areas - technology, manpower, industry and infrastructure - and for the promotion of public information and education.

For industry the programme focuses on accessing the latest technology and developing a commercial base through strategic alliances that capitalize on Singapore's infrastructure, location and other existing strengths.

More missions of industry, academic and government agency representatives will be sent to leading centres of biotechnology overseas to explore collaborative business opportunities.

To boost efforts under the NBP, the EDB has set up a $20 million Biotechnology Investment Fund. Through direct investment of equity participation in viable projects, the EDB aims to help stimulate commercial business activities in biotechnology.

For technology development, the EDB has created a $20 million scheme called the Biotechnology Competence Enhancement Programme (BCEP), applying the "supporting centres of competence" approach that has been well tested in other industries.

The BCEP covers two centres. One is a centre of competence for biological sciences to be set up at the National University of Singapore (NUS). The other is a centre of competence for food technology to be set up jointly by NUS and the Singapore Institute of Standards and Industrial Research. (Source: Tech Monitor, January-February 1991)

Spain

National Biotechnology Centre

In the early 1980s Spain climbed on the biotechnology bandwagon by launching a major funding commitment. Unfortunately the "jewel in the crown" of this programme, the National Biotechnology Centre, was never completed. Now, following a five-year hiatus in funding, Spain has decided to accelerate the official opening of its long-awaited centre.

The moribund national biotechnology programme has been given $20 million this year, $7 million of which will be used to bring the national centre into full operation. The almost-complete building has, since its inception in the mid-1980s, lacked the funds to install laboratories and workers.

The Centre will conduct basic research on recombinant DNA technology and methodology, including the development of expression vectors and appropriate cell culture systems. Human health-care projects will be directed towards new generation antibiotics, immunobiology, blood proteins, peptides and enzymes.

A large number of agbio food projects will include genetic improvement in plant breeding, nitrogen fixation studies, improvement of starter cultures and food fermentation, bioconversion of lignocellulose, and biopesticide production.

Some attention will also be paid to environmental biotechnology applications (heavy metal recovery, microbial mining, biotransformation of pollutants and water purification). (Source: Genetic Engineering News, May 1991)

R&D subsidies

The Spanish Government has notified the European Commission of its intent to provide subsidies for research in key industrial areas, constituting the country's technological action plan for 1991-1993. The overall budget of some ECU 450 million will provide up to 25 per cent of the cost of applied research and development projects and up to 50 per cent for basic industrial research projects. The action plan focuses on research in biotechnology, advanced chemistry and new materials, pharmaceuticals, electronics and computing. (Source: European Chemical News, 20 May 1991)

New National Biotechnology Association established

The Asociación de Bioindustrias has recently been established as the new NBA organization for the coordination of Spanish biotechnology companies. It has been formed initially from 12 companies working in many different areas of biotechnology but membership is available to all companies in this field in Spain.

Its aim is to provide relevant information on issues important to the successful development of biotechnology in Spain, such as public policy issues, regulations, research and training programmes and business opportunities and to develop collaborations between Spanish and other European institutions and associations. Further details are available from: Mr. Juan Guixer, Asociación de Bioindustrias, C/Bruc, No. 72-74, 6a Planta E-08009 Barcelona;
Tel.: (93) 318-33-83; Fax: (93) 302 35 68.
(Source: EBIS, No. 3, May 1991)

Thailand

Network of Aquaculture Centres in Asia (NACA)

NACA was established as a UNDP/FAO Regional Aquaculture Development Programme to expand aquaculture production of especially fish, shellfish and seaweed in the Asia-Pacific region. NACA started its operations in 1979 and was transformed into an autonomous inter-governmental organization in 1990. At present, nine countries have acceded to the NACA Agreement: Bangladesh, China, Hong Kong, (North) Korea, Nepal, Myanmar (formerly Burma), Pakistan, Sri Lanka and Viet Nam. NACA headquarters are in Bangkok, Thailand. NACA's priority is to upgrade aquaculture technology to a level on par with livestock husbandry. Programmes focusing on diseases, feeds, nutrition, water management and development of suitable species or varieties through selective breeding have been implemented by the network of Regional Lead Centres closely linked to a number of national centres in the participating countries. Biotechnology research is taking place in India, Thailand and China. At the Indian Regional Lead Centre, research is carried out on inter-genetic hybrids between Indian and exotic carp. Gynogenesis and sex reversal techniques are applied on carp varieties. Polyploidy progeny of rohu are produced as well. At the Regional Lead Centre in Thailand, research programmes for the commercial production of triploid oysters have been carried out. The methods to induce triploidy involved temperature shock, hydrostatic pressure and Cytochalasin B treatment. At the Regional Lead Centre in Wuxi, China, research is carried out on the Heyuan carp. A Heyuan hybrid can be grown to marketable size within one year. For more information contact: NACA, c/o UNDP, G.P.O. Box 618, Bangkok 10200, Thailand. (Source: Biotechnology and Development Monitor, No. 7, June 1991)

United Kingdom

UK to introduce environment standard

Britain could become the first country in the world to introduce an official national standard for environmental performance. The British Standards Institution has released its initial proposals* for public comment, and the final document is expected by the end of 1991.

Although the new BSI standard would be voluntary unless it is later cited in subsequent legislation, insurers and investors will probably expect industrial companies to seek accreditation.

To gain the BSI mark of approval, companies would have to meet or exceed standards in existing environmental regulations. Companies would be expected to implement comprehensive corporate policies, covering issues such as waste reduction, the use of energy and raw materials and product design. The policy would have to take a "cradle to grave" approach and account for both routine and emergency situations. Responsible managers would have to receive appropriate training and support.

The draft also calls for environmental audits, which could be conducted internally or by an outside agent. Audit protocols and documentation procedures would have to be included in a company environment manual.

While the costs of pollution prevention and environmental assessment can be high, the document notes that failure has its price, too. A new standard could yield benefits in terms of increased markets and revenues, BSI says. Furthermore, companies can avoid the growing costs of fines, litigation, high insurance premiums and money wasted on ineffective technology. (Source: Chemistry & Industry, July 1991)

Council of Bioethics

The UK will soon become the latest country to have a specialist bioethical committee. The Nuffield Foundation (London) has confirmed that it will fund the "Council of Bioethics" for three years. According to Nuffield's David Shapiro, the Council could be running by May.

The Council will have an advisory role and will probably consist of 12 members, the majority of whom will be non-scientists. Neither public interest groups nor industry will be directly represented. Unlike the French and Danish Bioethical Committees - whose concerns are restricted largely to issues in human biology - the UK Council will address questions raised by research on animals and plants. Shapiro anticipates that one of the first items on the Council's agenda will be the collection and use of information from genetic screening. (Extracted from Bio/Technology, Vol. 9, April 1991)

New guidelines for risk assessment

Amid a flurry of initiatives on managing releases of genetically modified organisms (GMOs), Britain's Royal Commission on Environmental Pollution has proposed a new risk assessment procedure.

Developed from the UK's HAZOP rules for assessing chemical plant hazards, the Royal Commission has drawn up a new package, called GENHAZ, to cover GMO releases. The Government and its Advisory Committee on Releases to the Environment (ACRE) have been asked to conduct trials aimed at refining the guidelines.

The UK has yet to introduce regulations on GMO releases, beyond the aspects covered under health and safety legislation. New regulations are to be introduced later this year, however, under last year's Environmental Protection Act. Planned releases will be assessed by ACRE, and researchers will need government approval before going ahead.

GENHAZ sets out a formal evaluation procedure, involving set-by-step analyses aimed at encouraging lateral thinking. Professor John Beringer of Bristol University, chairman of ACRE, says the system will help people to think in a structured fashion; but, with no fixed pathways, GMO releases are much more difficult to assess than chemical plant hazards are. (Source: Chemistry & Industry, 1 July 1991)

Grant for biotechnology

British Biotechnology has received the UK's largest grant to date under the pan-European

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* Environmental management systems. £33 (£16.50 for BSI subscribing members), available from BSI Sales, Linford Wood, Milton Keynes, MK14 6LE.

EUREKA initiative. The £7.86 million award will support the company's work on virus-like particle (VLP) technology.

Virus-like particles, developed at British Biotechnology and Oxford University, can stimulate a strong immune response but are non-infectious. The company is currently conducting phase I clinical trials of a VLP vaccine for patients already infected with the AIDS virus and results are expected this autumn.

This therapeutic vaccine, which carries the p24 AIDS virus protein, is expected to boost the immune response of HIV-infected patients. However, a prophylactic VLP vaccine will probably need to carry more than one HIV protein. With this in mind, company researchers are now looking at other possible protein candidates on both the human and simian AIDS viruses.

The company's partners in the EUREKA project are Farmitalia Carlo Erba and Antibioticos Farma. They will be looking at the use of VLPs in the production of pharmaceutical proteins for the treatment of cardiovascular diseases. (Source: Chemistry & Industry, July 1991)

United States of America

White House changes rules for genetic engineering

The White House proposed a new policy for deregulating the biotechnology industry in May and immediately ran into a storm of criticism. Environmentalists say that it would remove all controls on genetically engineered organisms, ignoring their special risks. The industry did not like it either, as some officials privately called the proposal vague and "a step backward".

The new policy was drafted by the White House Council on Competitiveness, which in the past has criticized "regulations that discourage or penalize innovation" in biotechnology. According to the new policy, genetically engineered organisms "shall not be subject to federal oversight" unless there is substantial evidence that they present "unreasonable" risks. Even then, federal regulators should not get involved if those risks can be "addressed by other mechanisms", such as the recovery of civil damages through the legal system.

A genetically engineered drug, for instance, would be tested for safety and effectiveness, just as any drug would be. A company that modified a strain of fish, however, might not have to inform any federal agencies of its work, because fish breeding is largely unregulated.

Sources in the Bush Administration tried to downplay the significance of the proposed policy. One said it was merely an attempt to make existing policies more precise. But officials of the Environmental Protection Agency were stunned when they saw the proposed guidelines for the first time. They fear that the White House initiative could scuttle their plans to publish their own regulations. Under the EPA plan, companies would at least notify the Government of new transgenic products, and the EPA would then analyse the risks that each product might pose.

Even the biotechnology industry was unpleasantly surprised. Earlier versions of the Government's regulations had defined a set of genetically altered organisms that would not require approval. They exempted organisms that could be produced by traditional breeding techniques or those that contain new genetic material that causes no change in the organism's function. The new draft dropped all mention of these exemptions, instead proposing that regulators ignore the process by which an organism is produced. (Source: New Scientist, 25 May 1991)

Genetic screening

Regulations due to be published in July could allow US employers to discriminate against job applicants on the basis of their genetic make-up. To avoid this possibility, Nancy Wexler, who chairs the US Genome Project Committee dealing with the ethical, social and legal implications of genome research, will ask the National Institutes of Health (NIH) to press for changes to the proposed rules.

The regulations in question were drafted earlier this year by the Equal Employment Opportunity Commission (EEOC). Their purpose is to implement the 1990 Americans with Disabilities Act - legislation supposed to outlaw discrimination against job applicants on grounds of disability.

The EEOC regulations state that employers should not decide whether to hire a person on the basis of medical tests that have no bearing on that person's ability to do the job. But the regulations, as they were drafted, would allow employers to conduct tests that are not job-related, once a conditional offer of employment has been made. Because employers are not bound to reveal which medical test they have done or why an offer of employment has been withdrawn, the regulations could do nothing to stop employers determined to discriminate.

This is a major concern in the case of genetic screening, because it may be possible in future to identify a whole suite of genes that either cause disease, or confer a high susceptibility to particular health problems. The worry is that, to minimize their health care provision costs, some employers will screen for these genes in order to exclude job applicants who are more likely to become ill.

The final regulations will be published in July, but will not come into force for another ear. (Extracted from Nature, Vol. 351, 27 June 1991)

Clinical progress

The Gene Therapy Subcommittee of the Recombinant DNA Advisory Committee of the National Institutes of Health (NIH, Bethesda, MD) has recommended approval for a third somatic cell genetic manipulation protocol. The experiment is designed to test whether the cancer cells which reappear following adoptive immunotherapy are due to incomplete purging of the patient by radio- and chemotherapy or whether they are derived from the bone marrow cell preparations removed from the patient. Removed cells will be marked with a

neomycin-resistance gene before being readministered to the patient.
(Source: Bio/Technology, Vol. 9, April 1991)

Federal regulatory action preferred

Researchers facing increasing state regulation have urged the federal Government to take a more active role in regulating biotechnology. Responding to calls for a federal policy, the USDA has issued proposed guidelines for research involving planned introduction of organisms with deliberately modified hereditary traits. The USDA is working with the Office of Science and Technology Policy to establish recommendations, and invited public comment on the proposal before issuing final guidelines. The comment period ended on 2 April 1991.

The guidelines will not be mandatory. "The proposed USDA guidelines are not intended for federal oversight of biotechnology research but only as guidance for institutions and researchers", the USDA proposal said. The guidelines establish principles for assessing research safety and designing appropriate confinement.

A stepwise process has been recommended to assess the level of safety concern. Investigators are advised to determine the level of safety concern for the parent organism, then the effect of the genetic modification; this will indicate the environmental threat of the modified organism and the resulting confinement measures necessary. Considerations in determining the level of safety concern for the parental organism include: the organism's potential to be a pest or pathogen, its potential to become established in the environment, how the organism is ecologically related to other organisms in the environment, its ability to induce genetic change in the natural population, and how effectively it may be controlled in the test environment.

Examples are given in the guidelines for five different organisms, including genetically altered rapeseed. Confinement precautions are also detailed. For more information: Federal Register, 1 February 1991, pp. 4134-4151.
(Source: INFORM, Vol. 2, No. 6, June 1991)

Mapping plant genes: USDA funding genetic research

A new programme at the United States Department of Agriculture (USDA) is designed to address current deficiencies in understanding plant genetics. Begun in 1991, the USDA Plant Genome Research Programme has two straightforward goals, according to director Jerome Miksche: "to locate plant genes of agronomic importance and to get new plant varieties into the market".

Farmers want new crop varieties genetically engineered for pest resistance and increased yield; processors want new varieties with reduced by-products and better quality. The rapid advances in biotechnology are putting a squeeze on plant breeders to develop, test and market altered crops in record time. Whereas traditional plant breeding required ten or more years to get a new variety into the field, now scientists can engineer genetic improvements and field-test a new variety in a significantly shorter time.

Plant breeders say that they cannot keep up with the demand for improved crops. Part of the problem is that plant gene systems are not well characterized. Only a handful of researchers are working to identify the genome (map of locations of genes on chromosomes) of crop plants, and there is currently no electronic database of genetic information on crop varieties. Furthermore, the technology involved in gene manipulation is not well understood, with a long way to go to make it cost-efficient and relatively accurate.

The major areas of funding are expected to correspond to the major crops - corn, soybean, wheat and barley - but according to Miksche, "this research is science-driven, and the commodity is not specified". In early 1991, on three weeks' notice, 125 research groups submitted grant proposals. Miksche expects to fund 20-30 of these, covering approximately half of the 40 major US crops.

The first ambition of the Plant Genome Research Programme is to develop the science of plant genetics. Three objectives will address this goal:

- Developing broad genetic maps of common crop plants, in which 70-80 per cent of the genome would be mapped.
- Intensified mapping of gene systems to pinpoint specific gene locations and to develop methods of transferring these genes.
- Improving the basic technology of genetics to increase efficiency and consistency, focusing on understanding the stereochemistry of protein coding.

Funding preference is given to teams of scientists with expertise in plant breeding, molecular biochemistry and plant physiology.

A second objective of the project is to compile a database for plant gene maps, funded through competitive grants awarded to individuals. Information will be gathered from all plant genetics researchers and centralized into a single database at the National Agricultural Library in Beltsville, Maryland. With such a database, a researcher looking at soybeans could call up the species on the computer and quickly see what other scientist had discovered about the soybean gene system. He could then go to work on a particular gene and not be repeating work already done in another laboratory. The database will be designed to go "from genetic research stock centres to gene maps to proteins to DNA sequences to amino acids to metabolic pathways", Miksche stated.

The ARS is working closely with the genome projects of the Department of Energy and the National Institutes of Health in developing the database. Eventually, Miksche said, "we want to tie in to all these genome databases, because much of genetics is the same across species".
(Source: INFORM, Vol. 2, No. 6, June 1991)

Public buying stock in biotechnology firms

After years of struggling to make high-risk investments pay off, biotechnology companies are

finding another source of financing: public stock offerings. In the first quarter of 1991, 11 companies have raised over $800 million, according to a report in the 8 April 1991 issue of Chemical Marketing Reporter. Eight other companies had public offerings pending. In March, Genzyme Corporation of Cambridge, Massachusetts, sold 3.5 million shares in the largest single public offering of a biotechnology firm, generating $124 million. The 1991 offerings to date have already surpassed the combined total of $777 million raised in 1989 and 1990.

Biotechnology consultant Peter Feinstein attributes the interest in such investments to the "tremendous potential" of biotech therapies in the pharmaceutical industry. Several biotechnology products have received marketing approval this year. Feinstein stated that capital investment will allow the companies to retain more control over their products by decreasing the need for the smaller biotechnology companies to rely on giant pharmaceutical companies to produce and market their products. (Source: INFORM, Vol. 2, No. 6, June 1991)

USSR

New office for HUGO in Soviet Union

The Human Genome Organization (HUGO), the body set up to help coordinate the international effort to map and sequence the human genome, is opening an office in Moscow. The aim, says HUGO vice-president Charles Cantor from Lawrence Berkeley Laboratory, is to improve the lines of communication between genome researchers in the Soviet Union and those in the rest of the world.

In terms of manpower, the Soviet genome project is second in size only to that of the United States. But poor communication links with the West hamper coordination between the Soviet programme and the other national genome efforts.

The Moscow office opened on 1 July and Cantor expects electronic communications to be established via a satellite link within several months. This should give Soviet genome researchers rapid access to the computer databases in which gene mapping and sequencing data are being accumulated. The costs of the plan have not yet been estimated, but Academician Nikolay Laverov, Soviet deputy prime minister, told HUGO's executive committee in Moscow that the Soviet authorities will provide most of the money.

The office is also expected to become the focus for internal coordination of the Soviet genome project. The Soviet pledge of financial support was welcome - HUGO's international coordinating role has so far been limited by its small budget.

The new office will be HUGO's fourth, adding to offices in London and Maryland, and a Japanese office in Osaka, still in the process of being set up. HUGO staff describe the Moscow office as a "satellite" of their office in London, which will continue to be the focus of HUGO's activities in Europe. (Source: Nature, Vol. 351, 27 June 1991)

C. RESEARCH

Research on human genes

Hepatitis gene is shown to cause liver cancer

Scientists in the US and Japan have solved the riddle of the link between liver cancer and hepatitis B. For years, epidemiologists have known that people infected with this virus (HBV) are more likely than others to develop liver cancer, but no one has been able to prove a direct link. Now experiments with transgenic mice (carrying a gene from the virus) have shown clearly that a protein made by one of the virus's genes is responsible. The finding should help to explain the molecular changes that lead to the disease and may improve prospects for treatment, says the team.

World-wide, more than 80 per cent of all liver cancers are linked with hepatitis B. In men who have longstanding infection with the virus, the risk of developing liver cancer is as high as one in two.

Gilbert Jay at the Jerome H. Holland Laboratory of the American Red Cross in Rockville, Maryland led the research with colleagues in Japan's National Institute of Health.

Three years ago, researchers discovered a protein, the HBx antigen, which is encoded by a hepatitis B gene. In laboratory cultures, they found the antigen could "upregulate", or amplify, the expression of certain other viral genes by hijacking the infected cell's own mechanisms. Jay and his colleagues suspected the HBx antigen might play a role in liver cancer. So they inserted the gene for HBx directly into mouse embryos. They checked that the gene had been integrated into the genome of each mouse, and selected six to breed.

All the transgenic mice carried the HBx antigen in their livers, kidneys and testes. When the team examined liver tissue from the animals, they found it contained areas of altered cells, in contrast to normal litter mates that did not carry the gene. At 10 months old, the transgenic animals were beginning to develop tumour nodules and by 15 months most had died of liver tumours.

In the past, scientists have inserted the entire genetic material of hepatitis B into mice and failed to see liver cancer develop. Jay and his colleagues believe this may be because other genes downregulate or switch off the HBx gene when the virus replicates.

"Our findings provide overwhelming evidence for the direct involvement of HBV in the development of liver cancer", they say. (Source: New Scientist, 25 May 1991)

Gene mutation may cause liver cancer

Two research groups have found a specific point mutation in a gene from human liver cancer cells that appears to be a cause of the disease. The findings were made by C.C. Harris of the National Cancer Institute and colleagues and Mehmet Ozturk of Massachusetts General Hospital, Charlestown, Mass., and colleagues. The studies

focused on liver cancer patients in China and in southern Africa, where liver cancer is prevalent, and where exposure to aflatoxins and hepatitis B virus are known risk factors for the disease. In both studies, tumour cells from half the cancer patients studied had a specific point mutation in p53, a putative tumour-suppressor gene. Four of five such mutations in the Chinese patients, and seven of eight in the African patients, were G-to-T substitutions, in which a thymine residue replaces a guanine. Most of the substitutions were at a specific site, the third base position of codon 249 in the p53 gene. According to Ozturk the work suggests "that p53 mutations caused by aflatoxins or other environmental carcinogens might contribute to the high incidence of [liver cancer] in these areas". (Reprinted with permission from Chemical and Engineering News, 8 April 1991, p. 45. Copyright (1991) American Chemical Society)

DNA fabricated into cubes

Chemists at New York University have fashioned DNA strands into a cube, 20 base pairs on an edge. Such highly functionalized molecular objects might serve as scaffolds to attach proteins or other molecules in known spatial relationships to one another for study. Chemistry professor Nadrian C. Seeman and graduate student Junghuei Chen began by cyclizing a DNA strand 80 bases long to form one face of the cube. Next they hybridized four more DNA strands to each "side" of the "square" such that sticky ends projected from each corner. They joined two such squares, using the sticky-end projections to form a third square between them. They liken the resulting three-square array to a belt, which they "buckled" into a cube with the remaining sticky ends. They verified the cubic structure by degradation with restriction enzymes, which produced gel electrophoresis fragments of expected molecular weights. (Reprinted with permission from Chemical and Engineering News, 22 April 1991, p. 27. Copyright (1991) American Chemical Society)

New dopamine receptors cloned

Reports from two groups of researchers add two more dopamine receptor subtypes to the three previously isolated and cloned. Dopamine receptors in the brain are primary targets for drugs used to treat disorders such as Parkinson's disease and schizophrenia. The three dopamine receptor subtypes previously cloned are called D_1, D_2, and D_3. Hubert H. M. Van Tol of the University of Toronto and colleagues have now cloned the gene for a D_4 receptor. The pharmacological characteristics of this receptor resembled those of the D_2 and D_3 receptors, but the D_4 receptor's affinity for the antipsychotic drug clozapine is an order of magnitude higher. Characterization of the D_4 receptor may prove useful in the design of new clozapine analogs, the researchers say. In addition, Hyman B. Niznik, also of the University of Toronto, and colleagues have cloned the gene for a dopamine D_5 receptor. The D_5 receptor binds drugs pharmacologically similar to those bound by D_1, but displays a ten-fold higher affinity for dopamine. The D_5 receptor, they say, "may contribute to the maintenance or expression of neuropsychiatric diseases". (Reprinted with permission from Chemical and Engineering News, 22 April 1991, p. 27. Copyright (1991) American Chemical Society)

Gene therapy eyed for lung diseases

A recombinant human α1-antitrypsin gene introduced into the respiratory tract of rats, using an adenovirus vector (carrier), causes human α1-antitrypsin to be secreted by rat epithelial cells. This suggests the possibility for gene therapy of respiratory diseases such as α1-antitrypsin deficiency (which causes emphysema) and cystic fibrosis (CF), the two most common lethal hereditary diseases of Caucasians. The research was conducted by Ronald G. Crystal of the National Institutes of Health and researchers there and at the Centre National de la Recherche Scientifique Unité Associée in Villejuif Cedex, France, and Transgene S.A., Strasbourg, France. When the researchers administered the modified adenovirus to live rats, they found secretion of gene product in the respiratory tract for periods of at least one week. Such a strategy could lead to gene therapy for emphysema patients with α1-antitrypsin deficiency and for CF patients. Abnormalities of CF epithelial cells were recently shown to be correctable by transfer of the normal CF gene in vitro. (Reprinted with permission from Chemical and Engineering News, 22 April 1991, p. 27. Copyright (1991) American Chemical Society)

Antibody oligomer enhances immunity

A newly discovered form of human immunoglobulin G_1 (IgG_1) antibody provides improved immunity against group B streptococcal infection, a major cause of infection in newborns. The antibody was discovered by Linda J. Harris and colleagues at Bristol-Myers Squibb Pharmaceutical Research Institute, Seattle. In the course of producing IgG_1, and immunoglobulin M (IgM) forms of an antibody to group B strep bacteria by recombinant DNA techniques, the researchers found that an oligomeric IgG was formed in addition to the normal monomeric I_gG_1. The oligomeric IgG turns out to have some desirable characteristics of both IgM and normal IgG antibodies. Like monomeric IgG, oligomeric IgG crosses the placental barrier in rats to protect offspring against disease, which IgM cannot do. However, like IgM, the oligomer provides immunological protection against streptococcal infection at a much lower dose than monomeric IgG_1. The enhanced protection could stem partly from higher antigen-binding activity of the oligomer compared with the monomer. (Reprinted with permission from Chemical and Engineering News, 6 May 1991, p. 30. Copyright (1991) American Chemical Society)

Gene mutations linked to bladder cancer

The first genetic alterations demonstrated to occur in a high proportion of bladder cancers have been found by Bert Vogelstein of Johns Hopkins University and colleagues. Of 18 tumours evaluated, almost two thirds were found to have mutations in the tumour-suppressor gene p53. The discovery is consistent with the view that alterations of tumour-suppressor genes play a role in the development of many human cancers. For example, p53 mutations are also known to occur with high frequency in colon and lung tumours. In each of three patients whose urine was tested for signs of the disease, the same p53 mutation identified in the primary tumour was also identified in the urine. This suggests that urine tests could be developed to screen

patients at high risk for bladder cancer, or for follow-up of post-operative patients. (Reprinted with permission from Chemical and Engineering News, 6 May 1991, p. 30. Copyright (1991) American Chemical Society)

Biotechnology approach to treating Parkinson's

A genetically engineered, temperature-sensitive neural cell line has been used to produce a functional improvement in rats with Parkinson's syndrome, according to Dale Bredesen, an assistant professor of neurology at the University of California, Los Angeles, School of Medicine. He described the research at a meeting in Boston of the American Academy of Neurology. Parkinson's disease results from a decrease in the number of neurons that release the neuro-transmitter dopamine in an area of the brain called the substantia nigra. Bredesen and UCLA colleagues inserted a temperature-sensitive tumour gene, which had been isolated from a virus, into immature neurons taken from the substantia nigra of rat embryos. The tumour gene was chosen because it would make the neural cells divide and proliferate, thus providing a large number of immature cells growing in culture. However, because the tumour gene is temperature sensitive, it ensured that the neurons would proliferate only below body temperature (37°C). Thus, once transplanted into rats the tumour gene would be turned off and the neural cells would stop proliferating and assume their mature role in the rat brain. The researchers observed what they describe as a 64 per cent improvement in Parkinson's symptoms in rats receiving the transplanted, dopamine-producing neurons. (Reprinted with permission from Chemical and Engineering News, 6 May 1991, p. 30. Copyright (1991) American Chemical Society)

Second gene for epilepsy mapped

The gene for a specific form of epilepsy has been traced by researchers from Finland. The gene leads to Unverricht-Lunborg disease, a rare type of epilepsy, and is only the second epilepsy gene to be mapped.

Epilepsy is thought to affect between 1 and 3 per cent of the world's population, making it one of the commonest neurological diseases. Despite this, scientist know remarkably little about the biochemical changes underlying the disorder.

People have epileptic seizures when their nerves fire electric signals in an uncoordinated way, causing fits and unconsciousness. Although epilepsy can be brought on by trauma, infectious diseases and oxygen deprivation, the cause is sometimes genetic.

Among the many known forms of epilepsy is a group called progressive myoclonus epilepsies, which are usually inherited and can lead to ser us illness. Unverricht-Lunborg disease is one of this group and is most common in the Baltic region of Europe, where it affects around 1 in 20,000 people. Not surprisingly, it was a group in Finland which set out to look for the defective gene.

The team at the University of Helsinki, led by a human geneticist, Albert de la Chapelle, studied the inheritance of dozens of DNA markers from generation to generation in 12 affected families. The markers detect small variations in DNA sequences between individuals. Should one marker always be inherited with the presence of epilepsy, the chances would be high that the marker signalled the chromosome containing the epilepsy gene.

Using markers from chromosome 21, the group successfully mapped the epilepsy gene close to one end of this chromosome.

The next step will be to use the markers as a starting point for isolating large stretches of the DNA. Then the researchers will sort and examine the sequences in order to identify the epilepsy gene.

They might be lucky. The position of the epilepsy gene on the chromosome map happens to coincide with that for a known gene called S100. S100 codes for a protein that binds calcium ions in the glial cells that are common in the central nervous system. De la Chapelle's group thinks S100 might just be the epilepsy gene it is looking for.

Two years ago, researchers from the Howard Hughes Medical Centre in Salt Lake City, Utah, mapped the first epilepsy gene - for a very rare form of seizure by the name of benign familial neonatal convulsions (BFNC). The group mapped the gene to chromosome 20, but they also have yet to identify the gene itself.

Understanding such minor forms of seizure may shed light on more serious forms. (Source: New Scientist, 25 May 1991)

Gene defect detected in Marfan's

Scientists have found the gene responsible for Marfan syndrome, which causes muscular and skeletal abnormalities and, in some cases, premature death.

The gene appears to cause the disease when it is defective, and the discovery means that a prenatal diagnostic test to identify carriers in the womb is now a possibility for couples with a family history of Marfan.

It is also expected to lead to earlier diagnosis in those suspected of having the disease and to improved treatments and earlier treatments for sufferers who until now were diagnosed only after they developed characteristic physical abnormalities.

The Marfan gene controls the production of a protein called fibrillin, which is a major component of tiny fibres in the connective tissue that binds various structures of the body. It has been suspected for some time that a fibrillin defect was implicated in Marfan, because the protein occurs in the ligaments of the eye lens and in blood vessel walls, both of which are abnormal in sufferers.

A team from the Shriners Hospital for Crippled Children in Oregon isolated the fibrillin gene. Working in collaboration with researchers from the Johns Hopkins University School of Medicine in Baltimore, they then showed that patients with Marfan had a particular mutation in the gene but that healthy people did not. (Extracted from International Herald Tribune, 26 July 1991)

Vaccine may help stop spread of malaria

A lead for a vaccine to prevent the spread of malaria in third world countries has been developed by workers at the National Institute of Allergy & Infectious Diseases, Bethesda, Md. The vaccine would not immunize the human host against the malaria organism but, rather, might block transmission from malaria-infected hosts to the mosquito vector. David C. Kaslow and colleagues report that they inserted into attenuated vaccinia virus the gene for Pfs25, a protein that appears on surfaces of Plasmodium falciparum (a species of the malaria parasite) at a stage in its life cycle when it is ingested by the mosquito. They next inoculated mice of varying genetic makeups with the virus. Three inoculations were needed to prevent transmission to mosquitos. This may be because the attenuated virus may not proliferate in mice enough to express much Pfs25 and produce sufficient antibody titers. (Reprinted with permission from Chemical and Engineering News, 3 June 1991, p. 22. Copyright (1991) American Chemical Society)

ZymoGenetics clones new member of glutamate receptor family

Scientists at ZymoGenetics Inc., a subsidiary of Denmark-based Novo Nordisk A/S, have cloned a gene coding for the Glug Glutamate receptor, which controls intracellular calcium release within nerve tissue. The DNA sequence is described in the 31 May issue of Science.

Because of its role as the predominant excitatory neurotransmitter in the central nervous system, Glutamate has generated tremendous interest over the last several years, as have synthetic Glutamate analogs. Glutamate is an amino acid that, through stimulation of several different types of receptors, has been implicated in activities ranging from learning and memory to development and specification of nerve contacts in the developing animal.

Normal stimulation of Glutamate receptors may promote beneficial changes in the brain, whereas overstimulation can cause damage to - or death of - the nerve cells in cases of neurological disease, trauma and stroke.

To determine the DNA structure of the Glutamate receptor, ZymoGenetics scientists used functional expression cloning techniques that are at the forefront of modern molecular biology. Sequence analysis and comparison of the amino acid sequence of this neuroreceptor with that of other receptors has shown that this Glutamate receptor identified a new family within the group of "G-protein-coupled" receptors. This is exciting because there are not many known receptor families in the brain and scientists can use this new receptor family to explore alternative ways to influence the course of central nervous system (CNS) diseases.

The precise characteristics of the DNA sequence provide important information regarding the evolution of this protein. ZymoGenetics scientists plan to use this information to determine the specific roles of various Glutamate receptors in the central nervous system. Further details are available from: Novo Nordisk A/S, Novo Alle, 2880 Bagsvaerd, Denmark or on +45 4444 8888. Fax: +45 4444 2314. (Source: Biotechnology Bulletin, Vol. 10, No. 5, June 1991)

Genetic imprinting

Biologists have long believed in at least one underlying equality between the sexes: a gene is a gene, no matter which parent it came from. Now they are not so sure. Genes are turning up which seem to work only if they have come from the father. Others need a mother's touch to switch them on. All this is a bit disturbing: it questions the established wisdom of nearly a century. But it is not inexplicable.

The phenomenon is called genetic imprinting. Normally, an embryo gets one set of genes from the father, and a similar set of genes from the mother. When two sets of genes from the mother were used, the resulting embryos developed virtually no placenta from which to draw sustenance. Paternal genes alone produced a placenta but not much of an embryo.

Without external meddling, embryos get two copies of each gene, one from the mother, one from the father, stored in two sets of chromosomes. But it is not unknown for small muddles to occur in the gene-shuffling which attends the beginning of a new life. In people, this shuffling can cause a disorder in which the foetus grows too fast. This comes about when two copies of one part of a specific chromosome arrive from the father, and none from the mother.

Another human disease - fragile-x syndrome - travels the distaff path. The x chromosome helps determine sex: women normally have two of them, while men have one x and one y. Fragile-x syndrome, a form of mental retardation, can occur in either sex - but only if the eponymous chromosome has come from the mother. Men with a fragile x do not have diseased daughters.

How all this happens is becoming clear. Not all of the genes in a cell are active all of the time. One way to turn genes off is to plaster molecules called methyl groups all over the DNA from which the gene is made. Imprinting seems to boil down to a difference between the sexes, in terms of which genes they choose to methylate. Imprinted genes appear to be methylated by one parent and not by the other - as though one parent wants them to be turned on, and the other is happy to let them lie.

How it happens is one thing; biologists also want to know why. Biological whys usually require a bit of detective work to unearth an evolutionary motive. What is the benefit to be gained from imprinting? There are three clues. First, most of the effects seem to occur in embryos. Second, the imprinted genes often regulate growth in some way. Third, parents may imprint genes with opposite effects in opposite directions. It is not a case of one sex simply being more disposed to adding methyl groups than the other.

For example, a hormone called IGF-2, encourages embryos to grow. The gene which tells

the body how to make this growth factor is imprinted: the mother's IGF-2 gene will be methylated and silent. But the maternal copy of another gene, one that produces a protein which makes IGF-2 inactive, shouts loudly in the developing embryo - while the paternal copy keeps quiet. The general rule is that the father imprints genes in such a way as to encourage growth. The mother discourages it. This fits with the original observation that male genes were promoting the placenta. It is the placenta which grabs resources from the mother to make the embryo grow.

To make sense of these clues, bear in mind that although all the embryos in a uterus have the same mother, they may not all share a father. Female cats and mice, for instance, often spread their favours widely. David Haig and Chris Graham, of Oxford University, suggest that in these cases imprinting by males has evolved as a sort of metabolic theft - stealing food from the mother which might otherwise be used by embryos unrelated to the father. Each father wants his offspring to do better than the rest of the litter; the mother wants all her offspring to do well. Hence the imprinting by which fathers prime the genes for growth and the grabbing of the placenta, while mothers try to damp such intra-uterine competition down. (Source: The Economist, 13 July 1991)

Schering solves interferon

Joint research by Schering-Plough (Madison, NJ) and the University of Alabama (Birmingham) has identified the three-dimensional structure of a variant of gamma interferon. It is the first time that the X-ray crystal structure of human interferon has been determined, says Schering-Plough. The firm is also trying to identify the three-dimensional structures of other cytokines, including granulocyte macrophage colony stimulating factor and interleukin-4. (Source: Chemical Week, 22 May 1991)

Scientists find allergy sufferers produce a unique T-helper cell

Barry Kay and his colleagues at the National Heart and Lung Institute in London have found evidence for a T-helper cell called Th2, that is produced in the immune systems of allergy sufferers; it appears in their response to pollen. In non-sufferers, there was no reaction and no cells were produced. The cell could be the source of the long-term reactions that allergens trigger in sufferers, including wheeziness and a stuffy nose.

The discovery could lead to future therapies, e.g., doctors could block this type of cell or the substances it produces, and thereby alleviate symptoms. (Source: Genetic Engineering News. May 1991)

Thrombin receptor cloned

Researchers at the University of California at San Francisco, headed by Shaun R. Coughlin, have identified and cloned a receptor on the surface of blood platelets and endothelial cells that is recognized and activated by the proteolytic enzyme, thrombin. The thrombin receptor regulates the activation of platelets and other cells through interaction with thrombin.

The scientists demonstrated that the thrombin receptor is self-activated through a mechamism involving a change in the receptor's molecular configuration. Through interaction with thrombin, a specific sequence within the receptor is cleaved, resulting in the exposure of a ligand that activates the receptor and elicits cellular responses. (Source: Genetic Engineering News. May 1991)

Research on animal genes

Dutch sanction human gene experiments in cows

The Dutch Government has approved experiments in which synthetic human DNA is introduced into cows. The agriculture minister Piet Bukman has announced that legislation to regulate this kind of research will be introduced soon. This contradicts earlier assurances that the Government would ban such experiments.

Gene Pharming, a company based in Leiden, is looking for ways to prevent cows contracting mastitis, a bacterial infection of the udder, a condition extremely painful to them.

Gene Pharming's researchers have inserted genes that code for a protein called lactoferrin into fertilized eggs. Lactoferrin is part of a mammal's natural defence against infection. Cows are unusual in that they stop producing the protein after a few weeks of lactation. The company hopes that cows with the extra gene will carry on producing lactoferrin for as long as they are producing milk. This should improve their resistance to Escherichia coli, one of the bacteria that can cause mastitis.

In December, the media made much of the birth of Adriana, the first calf with the extra gene, but little was said about the origin of the gene. Only in April did the Dutch animal rights association Dierenbescherming find out that the gene was human.

In fact, the gene was a synthetic copy of a human gene. It contained strings of DNA identical to human DNA but with certain segments of useless genetic material (introns) missing. This allowed the company to claim that the gene was not human at all.

Despite the doubts about the ethics of working with human DNA, the Dutch parliament has now followed Bukman and given Gene Pharming the go-ahead to continue its experiments. In the meantime, another 16 calves carrying the lactoferrin gene have been born.
(Source: New Scientist, 15 June 1991)

Antifreeze from fish

The winter flounder can survive in waters as cold as -2°C, thanks to a simple single-chain peptide manufactured in its liver.

The winter flounder antifreeze peptide (AFP) could be used to protect citrus crops, motorways and aircraft from ice and frost, according to Thomas Caceci of the Virginia Polytechnic Institute. A natural antifreeze could save billions of dollars every year in the US alone, he says. It might also be used as a cryo-protection agent for tissues, organs and research reagents.

The nature and arrangement of the amino acids in the peptide are "peculiar", Caceci says. Alanine accounts for 60-70 per cent of the molecule, while threonine makes up most of the remainder. The amino acid sequence is "unusual and repetitive".

"The activity of these molecules is much greater than would be expected from calculations based on their concentration", Caceci says. He believes "they must somehow interfere actively with ice formation", by binding to the face of an ice crystal and raising the free energy barrier to incorporation of water. Certain structural characteristics probably contribute to this activity, Caceci says. For instance the spacing of the threonine residues coincides with the spacing of oxygen atoms in ice. These residues have their active sites along one side of the molecule, "rather like teeth in a comb".

Using genetic engineering techniques, Caceci's group claims to have synthesized the first artificial AFP, and has applied for a patent on the peptide and the gene. He believes that a longer peptide should give a lower freezing point.

Meanwhile, researchers at DNA Plant Technology (DNAP) are working along similar lines, and they too have applied for a patent. Scientists at DNAP have introduced their own synthetic flounder antifreeze gene into baker's yeast. The company is also seeking US Department of Agriculture approval for field trials of tomatoes which have been modified to express the antifreeze protein. (Source: Chemistry & Industry, 20 May 1991)

Mouse diabetes genes discovered

Two genes that confer susceptibility to type-1 diabetes in mice have been located by researchers in the UK and US. Human type-1 diabetes is an autoimmune disease that causes tissue damage, blindness, kidney failure and reduced life expectancy as a result of the destruction of insulin-secreting (β) cells in the pancreas. Affected individuals require daily injections of insulin. Development of the disease is believed to be a multifaceted process in which environmental factors trigger an autoimmune reaction against β cells in genetically predisposed people. John A. Todd and colleagues at John Radcliffe Hospital (Oxford, UK), Transplantation Biology (Middlesex, UK), CEPH (Paris), and Merck Sharp & Dohme Research Laboratories (Rahway, N.J.), have found two genes that influence the onset of type-1 diabetes in diabetic mice. If corresponding human genes for diabetes susceptibility can be found, this could lead to tests for identifying susceptible individuals. In addition, an understanding of the biochemical function of the gene products could facilitate development of therapies for the disease. (Reprinted with permission from Chemical and Engineering News, 17 June 1991, p. 16. Copyright (1991) American Chemical Society)

Mice models for Alzheimer's testing

Scientists have created genetically engineered mice whose brains are beginning to develop the fibrous tangles that are the hallmark of Alzheimer's disease in human beings.

The creation of the first animal models for the devastating disease, whose cause and course have been nearly impossible to study in humans, was hailed as a milestone.

"We were at a standstill," said Zaven Khachaturian, associate director of the National Institute on Aging.

"Having these mouse models will open up whole new vistas."

Two teams of investigators have inserted a human gene into mouse embryos, endowing them with the ability to make the human protein found in the curious tangles that develop among the brain cells of Alzheimer's victims.

The new strains of mice were developed by two teams working separately. The first team was led by Barbara Cordell at California Biotechnology Inc. of Mountain View. The other team was headed by Dana Wirak of the Miles Research Center in New Haven, Connecticut.

The oldest genetically altered mice are now almost two, or about 50 years old in human terms.

As the mice age, the researchers plan to investigate how the plaques form. They also will subject the mice to tests to see if they lose their ability to learn or suffer from confusion. (Source: International Herald Tribune, 19 July 1991)

Research on plant genes

DNA plant technology field trials of recombinant crop resistance

Various plants and bacteria naturally produce chitinase as a self-defence mechanism against soil-borne pathogens. Chitinase breaks down chitin, a structural component of the cell walls of fungi. DNA Plant Technology scientists have engineered plants to express a higher level of chitinase by incorporating a gene isolated from a strain of Serratia marcescens bacterium.

In field trials, according to Biotechnology Business News, transformed (transgenic) plants were compared with untransformed plants treated with a commercial fungicide used to control a common soil-borne pathogen, Rhizoctonia saloni, which causes lesions on the stem, diminishing yields due to stress. Crop yields in the comparative trials were highest in the genetically engineered plants. Further details are available from: DNA Plant Technology Corp., 2611 Branch Pike, Cinnaminson, NJ 08077, USA or on +1 (609) 829-0110. (Source: Biotechnology Bulletin, Vol. 10, No. 5, June 1991)

Flowers start from a single gene

A single gene triggers the growth of flowers in plants. Researchers at the Agriculture and Food Research Council's Plant Science Laboratory in Norwich discovered the gene, which sets off the cascade of changes needed to produce a flower.

The discovery is part of a wider series of breakthroughs in the study of flower development, which have confirmed the theory, originally put

forward by the poet Johann Wolfgang von Goethe more than 200 years ago, that the different organs in a flower, such as petals and stamens, are all variations on a single theme.

It is well known that the length of daylight and other environmental factors affect when plants flower. Enrico Coen, Rosemary Carpenter and their colleagues at Norwich discovered that the process is mediated by a gene, named flo, which is somehow triggered into action by the plant.

Coen identified flo by looking for abnormal flowers in snapdragons, Antirrhinum majus, with so-called jumping genes. When a cell divides, genes can sometimes jump from one place on the chromosome to another, interfering with the normal action of the gene where they land. The genes in the 50,000 plants screened by Coen jumped once every 10 to 20 generations.

Coen eventually found a plant that failed to produce any flowers. Instead it kept on growing more green shoots. Armed with the identity of the jumping genes in the plant and standard gene mapping techniques, Coen identified the location of the jumping genes on the chromosomes. It turned out that one jumping gene had landed next to flo, disrupting its action.

Flo has subsequently been found by a group at the California Institute of Technology in a weed, Arabidopsis, which is only distantly related to Antirrhinum, supporting Coen's original suspicion that flo is common to all plants.

Coen has gone on to determine the genetic code of flo and hence the protein which it produces. Although not normally present in plants, this protein is produced less than two days after plants are stimulated to flower.

Flo is the first step on the path to a complete flower. During the past year researchers at Norwich, Caltech and the Max Planck Institute in Cologne have identified most of the remaining steps. They have identified five genes which, with one or two possible additions, determine which cells grow into which parts of the flower.

Intriguingly, the genes all share a common sequence of 150 nucleotide bases so they make proteins that have one end, amounting to a quarter of their structures, in common. In a genetic sense, this confirms Goethe's idea that in some way all the organs are related.

A typical plant has four different organs in concentric circles. Outermost are sepals which protect the bud, then there are petals, male stamens which produce pollen and, innermost, female carpels.

The researchers have discovered that the production of each organ is determined by a code composed of three elements, "a", "b" and "c". A single "a" generates sepals; "a" and "b" together produce petals; "b" and "c" stamens; and "c" carpels. The letters themselves correspond to the genes the researchers have found. So far in Antirrhinum they have found one gene which is needed for "a", three for "b" and one for "c". They expect to determine soon whether any more genes are involved.

The discoveries open the way for horticultural companies to develop both new ways of making plants flower to order and new varieties of flowers. (Source: New Scientist, 6 July 1991)

Soybean, bacteria are symbiotic

The symbiotic relationship between the soybean plant and the nitrogen-fixing bacteria Bradyrhizobium japonicum appears to be related to the production of the heme, according to scientists Indu Sangwan and Mark R. O'Brian.

Soybeans can thrive in nitrogen-poor soils because they harbour bacteria that trap nitrogen from the air and convert it into forms the plant can use. The bacteria are protected in nodules on the plants' roots and are supplied with nutrients from the plant. These nodules also have a supply of heme molecules, used by the bacteria as a source of oxygen.

Using a genetically altered strain of B. japonicum, the researchers found that when the bacteria could not make heme on their own, heme was still found in the nodules, suggesting a cooperative role between the bacteria and plant in producing the heme. O'Brian and Sangwan found that in soybeans with exposure to the bacteria, the ability to make heme-precusor ALA was ten times greater than in plants that were not exposed to the bacteria. O'Brian explained that the bacteria "seems to be telling the plant to turn up the activity" to make ALA. (Source: INFORM, Vol. 2., No. 6, June 1991)

Transgenic tobacco tolerates hydrogen sulphide

The National Institute for Environmental Studies of Japan has developed a transgenic tobacco plant tolerant to atmospheric hydrogen sulphide. Using an Agrobacterium vector, researchers engineered cells of a tobacco leaf to contain an E. coli gene encoding glutathione reductase. The enzyme detoxifies oxygen radicals that form when hydrogen sulphide penetrates cells, thus protecting them from damage. The regenerated plantlets remained unaffected at hydrogen sulphide concentrations which normally cause tobacco plants to wither and die. (Source: McGraw-Hill's Biotechnology Newswatch, 17 June 1991)

High-yield oilseed grows in seawater

Scientists at the Environmental Research Laboratory in Tucson, Arizona, have completed six years of field trials on the oilseed halophyte Salicornia bigelovii Torr. using seawater irrigation.

Halophytes are plants that can survive on salt water rather than fresh water. The oilseed yielded seed and meal equal to or exceeding quantity of soybean and sunflower, indicating that the oilseed source is a potentially valuable crop in subtropical coastal deserts, such as in Mexico, where the trials were conducted.

The seed contained 26-33 per cent oil, composed of linoleic (74 per cent), oleic (12 per cent) and palmitic (8 per cent) acids, and 31 per cent protein; fibre and ash content was low (5-7 per cent). When included as a source of calories and protein in chicken starter diets, the

oilseeds were comparable to soybeans in caloric value; however S. bigelovii resulted in poor growth due to the presence of growth-inhibiting saponins. (Source: INFORM, Vol. 2, No. 6, June 1991)

Rice/E. coli shuttle vector developed

Researchers at Japan's National Institute of Agrobiological Resources (NIAR) have used a shuttle vector to mass replicate an exogenous gene in rice cells. The vector, which consists of a wheat viral gene linked to an E. coli plasmid, is capable of replicating in both plant and E. coli cells. The research group introduced the shuttle vector into rice protoplasts by electroporation and found that it replicated several hundred times. (Source: McGraw-Hill's Biotechnology Newswatch, 17 June 1991)

Viral genes

A triple helix to cripple viruses

A technique to insert a third strand of DNA into the double helix of specific genes could be used to throw a spanner into the works of the cell's machinery. The American scientists who developed this triple helix, or triplex, technique hope to eventually cripple viruses in this way. The same approach could also inhibit the hormone progesterone, and so terminate pregnancies.

Ever since the discovery of the double helix, it has been known that there is room for a third strand of DNA, filling in a groove in the helix, says Michael Hogan of Baylor College of Medicine in Houston, Texas. But until recently, there was no way to predict which sequence of nucleotides - the letters of the genetic alphabet - would form this third strand.

Hogan worked from the exact sequence of a target gene, and deduced rules for designing a single strand of nucleic acids that would bind to that gene. He then synthesized a strand, generally only 25 to 35 nucleotides long. Such short pieces of DNA are readily assimilated into the cell's nucleus, where they attach to the gene.

At places where this third strand attaches, forming a triple helix, genes are prevented from functioning normally. Proteins known as "transcription factors", which normally bind to the double helix and switch on specific genes, cannot gain a foothold on the triple helix.

Adding a third strand of DNA to genes that respond to progesterone, for example, would block the effects of the hormone. Progesterone, when it combines with its receptor, normally activates these genes and causes the lining of the uterus to grow, providing a home for the fertilized egg.

Blocking progesterone in this way would be different from the mechanism of RU486, the abortion pill. RU486 is a steroid hormone that blocks the progesterone receptor in the uterus, preventing progesterone from taking effect.

Bert O'Malley, also at Baylor College, has shown that this actually works, at least in cells in a test tube. O'Malley has just begun experiments to see whether his single strands of DNA will block the effects of progesterone in mice.

The triplex technique may prove effective in shutting down viruses whose genetic structure is well understood. Much of the research of triplex is aimed at designing single strands of DNA that will bind to key parts of the genetic material of HIV and the herpes simplex virus type-1. The company hopes that shutting down activity at these sites will render the virus impotent.

As scientists accumulate more knowledge of the sequence and function of human genes, the triplex approach should allow scientists to turn genes on or off at will, says Hogan. It might be possible to stop the growth of tumour cells by turning off genes which cause cancer. He admits, however, that such applications are at present "wishful thinking". (Source: New Scientist, 13 April 1991)

For first time in vivo, antisense RNA in transgenic mice blocks leukaemia

For the first time, a genetically engineered antisense sequence has blocked a virus in an animal.

Doctoral candidate Lei Han and co-workers Jeung S. Yun and Thomas E. Wagner at the Edison Animal Biotechnology Center, Ohio University, Athens, created transgenic mice that expressed an antisense sequence that was designed to subvert retroviral replication. Offspring of the mice that carried the blocking sequence were challenged with the Moloney murine leukaemia virus - none developed any symptoms of the disease. However, 31 per cent of the non-transgenic, litter-mate controls developed leukaemia. But these results with recombinant rodents still do not answer the question of how antisense code blockers produced outside the body by drug companies can be delivered in vivo with efficacy.

Han was able to neutralize reproducing viruses by inserting an oligonucleotide sequence that coded for a stretch of RNA that blocked the binding of the viral RNA with the core protein, explained Wagner, who is scientific director of the Edison Center. Therefore, when the retrovirus reproduced it yielded only empty particles containing no genomic RNA. "It is important to target the packaging region of the virus with the antisense sequence", he cautions. "We have done other regions but that one is dramatically more effective."

"The next step clearly is to try gene therapy with antisense sequences in the bone marrow of mice", Wagner told Newswatch. This is a model for AIDS therapy, he suggested. "If you can get the antisense segments that target the HIV retroviral packaging sequences into the stem cells, you could repopulate the patient with T-4 lymphocytes that are able to resist the infection." (Source: McGraw-Hill's Biotechnology Newswatch, 3 June 1991)

Another twist in HIV's pathogenesis

Human immunodeficiency virus (HIV), which causes AIDS, possesses a particularly complex genome compared with other retroviruses. While the functions of two of the seven known regulatory proteins encoded by the HIV genome are fairly well understood, the functions of the other regulatory proteins remain elusive. One such protein,

designated nef, has been the subject of considerable controversy, with some AIDS researchers maintaining that it acts to suppress HIV replication and other researchers arguing that it acts in quite the opposite fashion. J. Victor Garcia and A. Dusty Miller, of Fred Hutchinson Cancer Research Center, Seattle, have shown that nef, acting by an unknown mechanism, prevents the cell-surface expression of CD4, the antigen that both defines the set of T lymphocytes that HIV destroys and acts as the molecular target that the viral glycoprotein coat binds to when HIV infects a cell. The research indicates that nef does not interfere with the transcription or translation of DNA that encodes CD4. In HIV-infected cells, nef is known to be associated with the interior portion of the cell membrane, so it is reasonable to suspect that nef somehow acts to block transport of CD4 across the membrane. Garcia and Miller suggest that "down-regulation of cell-surface CD4 by nef would be advantageous for the survival and spread of the virus" because such downregulation impairs a component of the immune response while simultaneously reducing the possibility of super-infection with a second virus. (Reprinted with permission from Chemical and Engineering News, 15 April 1991, p. 14. Copyright (1991) American Chemical Society)

Agouron solves an HIV puzzle

Agouron Pharmaceuticals (La Jolla, CA) says its researchers have solved the atomic structure of a protein required by HIV to complete its cycle of replication and infection. Using protein X-ray crystallography, the scientists determined the three-dimensional atomic structure of the protein, called HIV RNase H, including the chemical and structural details of the enzyme's active site, according to Agouron. The firm also reports the discovery of a prototype inhibitor, a compound containing uranium, that binds tightly to the protein. Agouron says that its structural discovery could provide clues to the development of new drugs for treating AIDS. Agouron has a standing relationship with Eli Lilly (Indianapolis) and says that down the road Lilly could be brought into the project. For now, however, Agouron is working alone with support from the National Institutes of Health (Bethesda, MD). (Source: Chemical Week, 17 April 1991)

Lymph clue to virus

Lymphoid tissues may be the main reservoir for HIV in the body. Researchers at the National Institute of Allergy and Infectious Diseases (NIAID) in the US have found large amounts of the virus in the lymph nodes, adenoids and tonsils of people with HIV. So the amount of virus in the body during the latent phase of infection may be 10 to 15 times greater than was thought, say the researchers.

The NIAID team measured the frequency of HIV-infected CD4 cells in both the blood and lymphoid tissues of five people with HIV. The frequency of infection in blood ranged between 1 in 10,000 cells to 1 in 50,000 cells. But the figure was between 10 and 15 times higher in lymphoid tissues.

The discovery helps to explain one of the great mysteries of HIV: why it causes so much damage to the immune system when it infects only a handful of immune cells in the blood. Previous studies have found HIV in only a tiny fraction of the body's CD4 cells, the main targets of HIV in blood. (Source: New Scientist, 6 July 1991)

Placental clues to HIV spread in pregnancy

Scientists in France believe they are closer to understanding how HIV passes from mother to child, a discovery which could bring them nearer to blocking the spread of the virus in pregnancy. Laboratory studies show that certain cells from the placenta can become infected with the virus. Although the work is at an early stage, the researchers say the cells may play an important role in transmission.

The World Health Organization estimates that there are already 1 million children world-wide infected with HIV. By the end of the decade, this will rise to 10 million. Most studies show that about one in three of the babies born to HIV-positive women is infected, although a Europe-wide study has found lower rates.

Researchers at the University of Luminy, Marseilles believe that the virus is transmitted during pregnancy rather than birth but they do not know how. The team is based at a laboratory of INSERM, the French medical research council.

The researchers found that placental macrophages mixed with cultured cells could be infected with HIV and could harbour the virus for at least six weeks. The virus was capable of replicating in the culture. Both findings are surprising because placental macrophages seem to lack CD4, a surface molecule that acts as a receptor for the virus.

But the behaviour of the cells is puzzling. When the researchers compared macrophages from the foetus and from the placenta, they found that the foetal cells were more easily infected with HIV than the placental ones. Placental macrophages produced virus only erratically and in small amounts. This could be because the macrophages in the placenta are more mature, or differentiated, than those in the foetus. Earlier researach has shown that highly differentiated macrophages are less sensitive to HIV.

One possibility, says the team, is that only a small fraction of the infected cells in the placenta actually produce replicating virus. The team hopes to discover what would distinguish these cells from the rest. (Source: New Scientist, 1 June 1991)

Is HIV coat the key to targeting cells?

A small portion of HIV's protein coat seems to be crucial in determining which types of cell the virus infects, say American researchers. The finding may help to explain how the different strains of HIV present in individuals' bodies mutate during the course of disease.

HIV's main target cells in the body are T cells and macrophages, a type of white blood

cell. Macrophages and their immature forms, monocytes, are the commonest target cell for the virus in most tissues and are important in the course of disease. Yet despite this, many laboratory strains of the virus seem incapable of replicating in cultures of macrophages.

In culture, strains of HIV can be divided roughly into two groups: those that infect cultured T cells but not macrophages and those that infect macrophages but not cultured T cells.

Now Stephen Hwang, Bryan Cullen and their colleagues at Duke University Medical Center in Durham, North Carolina, have in effect made a member of the first group turn into a member of the second. The team cloned and sequenced the envelope gene from a macrophage-infecting strain, called BaL. They then constructed a string of chimeric viruses by inserting parts of this gene into clones of another strain, IIIB, which normally infects cultured T cells.

They found that the crucial difference was due to a sequence of just 20 amino acids in the V3 loop, a highly variable region of HIV's coat protein which is also important in stimulating an immune response. The altered IIIB strain carrying this sequence from BaL infected macrophages but not T cell lines.

Strains that can infect cultured T cells usually predominate in the body in the late stages of disease, while macrophage-infecting strains predominate earlier on. T-cell infecting strains also tend to have V3 sequences that are atypical of the vast majority of strains analysed. The team thinks that evolutionary pressures select for atypical, T-cell infecting strains in the course of disease. Vaccines should be aimed at more typical macrophage-infecting strains, they say. (Source: New Scientist, 13 July 1991)

Natural protein provides clue in the hunt for drugs to combat AIDS

The discovery of a human protein that stops viruses replicating in cells has raised hopes of finding a "natural" therapy for AIDS. The protein seems to play a part in holding HIV in check during the latent period of infection.

Jay Levy of the University of California in San Francisco reports that the protein, a member of the cytokine family, is produced as part of the immune system's natural response to HIV infection. It is secreted by a class of immune cells known as CD8 cells and appears to inhibit viral replication in CD4 cells, the main targets for HIV in the immune system.

The cytokine was discovered in people who have been infected with HIV for a long period - up to 10 years - but have yet to develop symptoms of AIDS. According to Levy, the continued production of the cytokine in these individuals may be one of the reasons that they have survived for so long. The researchers also found that the cytokine gradually disappeared in AIDS patients as the disease worsened.

It has been known for some time that CD8 cells - which are not themselves liable to infection with HIV - can inhibit HIV replication in CD4 cells. The characterization of the protein gives researchers a firm idea of how it does so.

Stimulating the immune system to produce more of the cytokine might lead to a therapy, the researchers suggest. But they warn that they have not finished characterizing the cytokine's molecular properties. Even when they have done so such a therapy will still be a long way off.

Many researchers are now confidently predicting the development of therapeutic vaccines. Such vaccines are designed not just to protect against infection, but also to bolster the immune systems of people already infected with HIV, allowing them to stay healthy longer.

In the near future, though, most researchers expect any improvements in AIDS therapy to come from antiviral drugs. (Source: New Scientist, 29 June 1991)

Research on bacterial genes

Ancient bacteria eliminate nasty niffs

A team of researchers in Japan has discovered that a group of micro-organisms can prevent animal manure from giving off methane, a potent greenhouse gas.

Archaebacteria, which differ from ordinary bacteria in their biochemical constituents, have been found to reduce the amount of methane produced by between 45 and 65 per cent.

"The bacteria can be put into animal feed", says Masuo Nakano, of Obihiro University of Agriculture and Veterinary Medicine on Japan's northern island of Hokkaido. "Then they lodge in the animal's intestine. It has to be continuously applied to be effective."

According to Nakano, there are about 50 species of archaebacteria in Japan, occurring naturally in old rock formations and salt pans. Archaebacteria occur only in extreme environments where conditions are similar to those which prevailed at the true life originated on Earth.

"There is a commercial application as well because the bacteria can reduce bad smells", says Nakano. During experiments, ammonia was found to have been eliminated almost completely from animal manure compost and hydrogen sulphide was reduced by around 98 per cent.

The archaebacteria work by vitalizing or retarding other naturally-occurring or artificially ingested bacteria. It was found to be most effective when used in conjunction with nitrifying or methane bacteria.

Another beneficial effect of archaebacteria was that the time taken to produce a compost from the manure of pigs, chickens and cows was reduced from around ten months to one. (Source: New Scientist, 20 July 1991)

Research instrumentation

Guide to reading the gene map

The mapping of human chromosomes is to be speeded up with the help of an automated machine that transfers tiny portions of selected cells from the plate on which they are randomly grown to the ordered array in which they will be cultivated and tested.

In 48 hours it can do the work that three scientists would have taken two to three months to complete, according to the Medical Research Council (MRC) of Cambridge, where it was developed. A vision system developed by UK company Visionways is key to the machine. Using a colour video camera and specially-developed software the Visionways system scans the random location of cell colonies on each plate and identifies where they are. This information is then used to guide the computer-controlled "picking" unit to take samples. Comprising six radial pins, the "picking" unit can take 1,000 samples an hour. It is automatically sterilized every six samples.

The MRC is negotiating with a number of companies to market the machine so it should be commerically available within a year. (Source: Financial Times, 17 May 1991)

The new automated DNA sequencer

Researchers at the Institute of Physical and Chemical Research have unveiled Japan's first fully automated system for the analysis of DNA. Nicknamed the Human Genome Analyser (HUGA), the robot-run system is expected to play an important role in Japan's efforts to sequence the human genome.

HUGA, the end product of a project initiated by Akiyoshi Wada of Tokyo University in 1981 with the backing of the Science and Technology Agency and several private companies, consists of a production line of machines that carry out the different steps of DNA analysis from initial purification to input of the DNA sequence into a computer. Robots transfer microtitre plates and electrophoresis gel cassettes between various parts of the analyser under the control of a supervisory computer system developed at the Institute. This is the first automatic system to cover so many steps of DNA analysis, says Kenichi Matsubara, one of the leaders of Japanese human genome research.

The analyser can run unattended at night and has a potential raw output of up to 108,000 base pairs of DNA per day. Because of the need for duplicate sequencing to cover damaged parts of a given sequence and to provide controls, the actual output of correct and complete sequences is about 20,000-30,000 base pairs per day.

The Science and Technology Agency is considering setting up a semi-private organization backed by industry that will use HUGA.

But while industry may sell individual parts of the human genome analyser, there are no plans to commercialize the system as a whole. (Source: Nature, Vol. 351, 20 July 1991)

Perkin-Elmer Cetus reagent kit prevents PCR carryover contamination

The new GeneAmp PCR Carryover Prevention Kit from Perkin-Elmer Cetus prevents contamination due to PCR carryover. It contains ultrapure and nuclease free recombinant UNG, dUTP and a detailed protocol and is sufficient to perform 100 reactions of 100 uL each.

Substituting dUTP in the PCR reaction mix and using uracil N-glycosylase (UNG) for the excision of uracil residues as a pretreatment step for subsequent PCR reactions ensures that DNA products from previous PCR amplifications cannot be reamplified to give false positives. Further information is available from: Perkin-Elmer Ltd., Maxwell Road, Beaconsfield, Buckinghamshire HP9 1QA or on (0494) 676161. Fax: (0494) 678324. (Source: Biotechnology Bulletin, Vol. 10, No. 3, April 1991)

Kansai Paint uses high-pressure gas to insert DNA

Kansai Paint Co. Ltd., Osaka (Japan), in collaboration with Sunao Matsunaga of the Tokyo University of Agriculture and Technology, has developed a device that uses high-pressure gas to insert foreign DNA into cells. The Mach Impacter KPG10 propels recombinant-DNA-coated tungsten particles at a pressure of some 100 atm into cells at "supersonic speed". Kansai Paint has used the device to insert genes into the green algal Chlorella cells, which are surrounded by a rigid cell wall that resists penetration by conventional methods. (Source: McGraw-Hill's Biotechnology Newswatch, 17 June 1991)

Promega's restriction enzyme reference wheel

Promega's new Restriction Enzyme Reference Wheel is a handy way to access a wealth of useful product and application information. Through a combination of a rotating wheel, dual pull-tabs, data windows and reference tables, information on all Promega's restriction enzymes is provided.

The information provided includes recognition and cut sites; heat instability; freshness dating; frequency of cutting on various DNAs; methylation sensitivity and isoschizomer cross-reference. Further details are available from: Promega Corp., 2800 Woods Hollow Road, Madison, WI 53711-5399, USA or on +1(608) 274-4330. Fax: +1 (608) 273-6967. (Source: Biotechnology Bulletin, Vol. 5, No. 5, June 1991)

Sartorius offers disposable system for protein and pyrogen removal

A ready-to-use disposable system for the ultrafiltration of small volumes (several ml), which is usable in any laboratory centrifuge has been launched by Sartorius Filtration. Known as Centrisart I, this device filters centripetally in order to prevent concentration polarization. Packed in units of 12, Centrisart I is available in the following molecular weight cut-offs: 5,000, 10,000, and 20,000. Further details are available from: Sartorius, Longmead Business Centre, Blenheim Road, Epsom, Surrey KT19 9QN or on 03727-45811. Fax: 03737-20799. (Source: Biotechnology Bulletin, Vol. 10, No. 5, June 1991)

Custom non-isotopic labelled antibodies and oligonucleotides

Cambridge Research Biochemicals are extending their already wide range of custom services to include the non-isotopic labelling of oligonucleotides and antibodies. (CRB have had many years of

covalent conjugation chemistry experience and have applied it successfully in the conjugation of enzymes to a variety of molecules.)

Oligonucleotides can be readily synthesized and conjugated at the 3' or the 5' end to alkaline phosphatase, horseradish peroxidase or many other enzymes. The resulting conjugate can be used with colour or chemiluminescent substrate in a wide range of applications. Oligonucleotides substituted with biotin or fluorescein can also be manufactured.

A purification and custom conjugation service for antibodies is also available. Both polyclonal and monoclonal antibodies can be conjugated to a wide variety of enzymes using selective chemistry to ensure a 1:1 ratio of antibody to enzyme. Fluorescein and biotin antibody conjugation can also be carried out on request.

The scale of all conjugations can range from the small research user to the larger production batches for diagnostic products.

Manufacture is to GLP standard and can be to GMP standard on request. For more information please contact Simon Douglas, Senior Product Manager, Bioscience, Cambridge Research Biochemicals Ltd., Gadbrook Park, Northwich, Cheshire, CW9 7RA, UK. (Source: ICI Press Release)

Separex offers licosep continuous separation process

Researched and developed by the French Institute of Petroleum in association with Separex, the French company which also markets it, Licosep is a continuous separation process using liquid chromatography. Widely used in the pharmaceutical, chemical and food industries, liquid chromatography is a high-performance purification technique.

However, it has the disadvantage of being diluting and not continuous, and therefore expensive. Licosep, by contrast, uses the simulated counterflow technique, which has been used for many years for large-scale separation in the petrochemical industry and is now available for smaller-scale separation with processing rates from 0.5 to 30 tons a year. A liquid mixture can therefore be continuously separated into components not separable by distillation.

With continuous operation, fractions of the mixture that are not sufficiently separated are effectively recycled to undergo new elution through the chromatography column, through repeated injection and extraction.

By drawing off the required product where it is at its highest concentration, Separex says, almost all the product can be obtained in optimum conditions of concentration and purity. In addition, this technique produces significant savings in eluent and absorbent, with subsequent gains in output and productivity. Further details are available from: M. Nicoud, Separex, Chemin des Blanches Terres, BP 9, 54250 Champigneulles, France (Tel.: +33 83 31 24 24. Fax: +33 83 31 24 83. (Source: Biotechnology Bulletin, Vol. 10, No. 4, May 1991)

Lumi-Phos™ substrate kit - for all blotting applications

Cambridge Research Biochemicals have launched a new chemiluminescent detection kit containing Lumi-Phos™530 substrate and a blocking buffer. Lumi-Phos™530 is a substrate for alkaline phosphatase, which provides ultra-sensitive detection of any alkaline phosphatase conjugated molecule such as antibodies, oligonucleotide or double stranded DNA probes. The kit comes as a ready-to-use stable formulation consisting of Lumigen PPD, buffer, CTAB and enhancer. Enzymatic removal of the phosphate group from the stable dioxetone produced an unstable intermediate, which decomposes to provide the observed chemiluminescence.

The enhancer system consists of a fluorescein derivatized co-surfactant in micelles which provides a 370-fold increase in the chemiluminescent efficiency.

The blocking buffer is based on casein and is supplied as a 10 x concentrate. It has been optimized for use in Southern, Northern or Western blotting application on nylon or PVDF membranes. The chemiluminescent signal is recorded on normal X-ray film giving a permanent record of result that will not fade with time.

Two kit sizes are available, containing blocking buffer, and either 35 ml or 100 ml of Lumi-Phos. The Lumi-Phos is supplied in a convenient spray bottle which allows easy application and minimizes contamination. Extra blocking buffer is available separately. Further information is available from Simon Douglas, Senior Product Manager, Bioscience, Cambridge Research Biochemicals Ltd., Gadbrook Park, Northwich, Cheshire, CW9 7RA, UK. (Source: ICI Press release)

Sternberger monoclonals available in Europe

The internationally renowned SMI series of monoclonal antibodies and mouse monoclonal peroxidase-antiperoxidase (ClonoPAP®) are available in the UK and Europe from AFFINITI Research Products Ltd. AFFINITI Research Products Ltd., based in Ilkeston, Derbyshire, UK is a new company specifically formed to serve the needs of neuroscientists, working in disciplines from anatomy to zoology.

The range includes antibodies to non-phosphorylated, hypo-phosphorylated and phosphorylated neurofilaments, microtubule associated proteins tau and MAP2, myelin basic protein and an as yet unidentified synaptic protein. All the monoclonal antibodies are fully validated for use in immunocytochemistry and are complemented by a range of secondary antibodies and PAP complexes. For further details of the ranges, and an information pack, please contact Dr. Ian M. Varndell, AFFINITI Research Products Limited, 10 Cossall Industrial Estate, Ilkeston, Derbyshire, DE7 5UG, UK. Tel.: (+44/0) 602 442232; Fax: (+44/0) 602 442313. (Source: AFFINITI press release)

High-tech detection

DNA fingerprinting is now being used for more than just paternity suits and solving crimes. At

an Edinburgh Science Festival symposium on genetic engineering, Paul Debenham from ICI's Cellmark Diagnostics described recent advances in the technique, and some bizarre applications. These included testing blood on the steering wheel of a crashed Lamborghini to prove to an insurance company that the insured owner had actually been driving the car, and also trying to establish whether or not one particular duck-billed platypus of an Australian group was fathering all the offspring.

The US armed forces are about to conduct pilot studies on DNA-fingerprinting their personnel, so that corpses which, in modern warfare, may be otherwise unidentifiable, can be named. The plan is to ensure that no US soldier will ever again be buried as "unknown". This task involves testing some 100,000 people, at a rate of 1,000 to 1,200 a week, once the system is established. This would be one of the largest DNA screening projects yet undertaken.

In 1990, bone was used in forensic DNA fingerprinting for the first time, to prove beyond reasonable doubt the identity of a skeleton found buried in a Cardiff garden. Prof. Alan Jeffreys of Leicester University, who pioneered the original technique, took blood samples from the living parents of the suspected victim and compared their DNA with that taken from the skeleton.

The technical challenge here was firstly to extract the DNA from the bone successfully. The second problem was the small genetic size of the extracted material, which limits the genetic tests that can be undertaken.

This evidence helped to convict two men for murder earlier this year. (Source: Chemistry & Industry, 6 May 1991)

Filters provide traps for catching viruses

The viral contamination of drugs and blood plasma used for transfusions is a serious problem.

Over the past few months, a number of filters have become available which are reported capable of sieving out lethal viruses, including HIV, from blood plasma and other biological medicines, such as human growth hormone.

According to the companies which have developed the new filters, they provide the medical profession with an additional means of purifying plasmas and other drugs derived from biological sources. They have the advantage that they can be sterilized after use, to destroy any viruses that they may trap.

At present, suppliers of blood plasma and biological agents purge their products of any viral contaminants by heating them, usually at temperatures of around 60°C, for between 10 and 30 hours. Another option is to kill viruses with chemical solvents or detergents, such as chloroform or tri-n-butyl phosphate.

But, as haemophiliacs will testify, these methods are not foolproof. There is also a danger that the harshness of the treatments will damage the product and impair its effectiveness. The new filters could therefore provide an additional screening process to guarantee purity.

Millipore, a filter company based at Bedford in Massachusetts, launched "Viresolve", a membrane filter that is claimed to be more reliable than existing filters. The company says that uniquely, all the pores in the membrane are virtually identical in size. Moreover, the membrane works in an unconventional way, blocking rather than adsorbing viral particles. The filters, made from a polymer called polyvinylidene fluoride, successfully intercepted the polio virus which, at just 38.5 nanometres across, is one of the smallest known. HIV is around 100 nanometres in diameter.

Asahi Chemical, based in Tokyo, Japan, has spent $12 million devising a cellulose-based membrane specifically for filtering out HIV and the virus that causes hepatitis B from blood plasma. In laboratory trials, the hollow-fibre membranes, derived from cotton seeds, completely eliminated HIV from test solutions. Moreover, the filtrations work at low temperatures, and the membranes do not block the blood plasma itself, or most other biological protein-based products. The pores are between 20 and 100 nanometres across. Additionally, the flow rate through the filter does not change.

Already, Asahi has supplied two filters, one for purifying coagulation factor and one for purifying foetal bovine serum. (Source: New Scientist, 20 July 1991)

General

Human genome databases at the crossroads

As the Human Genome Project gets fully up to speed, genome researchers face a problem: information will soon be accumulating so fast that the prompt sharing of gene-mapping data threatens to become a bottleneck for the planned 15-year genome initiative. Data-handling experts and software engineers who design new computer databases say that action is needed now to handle the avalanche of data.

The main repository for human gene mapping data is now the Genome Database, run from Johns Hopkins University in Baltimore, Maryland. It contains a "consensus map", in which all the information has been carefully screened, to iron out any inconsistencies in data submitted by different researchers.

But as the volume of raw data coming into Hopkins increases, the delay between submission and the appearance of screened data in the database will increase. "People are going to have to give up on consensus data if they are to have rapid access to gene-mapping information", says Nat Goodman, an information scientist at the Whitehead Institute of the Massachusetts Institute of Technology.

Within two years, Goodman predicts, the consensus process will be overwhelmed. This makes it essential, he says, that a new system of intermediate databases be developed to act as clearing houses for unscreened data.

These intermediate databases could be the responsibility of the individual genome centres set up by NIH and the Department of Energy. Each centre is the hub for work on one or several individual chromosomes, and is supposed to act as a resource for investigators working on these chromosomes at other laboratories.

Although few of the main centres have made significant progress on the informatics front, database experts are hard at work at these centres, and if all goes as planned, should have intermediate databases ready within a couple of years.

That will still leave the problem of communication between the different databases, which may have different formats. Researchers expect that it will soon be possible to design a "mediator program' allowing researchers to communicate with each of the major databases via the NSFNET computer network.

Besides an understandable reluctance to share data with directly competing research groups without at least some delay, many biologists are worried about the potential embarrassment caused by the general distribution of gene-mapping data that have not been fully checked for accuracy.

Working out an acceptable data access policy for the next generation of genome databases will, however, require a greater degree of communication between the "two cultures" of scientists working on the genome project than has so far been the case. (Source: Nature, Vol. 352, 11 July 1991)

Genome researchers go hog wild

To the long list of animals that have their own genome project, one more may be added: the pig. In April, researchers at 16 European laboratories began PiGMaP - a three-year pan-European project to create a physical and genetic map of the pig genome. Supported by about 6 million ECU of European Communities and national funding, the project joins genome initiatives on worms, yeast, mice, rice and the common weed in taking advantage of the new mapping technology being developed for the human genome initiative. Pigs are a perfect species to map because they breed rapidly and their 18 chromosomes are of widely varying lengths, which are easy to sort by mechanical means, says University of Edinburgh biologist Alan Archibald, one of the project coordinators. PiGMaP's initial aim is to produce a porcine genetic map with about 150 markers, spaced 20 centimorgans apart, with which researchers can find genes that control such traits as growth speed and litter size. (Source: Nature, Vol. 352, 18 July 1991)

Japan's human genome project takes shape

Japan's Science and Technology Agency (STA) is planning to set up a new DNA analysis centre supported by private industry as part of Japan's effort to map and sequence the human genome. STA's move comes as the agency and two other ministries manoeuvre to cut up the pie of governmen -sponsored human genome research in Japan.

The centre, if established, will be Japan's third, following similar initiatives by the Ministry of Education, Science and Culture and the local government of Chiba prefecture.

STA's proposed DNA analysis centre is a top priority for submission in August in the agency's budget request for next year, according to people familiar with the agency's plans.

The education ministry, STA and the Ministry of Health and Welfare, which has a project to sequence disease-related human genes, have only recently come close to agreement on how to divide this year's budget for human genome research.

The education ministry is in the process of establishing its own new human genome analysis centre at the Institute of Medical Science of Tokyo University. The centre, to be headed by Minoru Kanehisa, a computer and database expert from Kyoto University, will get under way this fiscal year with a complement of four researchers in a "genome database division". It is hoped that Tokyo University centre will eventually have about 24 researchers.

In a move independent from all the national government projects, the local government of Chiba prefecture has also announced that it will establish a new DNA analysis centre in 1993 in a science park for private companies. The centre is expected to concentrate on sequencing DNA and will probably be manned largely by technicians.

The planned STA centre will adopt a "top-down" approach to look at the human genome as a whole, in contrast to researchers supported by the two ministries, which will use a "bottom-up" approach and focus on specific genes. The STA centre will concentrate on mapping the human genome until advanced sequencing technology is developed.

Under a separate budget, STA is hoping to start a project in 1992 to develop a next-generation automatic sequencing system at the Institute of Physical and Chemical Research where an automatic sequencer, HUGA, has just been unveiled. In the meantime, HUGA will probably be used at the planned centre to sequence DNA clones that have already been mapped. (Source: Nature, Vol. 351, 20 June 1991)

Gene amplification

The polymerase chain reaction - a method of making millions of copies of a piece of DNA quickly and reliably - is the most exciting new biotechnological technique to emerge in the past few years. PCR is particularly well adapted to developing new diagnostic tests and "genetic fingerprinting" techniques for forensic work. Besides these wordly applications, PCR opens up all sorts of new areas of research by making genes visible where before they had remained hidden. It is the key to the biological candy store.

Those who study extinct species, for example, have never had much chance of getting to grips with genes. Now the skins, bones, leaves and seeds in old museum collections are yielding DNA. Unsuspected relationships are turning up, to the delight of biologists. Their subjects might be less enthusiastic. Some extinct species are losing their specificity, as post-mortem genetics shows them to be barely different from other organisms.

The PCR techniques which allow all this are simple. Polymerase is an enzyme which duplicates DNA inside cells. PCR takes a type of polymerase

insensitive to temperature change, and puts it in a test-tube with some DNA. Increasing the temperature makes the DNA double helix come apart; the polymerase then copies each strand; the strands then reform double helices as the temperature drops. Every temperature cycle doubles the amount of DNA. The proverbial vizier who started with a single grain of wheat on the first square of a chess board, then put two on the second and four on the third, ended up walking away with the entire harvest of the kingdom. PCR puts a similar power in the hands of biologists.

One recent victim of post-mortem PCR is the quagga. Quaggas roamed South Africa until about 100 years ago, when they were killed off. They appeared to have been designed by a committee: the striped front resembled a zebra; the plain brown rump a horse. Zoologists have never agreed about whether the quaggas were a species or not. Now amplified fragments of DNA from specimens at the South African Museum in Cape Town have shown them to be a mere variety of the local Burchell zebra. Sad, perhaps, but not as sad as it sounds - the humble state brings with it the possibility of new origins. The museum's zoologists are trying to recover a quagga, or something like it, by selective breeding from quagga-like Burchells. They think it will take about 20 years.

Another species which is being tidied out of existence is the American red wolf. This is not yet extinct - a few individuals linger in zoos. But conservationists feared these last few had become impure through fraternizing with the more successful grey wolf and the coyote. Tests using PCR showed that that is what happened. The survivors are entirely hybrid. And when "pure" red wolves from old museum collections were examined, they turned out to be hybrids too. The red wolf, it appears, never really existed in the first place.

Not all PCR revisionism demotes its subjects - some merely shows them to have had unexpected relatives. Work on animals wiped out when people reached the antipodes shows that the Tasmanian "wolf" (thought to have finally succumbed to European sheep farmers in the 1930s) was related to mouse-like marsupials and the anteater-like numbat. The giant moas which once stalked New Zealand were cousins to the far-off South American rheas, not the little kiwis with which they shared their islands until the Polynesians arrived.

How far back can the long arm of PCR reach? About 17 million years ago, a lake in what is now Idaho was surrounded by magnolia trees. Their leaves were preserved in the mud at the lake's bottom in impressive detail. Edward Golenberg, of the University of California at Riverside, believes this detail includes double helices. He has extracted, from the fossils, DNA similar to that found in modern magnolia leaves - which seems to overturn the conventional wisdom that DNA needs to be dry to survive even a few thousand years, and never survives millions. If Dr. Golenberg's discovery is confirmed, it could be possible, in exceptional circumstances, to study the genetics of long-extinct creatures, rather than those who had been killed off by people. And maybe, just maybe, their genes can be stitched together again, and some of them ushered back. (Source: The Economist, 27 July 1991)

D. APPLICATIONS

Pharmaceutical and medical applications

"Altruistic vaccine" boosts hopes for halting malaria

A vaccine to control the spread of malaria could start trials within two years. Scientists in the US have found a way to block the malaria parasite Plasmodium falciparum while it is in the mosquitoes. Although such a vaccine could not stop infection in the first host, it should prevent its spread to the next, so reducing the size of malaria epidemics.

Malaria is a worsening problem world-wide. More than 110 million people suffer from it every year, and up to 2 million die. A growing number of countries are now affected by drug-resistant strains of the parasite and vaccines are urgently needed. P. falciparum, however, has a complex life cycle, and no single vaccine is likely to be capable of protecting against it at all stages of its development.

David Kaslow and his colleagues, in the Laboratory of Parasitic Diseases and Laboratory of Viral Diseases at the National Institutes of Health, based their experimental vaccine on one of the parasite's surface proteins. The protein, known as Pfs25, is produced in the ookinete. Researchers know that Pfs25 stimulates the immune system of mice to produce specific antibodies against it. "In some way the antibodies disrupt the ookinete from forming the cyst, and this blocks development", says Kaslow. Next time the mosquito bites, there are no sporozoites to infect the host.

"This is an altruistic vaccine; it would not protect the individual, it would protect the community", says Kaslow. When it is ready for field trials in people, he says, it will be essential to make sure people understand its nature. Transmission-blocking vaccines would probably have to be used with antimalarial drugs or vaccines that protect against infection.

An important advantage of transmission-blocking vaccines is that they could halt the spread of new mutant strains of the parasite. These mutants may evolve rapidly to evade vaccines that protect against disease.

Pfs25 is shaped by a network of disulphide bonds that create specific folds in it. That shape may be important in determining the strength of the immune response to the protein. Rather than make a synthetic peptide, whose shape may not be correct, the team inserted the gene for Pfs25 into whole, live vaccinia virus. When they infected cultures of monkey cells in the laboratory with the altered virus, the cells produced Pfs25, correctly folded to stimulate specific antibodies.

Next, the researchers inoculated mice with the altered virus and took blood samples from them. The mice had produced antibodies to Pfs25. After one shot, the level of antibodies was too low to block the parasite but, after three, the response was very strong. A human version of the vaccine would probably need several shots to stimulate several lasting batches of antibodies.

In a system designed to mimic mosquito bites in humans, the team put blood from the mice on one

side of an artificial membrane and allowed the insects to feed on it. Even when they diluted the blood, the antibodies in it completely blocked transmission.

Despite the success with mice, Kaslow warns that we cannot yet assume that the vaccine would work in humans. Vaccinia virus is normally harmless, but in people whose immune systems are suppressed it can very occasionally cause disease and even death. Kaslow is investigating other virus vectors, such as adenovirus, which may be safer. Safety trials will be done first in the US, then in countries where malaria is endemic. (Source: New Scientist, 8 June 1991)

Soap being used to fight malaria in Philippines

The soap was invented and patented by Thomas E. Simmons of Doncaster East, Victoria, Austrialia under the auspices of the World Health Organization, who gave the rights to the Medical Mission Sisters, an international Roman Catholic order headquartered in London. Sisters of the order operate the Holy Family Hospital at Bongao on Tawitawi at the extreme southwest corner of the Philippines.

Simmons taught the sisters how to make the soap. Local community health workers formed a cooperative, which is manufacturing it in a converted operating room in the hospital. The product, called mosbar, is sold exclusively to the Philippine Government for distribution. The proceeds are used to employ community health workers full time.

The soap combines a specified blend of fatty acids with from 0.2 to 30 per cent by weight of an insect repeilent and from 0.2 to 5 per cent of a residual insecticide. The preferred repellent is N,N-diethyl-m-toluamide; the preferred insecticide is a synthetic pyrethroid. Mosbar is designed to be used as a toilet bar that leaves a film on the skin. The repellent in the film, according to the patent, wards off mosquitoes by fouling up their sensors. Mosquitoes not deflected by the repellent are killed on contact with the insecticide in the film. (Abstracted with permission from Chemical and Engineering News, 1 April 1991, p. 64. Copyright (1991) American Chemical Society)

New claims for Retrovir cost-effectiveness

Early administration of Wellcome's Retrovir anti-AIDS drug to asymptomatic HIV carriers would be as cost-effective as many other medical treatments, claims a study published in Annals of Internal Medicine.

Researchers at the University of Pennsylvania examined the cost and benefit of medication with low doses (500 mg) of the drug, showing that "early zidovudine therapy is one of the more cost-effective medical interventions for which cost-effectiveness ratios have been calculated". Despite its cost, put at $2,200 per year for asymptomatic patients, Retrovir has the potential, says the researchers, to yield a survival benefit by delaying the progression to advanced HIV diseases.

Using one model, which assumed early administration of the drug prolonged life for over nine years, they showed that the cost of early Retrovir averaged $6,553 per year of life saved.

The authors of the report estimate that the continuous investment in zidovudine therapy for the estimated 400,000 people in the US suffering asypmtomatic HIV infection and impaired immunity could be expected to yield 200,000 to 3.74 million years of life saved, depending on the model used. The cost would be $1 billion, not taking into account costs for treatment of side-effects, most commonly nausea.

The report is likely to be of benefit to Wellcome, which has been criticized in the past for the cost of the drug. It will also help in the active debate over whether Retrovir should be given to otherwise healthy HIV carriers. (Source: European Chemical News, 20 May 1991)

Genentech begins clinicals

Genentech (South San Francisco) has begun clinical trials at the University of California (Los Angeles) to test a monoclonal antibody for treatment of breast and ovarian cancers. The monoclonal is aimed at an oncogene - HER-2 - thought to be linked to the cancers. Genentech says laboratory studies show success in inhibiting growth of tumour cells in culture and increasing the tumour's susceptibility to the body's immune system. The UCLA clinical trials will be one of the first efforts to treat cancer by targeting a specific oncogene product, according to Genentech. The firm says the HER-2 oncogene is present in about one third of all breast and ovarian cancers. (Source: Chemical Week, 17 April 1991)

Structure of promising drug found

Several teams of scientists have unravelled the detailed molecular structure of a compound - FK506 - showing promise as a powerful immuno-suppressive drug and have found the structure of the protein - FKBP - to which it binds. Chemists from Cornell University (Ithaca, NY) and Harvard (Cambridge, MA) say they have determined the structure of FK506 and FKBP. Meanwhile, scientists at Vertex Pharmaceuticals (Cambridge, MA) report solving the three-dimensional structure of the FKBP binding protein. FK506 is made by Fujisawa Pharmaceutical. While still not approved for clinical use, the promising compound could be far more effective than currently available immunosuppresants for controlling the body's rejection of transplanted organs. It could also have applications in treating autoimmune diseases. Vertex - which used nuclear magnetic resonance spectroscopy and supercomputer-based modelling techniques to solve the structure - says it will use the information to rationally design highly specific drugs to treat organ transplant rejection and autoimmune disorders. Last October, Vertex signed an agreement with Chugai Pharmaceutical (Tokyo) to develop novel immuno-suppressive drugs. Chugai investment in the effort will total over $30 million. (Source: Chemical Week, 22 May 1991)

Promising Down's syndrome test

A screening test for Down's syndrome could identify nearly 90 per cent of cases.

A current method of screening for Down's syndrome is to offer aminiocentesis to pregnant women over the age of 36. Amniocentesis involves drawing off fluid from around the foetus, culturing cells in the fluid, and looking directly for the defect on chromosome 21, which is responsible for Down's syndrome.

For the new test, developed at St. James's University Hospital in Leeds, a woman only needs to give a blood sample. The hospital sends the woman a test tube and a microscope slide. She must then ask her family doctor to take some blood, fill the tube and smear blood on the slide.

The blood is subjected to the "triple" test, a technique developed at St. Bartholomew's Hospital in London. Women carrying a Down's syndrome foetus have higher or lower than normal levels of certain hormones and proteins. The triple test is an analysis of three such substances - the hormones human chorionic gonadotrophin and oestriol, and alpha-foetoprotein, which is produced by the foetal liver.

The combination of the levels of these three substances indicate the degree of risk of having a Down's baby. Women who give a positive test then have amniocentesis for a firm diagnosis. The triple test can identify around 60 per cent of Down's pregnancies.

The St. James's "triple plus" test goes further. Blood smeared on the slide is stained red to reveal an enzyme called urea-resistant neutrophil alkaline phosphatase (UR-NAP), which is produced by white blood cells called neutrophils. An analyst then scores each sample according to the amount and depth of colour taken up by neutrophils. The activity of this enzyme is higher than normal in Down's sufferers.

According to models, when the risk measured with UR-NAP is combined with the risk estimated from the triple test, detection will go up to 80 per cent and probably near 90.

Clinical trials of the triple test have not been widely performed by groups other than the team at St. Bartholomew's. However, at least one recent trial concluded that the triple test should replace screening based only on maternal age.

A better understanding of the enzyme and of Down's syndrome, and the development of a test that can be performed in the first three months of pregnancy are the priorities for research at St. James's. (Extracted from New Scientist, 25 May 1991)

Growth hormone treats cancer

US firm Bio-Technology General is testing the efficacy of its recombinant human growth hormone Biotropin in cancer patients.

In collaboration with the New York-based Memorial Sloan Kettering Centre, the company is trying to ascertain whether rhGH can prevent or reverse cachexia - the loss of weight and degeneration seen in cancer patients. Two thirds of patients who exhibit this syndrome die.

The company believes it is the first to investigate the effects of growth hormone on cancer patients with or without clinical manifestations of cancer cachexia.

In some patients, the syndrome is caused by intensive breakdown of complex molecules, such as proteins, to simpler ones, such as amino acids - a process known as catabolism. To date, attempts to treat this have failed. Recent studies have suggested that rhGH has distinct anabolic properties that could make it therapeutically useful. (Source: European Chemical News, 29 April 1991)

Synthetic success for yew tree "anti-cancer" drug

Cancer researchers experimenting with taxol - a substance obtained from the yew tree Taxus - received some good news when it has announced that taxol can be synthesized. Furthermore a doctor in Houston, Texas, reports that the natural drug has helped to control cases of breast cancer.

Taxol, which is extracted from the bark of the Pacific yew of the northwestern US, has already been tested on several types of cancer. At one trial at Johns Hopkins University, it reduced the size of ovarian tumours in almost half the subjects. Its potential has led to calls for its conservation, since it is often cut down and burned during logging of nearby trees.

Years of failed attempts to synthesize taxol cast doubt on its availability, says Saul Schepartz of the US National Cancer Institute, and conservationists grew concerned that rising demand could wipe out the tree. Some 100 trees are needed for one patient, or about 10,000 trees for one kilogram of taxol.

Last week, Florida State University announced that one of its professors had won a US patent on a synthetic process for taxol.

In Houston, Frankie Ann Holmes of M.D. Anderson Medical Center reported that new results show taxol may help to stem breast cancer. In a study taxol shrank tumours in over half of 25 women with advanced breast cancer, and three women experienced remission. Holmes warned that taxol is not a cure for advanced breast cancer, but, if further study bears out her results, taxol may help to control it. Meanwhile Rhône-Poulenc Rorer and Bristol-Myers Squibb are racing to develop cancer therapies with the help of yew trees. In each case, the companies are developing methods for synthesizing large quantities of yew chemical analogues which have demonstrated early promise in breaking solid tumours.

Rhône-Poulenc Rorer is focusing on Taxotere, while Bristol-Myers Squibb is working on the related compound Taxol. These compounds are present in yew barks but their isolation is difficult and results in tree deaths. Both firms are now working on syntheses which use a chemical from yew needles as a starting block. (Source: New Scientist, 1 June 1991 and European Chemical News, 3 June 1991)

Hoechst to produce Factor VIII

Hoechst has commissioned a pilot plant in Japan to produce test quantities of Factor VIII blood clotting agent using a gene-splicing process. The plant is located in a new recombinant DNA research complex at Kawagoe, near Tokyo.

The product will be used in clinical trials over several years before Hoechst considers taking a Factor VIII drug to market, a spokesman said.

The research complex is part of the company's Advanced Technology Laboratory opened in October last year. The Japanese facilities are designed to give Hoechst a third geographic R&D base complementing those in Germany and the US. (Source: European Chemical News, 24 June 1991)

AIDS vaccine success?

Medical researchers greeted reports of successful trials of an AIDS vaccine, rgp 160, with cautious optimism. Researchers said test results are preliminary and may be based on too small a sample of patients, but they also said the results indicate vaccines may improve AIDS treatment, or even yield an outright cure for the disease.

Army doctors at Walter Reed Army Institute of Research, Bethesda, MD, said an 18-month study showed that injections of rgp 160, a vaccine produced by MicroGeneSys Inc., Meriden, Conn., strengthened the immune systems of 19 out of 30 people infected with AIDS and stopped the number of their CD4 immune cells from declining.

Fifteen patients received six injections of the vaccine, and 13 of the patients were able to fight the disease more effectively. Another 15 patients were given three injections of the vaccine, and six of these patients also improved.

Researchers cautioned that the vaccine cannot be considered a cure for the disease yet. Too few patients were given the vaccine, and its effects could be temporary or it could merely be eliciting immune responses in patients having the healthiest immune systems. Researchers even cautioned that the vaccine may actually shorten patients' lives by overstimulating their immune systems and increasing the rate at which the virus attacks immune cells.

Yet researchers see the success of the vaccine, however limited, as an important step towards curing the disease. (Extracted from Chemical Manufacturing Reporter, 17 June 1991)

Cutting the cost of AIDS testing

Due to the high cost of materials used in AIDS testing, third world countries have been losing the battle against the spread of the disease. However, a researcher at the University of Texas Health Science Center at San Antonio has devised an inexpensive test which will enable doctors to diagnose those infected with the human immunodeficiency virus which causes AIDS, and guard against tainted blood supplies. Parts for the test include Teflon-coated glass slides which contain drop-size wells where standard laboratory substances are mixed with blood, a colorimeter (to determine the presence of AIDS virus), a photographic light meter and filter, and a flashlight. The test, when manufactured in a third world country, is expected to cost about 10 to 30 cents in materials and labour, compared to $3.50 in developed countries.

For more information, contact Cary Corbin, Susan Karkoska or Donna Butler, Dublin-McCarter and Associates, 112 E. Pecan St., Suite 1300, San Antonio, Texas 78205, Tel: 512/227-0221. (Source: BioBytes, June 1991)

Ajinomoto's curdlan sulphate "more potent" than AZT

Ajinomoto Co. Ltd., Tokyo, plans to run clinical trials by the year's end of curdlan sulphate as an AIDS therapeutic in the USA. It developed curdlan sulphate, a beta-1,3 glucan, in collaboration with Toshiyuki Uryu of the University of Tokyo's Institute of Industrial Science. In vitro experiments using infected lymphocytes showed that the compound inhibits activity of the AIDS virus soon after it infects the host cells. Preclinical tests in Japan suggest that curdlan sulphate exhibits more potent anti-HIV action than the reverse transcriptase inhibitor, azidothymidine (AZT), the sole AIDS therapeutic currently approved world-wide. Trials will begin within the year. (Source: McGraw-Hill's Biotechnology Newswatch, June 1991)

Supervaccine technology promises one-shot, multivalent protection

As reported in Nature and the Wall Street Journal, two teams of US researchers have successfully engineered "foreign" genes from viruses and bacteria into the BCG microbe, a bacterium widely used as a vaccine against tuberculosis. Tested in mice, the vaccine showed signs of developing full immunity. The conclusion drawn is that it may be possible to use a genetically engineered BCG microbe as a one-shot vaccine against several diseases simultaneously, including tetanus, diphtheria, hepatitis, Lyme disease, measles and malaria. The technique might also be used as a vaccine against AIDS.

The company, which seems best placed to benefit from these developments, is a small US biotechnology firm, MedImmune Inc., based in Gaithersburg, Maryland. MedImmune obtained rights to the BCG-based vaccine technology from three academic institutions - the Whitehead Institute at Massachusetts Institute of Technology (MIT), in Cambridge, Massachusetts; the Albert Einstein College of Medicine in New York; and Stanford University in Stanford, California.

The scientists said they had inserted genes from the AIDS virus, the tetanus microbe and 17 other viral, bacterial and parasitic microbes into the BCG bacterium. To get the genes to produce large amounts of their protein in BCG, the researchers tacked on pieces taken from genes known as "heat-shock protein" genes. These can produce large amounts of protein when subjected to some stress, such as heat. In this work they were used, for example, to coax tetanus or AIDS virus genes to produce their proteins in large amounts.

So far, however, the researchers are being cautious when asked how quickly their findings will translate into commercial vaccines. "Although the immune responses reported here are encouraging", the Einstein-Pittsburg-MedImmune's team said, "Much remains to be learned before recombinant BCG can be perfected as a multivaccine vehicle". MedImmune's work on using the BCG microbe for a vaccine against AIDS is being funded by Merck & Co., while the Lyme disease and hepatitis B work is being funded by Connaught

Laboratories Inc., based in Swiftwater, Pennsylvania. (Source: Biotechnology Bulletin, Vol. 10, No. 5, June 1991)

Transgenic swine yield human blood

DNX Corp., Princeton, N.J., reports that the company has created a transgenic pig that expresses recombinant human haemoglobin. The company has filed patents covering the products and processes and expects to submit an IND application to the FDA in 1992. It hopes to be able to start clinicals in late 1992 or early 1993 for the putative human-blood replacement. Currently, DNX, a private company specializing in transgenic animals, has just three of the pigs that produce the blood substitute. The firm is awaiting the birth of others. Each pig, according to company estimates, should annually yield 20 units of haemoglobin. (Source: McGraw-Hill's Biotechnology Newswatch, July 1991)

Drug targets a tough leukaemia

Doctors have successfully treated a small group of leukaemia patients using a new therapy that prods unruly cancer cells to mature into normal cells. Conventional cancer drugs attempt to kill malignant cells, but their aim is so poor that they are often ineffective and destroy many normal cells, producing notorious side-effects.

In a new study, patients treated with a new type of medicine related to vitamin A routinely achieved remission from a severe form of leukaemia with so few side-effects that some could be discharged from the hospital in days.

Most exciting, as the patients recovered, doctors were able to watch the cancerous cells in their bloodstream slowly take on the appearance of normal cells.

In the test tube, scientists have been able to use vitamin A derivatives, called retinoids, to force cancer cells to develop into normal cells for over a decade.

But "this is the first time we have been able to consistently achieve the differentation of cancer cells in patients", said Dr. Michael Hawkins, chief of the Investigational Drug Branch at the National Cancer Institute. The new treatment, called differentiation therapy, is a "highly promising field", he said.

The 11 patients in the study had a rare but lethal disease called acute promyelocytic leukaemia. Among patients treated in the study, 80 per cent achieve remission with usual cancer drugs; with the new treatment the rate appears to be at least equal.

Leukaemia cells are immature blood cells that multiply uncontrollably and eternally, since they have not developed a sophisticated regulatory apparatus.

In doing so they take over the bone marrow and spill into the blood, squeezing out the normal blood cells, which do not divide once they are mature. Lacking the usual complement of normal blood cells, patients suffer from infections, anaemia and bleeding.

Scientists were at first surprised that the new drug, called all-trans-retinoic acid, was so successful in humans, since a closely related compound that had worked in the test tube had proved ineffective against cancer in man. (Extracted from International Herald Tribune, 23 May 1991)

Celltech's new anti-TNF antibody

Celltech has announced a new, second generation recombinant antibody, incorporating extensive human structural elements, for the treatment of septic shock. Dr. Mark Bodmer, head of immunomodulation research at Celltech, explained that trials are expected to confirm a higher degree of therapeutic efficacy than had been previously achieved with anti-TNF antibodies.

The novel antibody, designated CDP571, incorporates elements of an antibody which has been shown to be up to 100-fold more effective than previous antibodies in removing tumour necrosis factor (TNF) from the blood in laboratory experiments.

Recent scientific evidence indicates that the release of TNF in human septic shock may be a major cause of mortality. The fact that the new Celltech antibody is fully humanized means that it will not produce the kind of immune system reaction associated with murine antibodies. It is also anticipated that this antibody will offer a prolonged half-life in patients' circulation.

Celltech addressed three issues in developing its second generation anti-TNF antibody:

- The starting mouse antibody must be of the highest possible potency against human TNF. The starting antibody for Celltech's CDP571 was CB0010, which was shown to be 100-fold more effective at removing TNF from the blood in animal models than the reference antibody CB0006.

- The antibody must be engineered to be as human as possible in structure while retaining the full biological activity of the starting antibody. The recently described technique of CDR grafting allows mouse-derived specificities to be put onto substantially human-like antibodies. CDP571 has been engineered in this way and has the same ability to bind TNF as its CB0010 parent.

- The non-binding, or constant, parts of the antibody must be chosen to be the most effective at neutralizing the activity of TNF in the body. Human antibodies exist in various different forms, or isotypes. The antibody engineering process allows the selection of the most suitable. CDP571 is an IgG4, which Celltech has shown to be optimal for blocking the effects of TNF *in vivo*.

Details from: Celltech Group plc, 216 Bath Road, Slough, Berkshire SL1 4EN or on 0753-77866. Fax: 0753-36632. (Source: Biotechnology Bulletin, Vol. 10, No. 5, June 1991)

Prostaglandins from yeast could lower cost

"Far-reaching implications for the pharmaceutical industry and science" are forecast by Johan Kock of the University of the Orange Free State (Bloemfontein, South Africa), following his finding of evidence for the existence of pharmacologically active prostaglandins in yeast.

Prostaglandins are becoming widely used in clinical practice for purposes as diverse as inducing labour and inhibiting the aggregation of blood platelets. Their natural roles in mediating inflammatory responses and in acting as hyperalgesics suggest that they and the closely related prostacyclin may well find other applications in future. But they remain extremely costly, because of the complex chemical syntheses necessary in their manufacture. Production by yeasts, grown on inexpensive substrates, could result in a dramatic fall in their price.

In scientific terms, the new discovery raises the intriguing question of the role of prostaglandins in the metabolism of micro-organisms. It may also offer a system to be used in studying more closely the biochemical basis of their diverse and potent effects in human physiology. The common threads behind certain of these effects are the control of adenylate cyclase and cyclic AMP levels. A similar adenylate cyclase system, which is involved in controlling growth and sexual reproduction, has been demonstrated in at least one yeast, Saccharomyces cerevesiae. (Extracted from Bio/Technology, Vol. 9, July 1991)

New delivery system for interferon

In collaboration with the Swiss pharmaceutical company Roche, at the Macromolecular Clinical Research Center in South Korea, Cortecs of Isleworth, UK has developed a drug delivery system that could permit interferon to be taken orally. Protein-based drugs such as interferon and insulin have to be injected - if they are swallowed they are digested in the stomach in the same way as other proteins. The scientists have demonstrated that specially treated interferon could pass through the gut wall into the bloodstream without being digested. To achieve this, the interferon was wrapped in a lipid envelope. Since fat passes relatively unchanged through the stomach, the drug was protected, so it could carry out its medicinal function. (Source: Genetic Engineering News, May 1991)

Test for toxins

At the National Hospital in Oslo (Norway), a test has been developed that indicates the presence of toxins or abnormalities in human cells exposed to environmental poisons. The work was led by Professor Egil Jellum at the Institute of Clinical Biochemistry. He used two-dimensional electrophoresis to trace the effect of the poisons on living human cells in a culture. So far white blood cells or cells raised in the absence or presence of the agents being tested have been examined. If the agents have an effect on the DNA, RNA or components of protein synthesis, a deviation in protein patterns can be registered. (Source: Genetic Engineering News, May 1991)

Livestock applications

Integrated agriculture-aquaculture systems

A higher net income can be obtained from integrated rice-fish farming than from rice monoculture. Apart from raising the production potential of the land, the fish can also function as insectivorous biological control agents for rice pests. Intensified cropping and chemical inputs have degraded many irrigated rice ecosystems. Growing rice and fish may facilitate the adoption of low chemical input practices. Small fishponds on irrigated and rainfed rice farms, whether isolated from the paddy fields or connected to them, can therefore be a highly productive asset for the farmer. Cooperation between ICLARM, the Freshwater Aquaculture Center (FAC) of Central Luzon State University (The Philippines), the International Rice Research Institute (IRRI) and national rice-fish research programmes within the IRRI-based Asian Rice Farming Systems Network (ARFSN) generated several collaborative projects in India, Indonesia and Thailand. Experiments in these countries showed that increases in net returns over rice monocropping occurs in all situations. Tilapia, common carp and silver barb were confirmed to be the most appropriate species for rice-fish systems.

These encouraging tests have resulted - although more investigations and testing of different systems are needed - in an increasing adoption of the technique in Indonesia and Thailand with involvement of governments and NGOs. The Government of Indonesia, for instance, has announced a plan to expand rice-fish farming in West Java by 20,000 hectares and in North Sumatra by 2,500 hectares. (Source: Biotechnology and Development Monitor, No. 7, June 1991)

Fish gene banks and gene transfers

Conservation of genetic resources is critical to aquaculture. Wild stocks of fish and shellfish have been and continue to be the principal gene banks for aquaculture. Future genetic material for aquaculture may be obtainable only from natural reservoirs of indigenous species, but wild populations are under threat of irreversible change or loss from factors such as fish and water transfers and habitat disturbance.

There are mainly two methods of fish gene banking: cryopreservation and broodstock collections, both hardly yet in practice. Cryopreservation refers to preservation through freezing. Because it is not yet possible to freeze eggs or embryos of any fish, this method is, as a tool for fish gene banking, only applicable to sperm. Broodstock collections refer to the maintenance of living fish in separate ponds. The Philippine based International Center for Living Aquatic Resources Management (ICLARM) has recently established a broodstock collection of one tilapia species, the Nila tilapia.

Tilapias are African fish that are used in warm-water aquaculture throughout the world. Some species, such as Nile Tilapia, are highly versatile, herbivorous-microphagous feeders, well-suited to low technology farming systems in third world countries. Tilapia culture has made great advances in the last 10 years in some Asian countries, including the Philippines, Thailand and China, but is based on a very narrow genetic base from a few small founder populations. African countries hold the global wealth of tilapia genetic resources.

In 1988 and 1989, "tilapia germplasm" from Egypt, Senegal, Ghana and Kenya was shipped to the Philippines. In the ICLARM ponds, a collection of strains from African and Asian stocks has been established to develop genetically improved strains

for distribution to national broodstock distribution channels. ICLARM sees its future role in (a) developing methodologies for breeding programmes which can be undertaken by national governments, and (b) maintaining a register of wild stocks, while promoting in situ preservation of important stocks in their natural habitats. (Source: Biotechnology and Development Monitor, No. 7, June 1991)

Agricultural applications

Fast-breeding pea keeps disease on the run

Farmers throughout India, Africa and the Caribbean may soon be able to buy a superior, hybrid variety of pigeon pea, a pulse that provides a major source of protein for millions of people in semi-arid zones. People throughout these regions consume cooked dishes - usually called dahl in India - made from pigeon peas that have been peeled and split.

The Indian Government became the first in the world to approve the sale of a pigeon pea hybrid. India grows nine-tenths of the world's pigeon peas, but must still import other varieties of pulse to meet domestic demand.

The Government expects the hybrid varieties to begin reaching farmers within five years, once local seed producers have scaled up production of the hybrids. Parent varieties from which the new pigeon pea, code-named ICPH 8, was produced will provide breeders throughout the world with genetic material from which to make improved hybrids.

The International Crops Research Institute for the Semi-Arid Tropics, a non-profit-making organization based at Hyderabad in Andhra Pradesh, India, developed the hybrid. The Institute says that it resists the fungal and viral diseases which usually ravage ordinary varieties of pigeon pea, causing $100 million worth of damage each year. It owes its hardiness to the fact that it only takes 100 or so days to mature.

Conventional varieties of pigeon pea may take 200 days or more for reproduction, or are perennial. These long periods before maturity give fungal disease such as fusarium wilt and viral disease such as sterility mosaic time to establish themselves and wipe out the crop. The rapidly maturing hybrid does not give these diseases time to take hold.

The new hybrid also increases yields by 30 to 40 per cent because each plant produces more pods and there are more peas per pod. It is also more tolerant of abnormally wet and dry conditions.

An international multidisciplinary team, led by Kul Saxena, a plant breeder at the Institute, faced formidable problems when setting out to cross-breed pigeon peas. Under natural conditions, cross-breeding cannot be controlled because it occurs at random between the plants of a population. Sometimes the plants fertilize themselves.

The trick with pigeon peas was to select from the Institute's gene banks natural variants that were incapable of producing pollen. These so-called "male-sterile" plants could only regenerate themselves by cross-breeding with normal, fertile male varieties. And offspring of plants incapable of producing pollen were obviously hybrids because the male-sterile parent line was incapable of regenerating itself.

The Institute tested the first nine hybrids it produced in 1977, and more than 1,000 more have been tested since then. Of these, ICPH 8 had the best characteristics and underwent further evaluation to satisfy rigorous criteria laid down by the Indian Government's Central Varietal Release Committee.

Scientists at the Institute worked alongside researchers from the All India Coordinated Pulses Improvement Project to test it in 100 field trials in several climatic zones of India. Mahyco, an Indian seed company based in Maharashtra, is interested in producing and selling the hybrid seed. Material has also been sent to Kenya for use in agro-forestry and crop rotation projects. (Source: New Scientist, 13 July 1991)

Plantech to register virus-resistant rice

Plantech Research Institute, the Tokyo-based research organization established by Mitsubishi Kasei Corp. and Mitsubishi Corp., has applied to Japan's Ministry of Agriculture, Forestry and Fisheries to register Yumei Kahori, a new breed of rice resistant to the rice stripe virus (RSV). Plantech developed Yumei Kahori by repeated selection of vigorous, RSV-resistant plants regenerated from protoplasts formed from cells of the existing Tsukinohikari breed of rice. The new breed has improved growth characteristics, a higher grain yield, and a more palatable flavour compared with the parent. It is undergoing field cultivation tests throughout Japan. (Source: McGraw-Hill's Biotechnology Newswatch, June 1991)

Mycogen gets EPA approval for pesticides

The US Environmental Protection Agency has approved for commerical sale Mycogen Corporation's genetically engineered bioinsecticides. "MVP" and "M-Trak" are the first genetically engineered pesticides to be approved. "MVP" controls caterpillar insects including the diamond back moth that attack cabbage, broccoli, lettuce and other crops. "M-Trak" controls the Colorado potato beetle which attacks potato, tomato and eggplant. Both products use recombinant DNA technology with Mycogen's "CellCap" encapsulation system.

"MVP" and "M-Trak" are the first of many commercial products based on the "CellCap" encapsulation system that Mycogen plans to market to control pests.

"CellCap" encases these products much like the gelatin capsule for medicine. The active ingredient in both products are proteins produced by a naturally occurring bacterium Bacillus thuringiensis (B.t.). Using recombinant DNA techniques, Mycogen researchers insert the gene that produces B.t. toxin into another naturally occurring bacterium. After mass fermentation, the recombinant bacteria are killed with a process that stabilizes the microbial cell wall forming a protective capsule around the insecticidal protein. When applied to crops, the material kills leaf-eating insects as they ingest the toxins. (Source: Chemical Market Reporter, 8 July 1991)

Kirin markets tissue-cultured asparagus

Kirin Brewery Co. Ltd., Tokyo, has begun supplying vegetable markets with asparagus harvested from plants grown by tissue culture. Kirin developed the technology to culture TX86, a new breed of male sterile asparagus developed by Hokkai Can Co. Ltd., Tokyo. TX86 produces asparagus shoots with soft stalks containing little unusable tough fibrous tissue. They yield a 40-50 per cent larger harvest than asparagus plants grown by conventional methods. Kirin plans to supply only 500 kgs of its Spring Valley brand of asparagus in the first year. (Source: McGraw-Hill's Biotechnology Newswatch, June 1991)

Industrial microbiology

Biotech role in industry grows

By the year 2000, 20 per cent of pharmaceuticals will be biotechnological products.

This prediction comes from a paper on the promotion of competitiveness in the growing field of biotechnology.

Presented by the European Commission (EC), this major strategy document estimates that 800 companies are already using biotechnology in Europe, 1,000 in the US and about 300 in Japan. Latest estimates put world sales at ECU 26-41 billion by the year 2000.

It cites insufficient patent protection. Community market fragmentation and a bad public image are areas that would inhibit the sector's competitiveness. (Source: Manufacturing Chemist, June 1991)

Towards "living computers"

Conducting proteins, such as those involved in photosynthesis, could be used in computers and optical devices within 10 years, according to Stephen Sligar of the Beckman Institute at the University of Illinois. These proteins can transfer electrons without the loss of heat which typically limits the size of such devices, Sligar says.

Sligar and his colleagues have succeeded in controlling the arrangement of conducting proteins on a surface - a "small first step" towards using genetically engineered proteins as sensors and computer chips. Recent work has focused on recognition and electrostatic interactions between cytochromes c and b_5. Sligar's group has applied for a patent on their method of modifying protein linker sites, which connect the molecules to a surface.

Sligar says his group is trying to give rise to a surface with a totally ordered array and adds, "we're beginning to succeed". Eventually, they hope to assemble the molecules in two dimensions, and to incorporate more than one protein at a time into an array. (Source: Chemistry & Industry, 6 May 1991)

Microbe maintenance

A new generation of biological agents is being developed to challenge the traditional chemical methods for wood preservation. Wood scientists are looking for the fungi or bacteria that could keep decay-causing microbes at bay.

According to Alan Bruce, of the Dundee Institute of Technology, there has been a significant shift in attitude towards biological control by the big wood preservation companies over the past few years. While creosote, pentachlorophenol, chromated copper arsenate and other traditional chemicals continue to dominate the market world-wide, concerns are being raised about their potential toxicity.

But the development of an effective system for biologically protecting wood is proving a tough nut to crack. It seems unlikely that in the short term any formulation will be developed offering the same degree of protection as the chemicals against the spectrum of decay-causing organisms.

The protecting organisms must be able to live on the wood without altering the structurally important lignocellulose matrix; they must be able to survive on the soluble sugars within the wood, or be supplemented with nutrients during inoculation. Given that wood products may need protection for up to 40 years, providing residual protection is a big challenge.

"Initially the uses of bioprotection are likely to be quite specialized, with control agents being targeted against a limited range of decay organisms", Bruce says. He has been studying creosoted electricity distribution poles, where one fungus, Neolentinus lepideus, is responsible for the bulk of decay. Dry rot, which is caused by Serpula lacrimans, is also a possible candidate for biocontrol. (Source: Chemistry & Industry, 15 July 1991)

Lactic acid polymer soon to be commercialized

Biodegradable polymers produced from lactic acid are close to commercialization by Ecochem, a joint venture between Du Pont Chemicals and food company ConAgra. A pilot plant is scheduled for start-up later this year, with a world-scale unit targeted for operation by late 1994.

The polymers, known as polylactides, are made from renewable resources such as cheese whey and corn. They degrade into water and carbon dioxide in the presence of moisture, air and common bacteria.

Ecochem is initially targeting uses in packaging products made of paper. The polymer can be used as a coating, or to formulate inks and adhesives. When the pack is recycled, the polylactide can be "dissolved" away, taking with it any printing ink, adhesives and toners, etc. This enables the paper to be recycled into a higher quality use than currently available.

The first commercial trials with the polymers are expected early next year. Trials of recyclability of packaging have so far proved very promising. Ecochem expects to offer polylactides commercially to paper, printing, packaging and speciality product companies by 1994.

The key to the development is the high efficiency of Ecochem's proprietary lactic acid technology and the high purity of the product. The company is currently building a $20 million lactic

acid facility in Adell, Wisconsin. (Extracted from European Chemical News, 24 June 1991)

UK genetic soap

A washing powder containing a genetically engineered lipase enzyme went on sale for the first time in the UK in May 1991. The enzyme is an ingredient in Lever Brothers' compact powder, Radion Micro.

Lever says the advantage of using the genetically engineered lipase, produced by Novo Nordisk, is that it is produced by a modified micro-organism that generates the enzyme in much larger quantities than the original micro-organism. Lipase enables the removal of fatty, oily and greasy stains from fabrics at low temperatures.

Lever says the current fermentation technology now makes it possible for the lipase to be produced in commercial quantities. It points out that the enzyme is chemically identical to that from the original micro-organism and does not classify as a new substance under EC regulations.
(Source: European Chemical News, 20 May 1991)

Extraction and bioremediation

Sulphur bacteria leach metals

The Dutch Organization for Scientific Research (TNO) has demonstrated, in a partly EC-funded project, that sulphuric acid-producing micro-organisms can be used to remove metals from contaminated solid wastes and soils.

The TNO environmental research group carried out a study to determine whether metal-contaminated wastes could be cleaned to meet the requirements laid down by Dutch law, using mixed cultures of Thiobacillus ferrooxidans that produce sulphuric acid.

Hans van der Steen of TNO said this type of microbial culture does not need expensive growth media and so results in low processing costs. The group has used the same species to remove sulphur from coal in previous studies. The sulphur is used as an energy source.

In the study, several types of soils and wastes from the priority list of the Dutch environment ministry were selected, including 10 industrial solid waste streams and two contaminated soil samples.

The study found that most metals, such as zinc, cadmium, arsenic, copper and nickel, were leached well - up to 98 per cent - in the presence of sulphuric acid. However, the efficiency of the process with chromium was much lower (6-7 per cent) although the researchers point out that chronium levels in the sample used were exceptionally high.

The group concluded that soil and solid wastes can be brought to within required standards, except for lead. High enough quantities of heavy metals are removed to enable deposition of waste materials. (Source: European Chemical News, 29 April 1991)

Bioremediation of soil spills favoured

In a recent background paper titled "Bioremediation for Marine Oil Spills", the US Office of Technology Assessment said using micro-organisms to accelerate breakdown of oil spills into less harmful products has some promise. Because of research conducted following the spill by the Exxon Valdez in 1989, much more is known now about the possibilities and limitations of such bioremediation. OTA says fertilization appears to be the most promising method. Nutrients such as nitrogen and phosphorus are added to the oil to permit naturally occurring micro-organisms to grow faster. Seeding is the other method, and it involves adding more micro-organisms to the spill, but is usually limited by the availability of nutrients. From the Valdez experience, OTA says bioremediation seems to work better on beaches than it does in the open sea. Copies of the background paper can be obtained from the Superintendent of Documents, US Government Printing Office, Washington, D.C., 20402-9325. Stock number is 052-003-01240-5 and the price is $2.00. (Reprinted with permission from Chemical and Engineering News, 10 June 1991, p. 21. Copyright (1991) American Chemical Society)

Energy and environmental applications

Environment charter: Industry signs on for sustainable development

A new charter on sustainable development has been launched by the International Chamber of Commerce.

The charter, so far signed by 200 of the world's leading companies and business organizations, is a voluntary agreement on environmental policy, aimed at promoting the environment as "one of the highest corporate priorities" - a "moral commitment", according to ICC president Joseph Connor. It provides the set of principles that the business community needs in all collective approaches on environmental matters", he said.

Signatories include most of the large North American and West European oil and chemical firms, plus an assortment of other manufacturing companies, banks and insurance companies. The glaring omission from the developed world was Japan, apparently due to delays in approving corporate policy statements.

The charter is less far-reaching than the chemical industry's Responsible Care programme already adopted in many countries. Furthermore, the charter will operate on a entirely voluntary, self-policing basis.

The business charter for sustainable development:

- To recognize environmental management as among the highest corporate priorities and as a key determinant to sustainable development;
- To integrate these policies fully into each business;
- To continue to improve performance, taking into account technical developments and community expectations; and to apply the same criteria internationally;
- To educate, train and motivate employees to conduct their activities in an environmentally responsible manner;
- To assess environmental impacts before starting a new project;

- To develop and provide products or services that have no undue environmental impact and are safe, that are efficient in their consumption of natural resources, and that can be recycled, reused, or disposed of safely.

- To advise, and where relevant educate, customers, distributors and the public in the safe use of products;

- To develop, design and operate facilities and conduct activities taking into account the efficient use of energy and raw material;

- To conduct or support environmental research.

(Source: Chemistry & Industry, 6 May 1991)

The Bioindustry Association: Is biotechnology sustainable?

As the trade association for biotechnology in the UK, the BIA is planning to review the environmental implications and applications of biotechnology. A working group, chaired by Biotechnology Bulletin editor John Elkington, is being formed to consider how the biotechnology industry can contribute to the world-wide drive for "sustainable development".

The World Conservation Strategy, published in 1980 by the United Nations Environment Programme (UNEP) and two conservation bodies (IUCN and WWF) introduced the phrase "sustainable development" - that is, economic development that respects and protects the natural resources on which much wealth creation depends. The concept was further developed in the UK response to the Strategy - The Conservation and Development Programme for the UK, published in 1983 and in the 1987 report of the World Commission on Environment and Development, Our Common Future. Better known as the Brundtland Report, because the Commission had been chaired by Norwegian Prime Minister Gro Harlem Brundtland, Our Common Future noted that biotechnology would bring threats and opportunities.

The Brundtland Report's conclusions were based on a study of the environmental implications and applications of biotechnology published in 1986 by the US World Resources Institute - Double Dividends: US.

Biotechnology and Third World Development. The WRI report was written by John Elkington, who had also written the industry component of the UK response to the World Conservation Strategy and had identified biotechnology as potentially one of the building blocks for a sustainable economy.

Elkington, founder-editor of Biotechnology Bulletin since 1982, had been involved in the environmental field since the early 1970s and had visited scores of biotechnology companies in Europe, the US and Japan during the 1980s. "We tried to get the UK biotechnology industry interested in the environmental agenda in the early 1980s", he recalls, "but most companies felt that these issues were remote at best. It has only really been in the last couple of years that we have seen the biotechnology industry waking up to the significance of the greening of public and political opinion." As a director of a leading environmental consultancy, SustainAbility, founded in 1987, Elkington had also co-authored a book which had helped increase the environmental pressure on business. The Green Consumer Guide was published in 1988 and has since sold a million copies. He is convinced that the environmental pressures on the biotechnology industry can only intensify in the 1990s.

"The recent controversies about BST and recombinant yeast are just the beginning", he says. "The biotechnology industry, or at least those companies that use biotechnology, have an enormous opportunity in this new area, but only if they get actively involved in the debate. Among the leaders in this respect are companies like Novo-Nordisk and Shell, which has linked up with Mycogen on the biopesticides front. The BIA initiative should provide a useful opportunity to get many more companies involved.

The BIA, formed in February 1989, was built on the foundations formed by the Association for the Advancement of British Biotechnology (AABB). Incorporated in 1985, the AABB had aimed to promote the development of biotechnology in the industrial, academic and service sectors. The BIA, by contrast, focuses specifically on the promotion of the commercial interests of companies actively involved in biotechnology in the UK.

The BIA's overall objectives are to:

- Provide the national forum for identifying and informing members of key issues affecting the development of biotechnology in the UK;

- Formulate strategies that promote the interests of members in national, European and international markets, including influencing Government investment in and grants for biotechnology;

- Develop and exploit links with policy-making institutions, particularly in the UK, Europe, USA and Japan;

- Promote the international commercialization of UK biotechnology;

- Promote a positive public perception of biotechnology;

- Promote manpower supply and training for biotechnology.

The BIA already has a number of expert committees covering: regulatory affairs; biotechnology finance; manpower, education and training; bioprocessing, manufacturing and technology; and public awareness and information. "The invitation to chair the new Working Group on Biotechnology, Environment and Sustainable Development came from BIA director Louis da Gama early in 1991", says Elkington. "It didn't take me long to make up my mind. We are now asking interested companies to get in touch." Further reports will appear in Biotechnology Bulletin as the initiative develops. Further information is available from: Louis da Gama, Executive Director, BioIndustry Association, 1 Queen Anne's Gate, London SW1H 9BT or on 071 222 2809. Fax: 071 222 8876. Or John Elkington, Director, SustainAbility Ltd., The People's Hall, 91-97 Freston Road, London W11 4BD or on 071 243 1277. Fax: 071 243 0364.
(Source: Biotechnology Bulletin, Vol. 10, No. 3, April 1991)

Chemical-biological approach to oil spills

A combined chemical-biological oil-spill clean-up technique has been developed by International Science Centre, a contract R&D firm in Bubendorf, Switzerland. The chemical treatment converts the oil carpet, on sea water or fresh water, into a non-toxic, water-soluble microemulsion using special emulsification agents. The biological treatment consists of selected microbes that degrade the oil and emulsifiers in the microemulsion. According to International Science Centre, the degradation occurs a billion times faster than with crude oil floating on an aqueous surface. During degradation of the microemulsion, the firm says, all components are converted into non-toxic biomass, without the generation of any carbon dioxide. (Reprinted with permission from Chemical and Engineering News, 1 April 1991, p. 28. Copyright (1991) American Chemical Society)

Bacteria take on groundwater

Cornell University (Ithaca, NY) researchers report a method that provides the first evidence that underground bacteria are actively degrading organic pollutants in groundwater. By measuring levels of protozoa - which feed on the bacteria - the scientists indirectly determined underground bacterial activity and growth. They found that organisms near a buried coal-tar waste site were breaking down organics leached into a nearby aquifer. The Cornell scientists say the finding suggests it could be feasible to predict and manage indigenous underground microbiological processes as an inexpensive means of purifying groundwater. (Source: Chemical Week, 22 May 1991)

Bacteria can directly reduce uranium

Researchers at the US Geological Survey in Reston, Virginia, have shown unequivocally that bacteria can directly reduce soluble uranium (VI) to insoluble uranium (IV). In fact, thermodynamic calculations performed by another group indicate that bacteria that normally obtain energy by reducing iron (III) to iron (II) can potentially get twice as much energy by reducing U(VI) to U(IV). The role of bacteria in reducing uranium has generally been thought to be indirect. For example, microbial metabolism produces reducing agents such as hydrogen sulphide that may go on to reduce U(VI) in the environment. The Reston researchers, Derek R. Lovely, Elizabeth J. P. Phillips, Yuri A. Gorby, and Edward R. Landa, have shown that two Fe(III)-reducing micro-organisms live quite well on uranium instead of iron. In fact, the bacteria reduces U(VI) much faster than does hydrogen sulphide. These observations suggest that microbial reduction of U(VI) could account, at least in part, for the presence of U(IV) in aquatic sediments and the distribution of some uranium ores. And it may be possible, the researchers suggest, to mobilize bacteria to clean up aquatic environments contaminated with uranium. (Reprinted with permission from Chemical and Engineering News, 8 April 1991, p. 45. Copyright (1991) American Chemical Society)

Bugs get tough on PCBs

Scientists at GE Research and Development Center (Schenectady, NY) have shown that anaerobic bacteria can strip off chlorine atoms from the inner - ortho - position on polychlorinated biphenyls (PCBs) molecules. While anaerobic bacteria are generally far more effective in attacking highly chlorinated PCBs than are aerobic organisms, GE says this is the first report of such bacteria removing the ortho chlorine atoms. While aerobic bacteria are usually limited to degrading PCBs with 1-3 chlorines, Daniel A. Abramowicz, manager, environmental technology programme, says the finds mean all chlorines on PCBs are now vulnerable to anaerobic bacterial attack. It is particularly important, he adds, because it suggests anaerobic bacteria could be used to completely eliminate PCBs in aqueous sediments. GE is preparing a field test this summer to study the bacterial degradation of PCBs. Based on the recent findings, says Abramowicz, the field test could depend on the use of anaerobic organisms. (Source: Chemical Week, 22 May 1991)

Biodegradable absorbent for oil spills

Made of incense cedar, absorbent "OIL TRAPPER" offers a totally organic and biodegradable way to contain oil spills. It is an industry by-product that uniquely functions as a superior oil absorbent while repelling water, says the company. This product recovers oil in all forms ranging from sheen to mousse, floats even when fully saturated with oil for reuse, and allows easy removal of absorbed oil. End-users include offshore oil operations, ships, fire departments, and municipalities. For further information contact: Howard H. Hanisch, Sales and Marketing Systems International, Inc., Dept. CN, 510 Hartbrook Dr., Hartland, Wisconsin, 53029-1415 USA. Tel.: (414) 367 2994. Fax: (414) 367 6774. (Source: Commercial News USA, No. 6, July 1991)

Sewage into trees

An Indian scientist has developed a way of growing trees on raw sewage that could turn sewage lakes around the country's cities into forests and prove a cheap and profitable way of treating effluent.

At the Karnal-based Central Soil Salinity Research Institute (CSSRI), soil-chemist Ranbir Chhabra grows trees on ridges along shallow trenches receiving sewage water. Depending on season and plant type, up to one million litres of sewage per day per hectare (90,000 gallons per day per acre) can be disposed of. The trees act like bio-pumps and quickly absorb sewage water.

Chhabra has successfully grown eucalyptus and poplars. A crop of five-year-old poplars earned $3,750 for the Institute. According to Chhabra, heavy metals such as lead and cadmium are not accumulated in the soil of sewage water plantations and the land can safely be used for agriculture. Says N.T. Singh, director of CSSRI: "It is a clean system of forestry from dirty water."

Sewage treatment is costly and hundreds of millions of litres of raw sewage are channelled into the rivers of India every day. Farmers divert free-flowing sewage to their farms and use it for growing vegetables, a dangerous practice as vegetables absorb harmful substances from effluents. Warns Chhabra: "Raw sewage should only be used for growing non-edible crops such as trees."

So far, the technique has been used in locations around Haryana and Punjab. (Source: Development Forum, July/August 1991)

Tethered bacteria wash Sydney's waste

An Australian process which could revolutionize the treatment of domestic and industrial effluent has undergone successful trials in Sydney, a city which is struggling to clean up its urban coastline.

The pilot plant, built by a company called Memtec based in Windsor, New South Wales, processes effluent in one-tenth the time of a conventional plant and generates virtually no smell. The water it produces is just as clean as that from teritary treatment, the most thorough form of conventional treatment available. The water is also considerably cleaner than water undergoing conventional secondary treatment and disinfection, which is the norm.

Tony Fane of the Centre for Membrane and Separation Technology at the University of New South Wales unveiled the results at a symposium at Valletta in Malta on desalination and water re-use. Fane, who worked on the project alongside Warren Johnson and colleagues at Memtec, explained that the two key elements of the system are a new type of bioreactor and cartridges that contain membrane filters.

Conventional bioreactors, known as "activated sludge" units, support bacteria that degrade organic compounds and other contaminants in the sewage. These pollutants are often toxic and many of them deplete water-borne oxygen that aquatic life needs for survival.

Memtec's bioreactors support similar bacteria; the difference is in design. In the activated sludge process, the bacteria and the sewage swirl around in a huge tank from which air, which kills the bacteria, is excluded. The cycle takes around five hours, and then the effluent has to be transferred to a settling tank to separate sludge from the cleaned water.

In Memtec's bioreactor bacteria are anchored to a solid support formed of purpose-built particles. Because the bacteria are immobilized, there is no need for a settling tank, so treated effluent passes through to the next stage in one-tenth the time and is much clearer of solid matter.

Fane says that the other key element is the microfiltration cartridge which receives and polishes water from the bioreactor. The filter has a patented self-cleaning process for keeping the tiny membranes in the cartridge free from blockage by solid material in the effluent. Air is blown backwards through the system to clear any obstructions in the hair-like hollow membranes, which are packed into the cylinder in bundles and have pore sizes less than a micrometre across.

As a result of the short reactor residence time, the absence of large settling areas and the compact nature of the microfiltration system, Memtec's process has a much smaller "footprint" than alternatives said Fane. The pilot plant occupies only one third the area of the conventional Cronulla sewage treatment plant in Sydney, where the tests took place.

Fane explained that this would allow industrial plants to build on-site treatment works for effluent that they would otherwise discharge raw to municipal sewerage systems. (Source: New Scientist, 4 May 1991)

Water treatment

With the impending enactment throughout Europe of the European Commission's (EC, Brussels) directive on nitrate levels in drinking water, opportunities for biological denitrification abound. Researchers in Germany, which already has tight limits on nitrate levels, are developing bioreactors to take advantage.

The Kernforschungsanlage (KFA, Jülich) has developed a novel pilot-scale bioreactor for nitrate removal - called the Roto-Bio-Reactor (RBR) - that is marketed in Germany by Ambs-Apparatebau (Emmendingen, Germany). RBR, with a volume of 1,700 litres, is made up of a column containing denitrifying bacteria immobilized on ceramic beads. It is continuously axially mixed, thereby avoiding the problems of clogging and channeling that have dogged other column reactors. RBR, which has run continuously for over a year, treats 120,000 litres of water a day, reducing nitrate levels from 65 mg/l to 5 mg/l. It also reduces microbial contamination to permitted limits. Success with the reactor led to a larger-scale project for water bioremediation with the state government of Baden-Württemberg, says Ambs-Apparatebau's Freidel Hoppe.

Another solution to the denitrification problem is at an earlier stage of development at the Technical University (Berlin). Based on studies of natural denitrification in lakes, Wilhelm Ripl designed the Biofilm Ribbon Reactor. Ripl noted that natural denitrification often involves the close association of mixed cultures of bacteria and algae. In the water-sediment contact zone around the edge of a lake, chemoautotrophic bacteria create an anaerobic environment - a film some 100 μm thick - in which denitrifying bacteria thrive. Algae in the film provide the bacteria with carbon nutrients.

Ripl has simulated that environment in the biofilm reactor by immobilizing a mixed culture of algae and bacteria on a polyethylene sheet or a nylon ribbon sheet. Treated water is then continuously passed over the sheet, providing a form of mixing. The algae grow photo-synthetically, so the biofilm reactor has a high surface-to-volume ratio, practically 20 m^2/m^3.

The biofilm reactor may have applications beyond denitrification. Ripl believes that the reactor's bacterial composition could be manipulated to deal with specific nitrogenous organic compounds. The presence of algae also means that the reactor could reduce high levels of inorganic phosphate. (Source: Bio/Technology, Vol. 9, July 1991)

Algae help to clean up contaminated water

Enterprising chemists in the US have found a new use for algae in the clean-up of hazardous waste. Dennis Darnall of New Mexico State Univeristy and his colleagues have developed "AlgaSORB" - an algae-based material for extracting heavy metal ions from contaminated water supplies. Darnall described the materials at the meeting of the American Chemical Society in Atlanta in April 1991.

Microorganisms, such as bacteria, are often used to clean up toxic chemicals and oil spills. But heavy metal ions, such as mercury and uranium, prove too much for them. The heavy metal ions

bind to the cell walls of micro-organisms, disrupting their metabolism and killing them.

Ironically, it is precisely this property of the heavy metal ions that makes the algae so effective. In the AlgaSORB process, which Darnall and his colleagues have patented, algae are packed in a column-shaped matrix of solid silica gel, immobilizing them.

The process of packing the algae in the solid matrix kills the micro-organisms. Nevertheless, their cell walls still provide a plentiful source of binding sites which can hook the heavy metal ions out of solution. The nature of these binding sites is the key to the novelty and potential of the AlgaSORB.

At present, the technique for extracting heavy metal ions from solution involves "ion exchange resins". These bind the metals to compounds known as "hard" ligands, such as sulphonate or carboxylate groups. The glue is simply the electrostatic attraction between the ligands and heavy metal ions.

There are two problems with this technique. In many cases, the contaminated water also contains large quantities of calcium and magnesium ions. These ions compete with the toxic heavy metals for electrostatic binding sites, so they rapidly clog up the resin.

The second problem with exchange ion resins is that many of the heavy metals which are of interest, such as mercury, copper and gold, prefer to bind to "softer" ligands, such as sulphur- and nitrogen-containing groups. Because hard ligands do not bind the metals as strongly, the metals "leak" from ion-exchange resins. As a result, it is difficult to reduce the concentration of heavy metals below several hundred parts per billion.

But things are better with algae. The binding sites for heavy metal ions are predominantly softer ligands. So the uptake of heavy metals is virtually unaffected by the presence of calcium ions. AlgaSORB can also reduce the concentration of uranium and mercury below one part per billion, because the metals are more tightly bound.

Darnall and his colleagues are now testing AlgaSORB at the pilot plant stage. They say the material has potential applications in the nuclear industry and in cleaning up toxic metals which have leached into ground water from old dumping sites. There is even a possibility that AlgaSORB could be used in the gold mining industry, for extracting the last milligram of the precious metal from the waste water. (Source: New Scientist, 25 May 1991)

How straw in the pond keeps algal slime at bay

Rotting straw releases a chemical which inhibits the growth of algae, according to scientists in Britain. This confirms an observation made by a farmer several years ago. He noticed that the algae in a lake virtually disappeared when some old, rotten bales of straw fell in.

Algae have become a particular problem in Britain during the past two summers, which have been hot. Algae flourish when there is plentiful sunshine and also when there is a supply of phosphates in the water, usually from detergents. Many lakes and waterways have become smothered with blankets of algal slime. The algae block drainage ducts and deoxygenate the water, killing the fish. Some even produce chemicals that are highly poisonous to animals and humans.

Pip Barrett and his colleagues at the Aquatic Weeds Research Unit near Reading, confirmed the farmer's observation that rotting straw reduces algae. They then carried out a series of experiments to investigate four possible reasons for the effect.

In the course of their experiments, Barrett and his colleagues found that the water retained its nutrients when straw was added. They also found that algae were killed even if the straw had been grown without the use of pesticides.

Barrett and his colleagues believe that rotting straw kills algae because it produces a natural algicide as it decomposes. "We still don't know the exact identity of the molecule - factor X. But we do know it is one of the common algicides produced by fruit", he says.

The algae take up the chemical quite rapidly, and it is absorbed by the mud in lakes as well. According to Barrett, it does not appear to harm higher plants, and fish flourish in the region of the straw.

For rotting straw to have its effect on algae, the water must contain plenty of oxygen. But remarkably little straw is needed - only 10 grams per cubic metre of water, the scientists say. Barley straw proved to be the most potent.

Barrett recommends that straw should be applied to a lake twice a year: once in the autumn, because it takes at least a month to start working, and once again in the spring, because the effect only seems to last about six months. He believes the straw offers the first satisfactory solution to the algae problem. (Source: New Scientist, 13 April 1991)

New tactic against erosion

Many rangelands in the drier areas of the world have been badly damaged by overgrazing, making much of the land completely bare of vegetation. When it rains, the water and topsoil just run straight off, leaving the land just as dry as before. Bringing such damaged land back to life is expensive and time-consuming and few village people have either the money or the time to put into it.

However, in southern Tanzania, the Matanga people have developed a simple and cheaper method for rehabilitating the land. They build new catchments and plant them up with a cash crop like cowpeas.

These micro-catchments are semicircular hollows dug into the hillside. Water collects in the hollows and soaks into the ground rather than running off and causing soil erosion. Cowpeas are planted on the small bank and benefit from the extra moisture provided by the micro-catchments. When the cowpeas are harvested, they can be sold for cash and more than pay for the time and effort put into digging out the micro-catchments.

The idea has now been successfully introduced to people who have the problem of degraded land near Machakos, in Kenya. They have found that plenty of shrub and grass seeds get washed down. These seeds soon germinate and at the end of the season, after the cowpeas have been harvested, there is a good cover of grass and shrub. These, of course, benefit from the extra water collected the following season. At the end of two or three years, a good cover of vegetation develops. (Source: Development Forum, July/August 1991)

E. PATENTS AND INTELLECTUAL PROPERTY ISSUES

EC extends pharmaceutical patents

The EC Commission has prepared a new regulation to adapt patent protection for pharmaceutical products to the schemes adopted previously in the United States and Japan. The new regulation, if approved by the EC Council, opens up the way to extend patent protection up to a maximum of 16 years from a drug's introduction into the market. A standard 20-year patent does not take into account the long periods of exhaustive testing and clinical trials required for new drugs. (Source: Biotechnica Journal '91)

Campaigners target EC "patenting of life" plans

An alliance of pressure groups has launched a campaign to halt EC legislation that would allow companies to patent genetically engineered plants and animals.

The groups have written to UK Prime Minister John Major and the President of the EC Commission, Jacques Delors, outlining their concerns and demanding a moratorium on the "patenting of life". Such patents could increase genetic uniformity and cause environmental impoverishment, they say, and large companies would have increased control over agricultural resources in the third world.

The letter claims that consumers may have to pay more for their food and have less choice. Some campaigners are particularly concerned that patents would encourage companies to gentically engineer crops to tolerate high inputs of pesticides. (Extracted from Chemistry & Industry, 20 May 1991)

Patent bill resurfaces

A mid-1980s court decision is the impetus behind the new biotechnology patent protection bill recently introduced in the US Congress. The bill seeks to extend coverage so that inventors and companies receive patent protection not only for products but also for the processes used in making them.

Versions of the bill, initially introduced in 1990, were reintroduced this session by Senator Dennis DeConcini and Representative Rick Boucher. Because justification for the legislation is couched in terms that promote US international competitiveness, it enjoys widespread bipartisan support, and thus has a good chance of passing.

In principle, current patent laws cover both biotechnology products and novel manufacturing processes. However, a 1985 court decision, named after the chemist Durden who brought the lawsuit, sharply restricted the manufacturing processes that are deemed patentable by the US Office of Patents and Trademarks (PTO). That decision revolved around a carbamate insecticide, which itself was granted a product patent. Despite the novelty of the product, however, PTO examiners ruled that the chemical reactions needed to produce it could not be patented because they were already well known.

The effect of the Durden case has proved "devastating for the biotechnology industry" as well as the chemical industry, according to patent attorney Allen Bloom. Subsequent patent court decisions tended to strengthen this PTO position, he notes.

The restrictive stance on processes is particularly difficult for biotechnology companies because many of their products are not eligible to receive product patent protection. Indeed, for many biopharmaceuticals and other biotechnology products the main inventiveness revolves around tricks, such as isolating genes or developing special types of living cells, to make large amounts of pure materials. Referring to the Durden decision, however, US patent examiners deem those tricks to be standard practice unworthy of patent protection. In some cases, a limited patent may be awarded for the cell line used for production purposes, but not for the processes or products themselves.

Criteria for granting patents for biotechnology-based processes are less restrictive in Europe and Japan. So competitors may exploit a company's biotechnology manufacturing process to make a product outside the US. Because neither the product nor the manufacturing process can be covered by US patents, the competitors may then export and market the 'me-too' product in the US without technically infringing on the initial developer's proprietary process. (Source: Chemistry & Industry, 15 July 1991.

Bioengineering patent

After five years of research and development, DNA Plant Technology, Cinnaminson, N.J., and Firmenich SA have received a patent for a new tobacco plant which yields high amounts of sclareol, a raw material for the synthesis of ambrox - a main constituent of amber-type fragrances.

Firmenich says ambrox is the most important amber-type fragrance material especially since it replaces the no-longer available natural grey-amber, a secretion of the pot-whale.

This year, DNA Technology is sampling out large quantities of its sclareol and next year, the company is planning to commercialize its production. The company is currently in the process of scaling up manufacturing. It is searching for growing areas in and outside New Jersey where it can grow the plant on a large-scale basis.

Dr. Evans, vice-president, business development division of DNA Technology, comments, "Until we are growing 1,000 acres of the plant, we cannot target exactly what its selling price will be".

In conjunction with using bio-engineering techniques called somaclonal variation, DNA Technology modifies both conventional fertilizing techniques and traditional harvesting practices to generate 20 times more sclareol than that produced by one plant under normal growing conditions.

Both sclareol and abienol have broad applications in the fragrance industry. In addition to its use in deodorants and after-shave lotions, sclareol can serve as a flavour enhancer.

DNA Technology is developing approximately 20 different aroma chemicals via the "somaclonal variation" method. They are using another plant variety from the nicotiana genus to produce abienol. (Extracted from Chemical Marketing Reporter, 13 May 1991)

Legal loophole allows altered organisms to travel by post

Scientists may not be allowed to release genetically engineered organisms into the environment willy-nilly, but they can send them to each other through the post. Researchers wishing to experiment with genetically engineered organisms outdoors must satisfy the strict approval procedures now in place in most industrialized nations. But there are no fixed rules about sending altered organisms by mail.

International law governing transport of such organisms is fragmented and confused, even for unaltered organisms. France and Spain, for example, are "hyper-restrictive", and forbid postage of all pathogenic material.

Efforts to end the confusion are now under way. The UN Committee of Experts on the Transport of Dangerous Goods is working on a set of recommendations which will apply to the transport of genetically modified organisms. The committee is thought to have agreed at a meeting in December to treat such organisms and animals in the same way as pathogens.

Governments and international organizations are likely to adopt the Committee's recommendations as benchmarks for their own legislation.

Mail carriers are also keen to see the legislation sorted out. The International Civil Aviation Organization in Montreal, for example, is known to be waiting for the UN guidelines so that it can introduce its own regulations for the carriage of altered organisms. Because most civil airlines are affiliated to ICAO, they are likely to follow its line.

The legal position in the US is unclear. The US Department of Agriculture has issued guidelines stating that genetically manipulated organisms must be packaged according to the nature of the host organism. The National Institutes of Health has also issued guidelines. These go slightly further and recommend that even harmless organisms such as brewer's yeast must be packaged securely if they contain alien DNA which codes for highly toxic substances such as the botulinum toxin.

The European Commission is investigating the matter through its transport directorate because neither of the two existing directives related to biotechnology tackle this issue. It is not clear whether any directive on the transport of genetically modified organisms would clash with recommendations by the UN's Committee on transporting dangerous goods.

In Britain, the Health and Safety Executive's Advisory Committee on Genetic Manipulation is drafting guidelines tailored to the transport of genetically engineered organisms. It hopes they will become law by October. The ACGM's guidelines will cover all types of organisms, from microbes to mice. In Britain, GMOs are packaged according to the nature of the organism hosting the new or altered genetic material.

A separate directive from the Commission on infectious organisms is to be finalized this month. At present, most countries class infectious organisms into four internationally agreed categories according to the risks they present to people or to the environment.

Class Four organisms are the most dangerous. They cause diseases for which there is effectively no cure, such as Lassa fever, green monkey disease and smallpox. These organisms cannot be posted. The negotiators working out the draft directive will decide how to frame rules for Class Four organisms.

They have already agreed on rules for the other three categories of organisms. Most genetically engineered organisms would fit into these first three categories.

Anyone intending to dispatch Class Four organisms would have to notify national authorities that they are about to send a consignment, which would have to be accompanied throughout the journey. The sender would also have to notify the receiver that a consignment is on its way. (Source: New Scientist, 25 May 1991)

F. BIO-INFORMATICS

Ecoforum, Environment Liaison Centre International (ELCI), Nairobi, Kenya

A bimonthly bulletin published in English, French, Spanish and Arabic, Ecoforum functions as a networking tool for NGOs active on issues relating to environment and sustainable development around the world. It also acts as a window on the UN Environment Programme (UNEP). The November 1990 and December 1990 issues comprehensively dealt with biodiversity and biotechnology respectively, giving in-depth background information on various aspects of the two issues. The publication is available from: ELCI, P.O. Box 72461, Nairobi, Kenya.

Ecoafrica, Africa NGOs Environment Network (ANEN), Nairobi, Kenya

Ecoafrica, published in English and French, is a bimonthly environment and development magazine addressed to African NGOs with a particular focus on grass-roots NGOs. It promotes environmentally sound, sustainable development and natural resources management for Africa. Acting as an indigenous forum for networking, exchange of experiences and sharing of ideas it services ANEN, who work to strengthen African NGOs' capacities and technical competence to deal with environment

and development issues and provide links between ANEN members and national Governments, UN and other international organizations. This publication is available from: ANEN, P.O. Box 53844, Nairobi, Kenya.

Briefing on Diversity, Genetic Resources Action International (GRAIN), Barcelona, Spain

As a contribution to the NGO preparation work towards UNCED, Rio de Janeiro, Brazil, 1992, GRAIN started to publish the series of Briefings on Biodiversity in October 1990. The first issue gave an introduction to UNEP's challenging task of drawing up a global convention on biological diversity. The second, February 1991, issue entitled Genes for Sustainable Development discusses the obstacles to a global agreement on conservation and sustainable use of biodiversity. The publica- tions are available from: GRAIN, Apartado 23398, E-08080 Barcelona, Spain.

The Impact of Intellectual Property Protection in Biotechnology and Plant Breeding on Developing Countries, Study Committee on Biotechnology and Intellectual Property Rights with Respect to Developing Countries, The Hague, the Netherlands, October 1990, 46 pages

This report reviews recent international developments in patent protection of plant material and plant breeders' rights and analyses their impact on the South and public agricultural research centres. The study comes to the conclusion that the desirability of patents and monopoly rights for plant material must be related to the stage of development of a country. Consequently, if third world countries were forced to introduce patents for biotechnological innovations or plant varieties, the system would primarily promote biotechnological innovation in industrialized countries. Therefore the report calls upon industrialized countries to stop pressurizing third world countries to adopt a patent system incongruous with their national agricultural developments. The publications are available from: Directorate General International Cooperation, Ministry for Foreign Affairs, The Hague, the Netherlands.

Further issue of EBIS published

Anyone wanting to keep abreast of developments in the European Commission's biotechnolgoy-related activities should track down a copy of EBIS (European Biotechnology Information Service). If you need to navigate among the profusion of EC programmes (e.g. BRIDGE, ECLAIR, FLAIR, HUG, SCIENCE), this is the place to start. For further information contact: Dr. M. F. Cantley, Commission of the European Communities, CUBE, DGXII, Rue de la Loi, B-1049 Brussels, Belgium. Tel.: +32 2 235 81 45; Fax: +32 2 235 53 65.

GATT Briefing, European NGO Network on Agriculture and Development (RONGEAD), Lyon, France

GATT Briefing is a series of 10 comprehensive bulletins on the Uruguay Round negotiations compiled for NGOs working in the areas of development, environment and agriculture by RONGEAD in associa- tion with GRAIN, Spain, GRESEA, Belgium, and CIIR, UK. So far GATT Briefings on the negotiations concerning agriculture, the Trade-Related Aspects of Intellectual Property Rights (TRIPS), services, food security, environment and economy have been published. They are most valuable contributions to a critical understanding of the complex issues at stake at the Uruguay Round. GATT Briefing is available in French, English and German, the latter as a translation by the German development NGO network BUKO. For more information contact: RONGEAD, 14 rue A. Dumont, F-69372 Lyon Cedex 08, France; the German version is available from: BUKO-AgrarKoordination, Nernstweg 32-34, D-2000 Hamburg 50, FRG.

Disclosures, GRAIN, Barcelona, Spain

Disclosures is an irregular briefing paper servicing the international campaign against patenting life forms. It informs about trends in the intellectual property rights discussion at the international level. Implications for food production, environmental security, farmers, consumers and the third world as a whole are expounded. The second issue of December 1990 is devoted to the upcoming revision of the current plant breeders' rights (PBR) system governed by UPOV. The suggested changes are expected to have serious detrimental effects on the food system, innovation in crop breeding, genetic diversity and the third world. Further information is available from: GRAIN, Apartado 23398, E-08080 Barcelona, Spain.

Biotechnology and the Future of World Agriculture, by Henk Hobbelink, Zed Books, London, UK, and New Jersey, USA, 1991, 159 pages

This book forcefully argues for more control over the new biotechnologies as giant corporations dominate the direction of biotech research and put pressure on national and international bodies to bring genetic materials under monopoly patent control. Since the fulfilment of biotechnology's promise of a brave new world depends on the context in which the powerful new technology is developed, used and controlled, it is imperative to set the priorities in the public interest. The alternative, as is demonstrated here, may be increasing environmental destruction and impoverishment of millions of people in the South, but also in the North. Further information is available from: Zed Books Ltd., 57 Caledonia Road, London N1 9BU, UK, and GRAIN, Apartado 23398, E-08080 Barcelona, Spain.

ABA to start new journal

The ABA has agreed with Australian Industrial Publishers, Adelaide, that it will cease publication of the Australian Journal of Biotechnology as from June 1991. This has been brought about by a combination of factors including the deleterious effects of the recession.

The ABA Council of Directors decided at its May 1991 meeting that it would also cease publication of the in-house ABA Bulletin and replace both publications with a new journal entitled Australasian Biotechnology. The first issue of this new journal will appear in August 1991.

The new journal will contain some advertising, and member companies wishing to take out prime advertising space in the new publication

should contact the ABA immediately. Other plans for the journal include a very active promotion compaign to increase subscriptions so that it achieves a genuine world-wide coverage.

The journal will maintain a high quality of presentation. Members wishing to be involved in the publication in any way at all are invited to contact Martin Playne, who was appointed Managing Editor of the journal by the ABA Council at its last meeting. Other members of the Editorial Board will be Peter Rogers, Barbara Arnold, Saliba Sassine and Ian Maddox. For further information on the journal, please contact: Martin Playne - Tel.: (03) 556 2211 or Barbara Arnold - Tel.: (03) 558 6988 or write to the Australian Biotechnology Association, P.O. Box 303, Clayton 3168, Victoria, Australia.

Directory of biotechnology in France

The new edition of the French biotechnolgy directory (ADEBIO) has been published. It contains 2,400 references covering many different aspects of biotechnology: health, agro-food, agriculture, chemistry, energy, environment and pollution, instrumentation and finance. More than 1,100 industrial organizations are mentioned and 3,800 biotechnology specialists. References are classified in four areas: industrial by areas of application; major research centres; professional organizations in public and private sectors; and financial organizations. ADEBIO's directory is available from Elsevier, Editions Scientifiques, 29 Rue Buffon, F-75005 Paris, France.

NIABA - profiles of members

The Netherlands Industrial and Agricultural Biotechnology Association (NIABA) has published the third edition of the book "Profiles of Members". NIABA's membership includes the majority of Dutch biotechnology companies representing five groups: industrial enterprises; agricultural companies; new biotechnology firms (NBFs); trade organizations; and suppliers of processes or equipment. As indicated in its introduction, the publication is intended to help you find your way around Dutch commercial activities in biotechnology, and as such it is a very useful document. Each profile describes the company and its interests in biotechnology: its field of activities, as well as its products, number of employees, etc. Further information is available from: J. H. L. van Lissa, Director, NIABA, P.O. Box 185, NL-2260 AD Leidschendam. Tel.: (31) 70 32704 64; Fax: (31) 70 32036 71.

Policy studies for biotechnology

The Senior Advisory Group on Biotechnology (SAGB) of the European Chemical Industry Federation (CEFIC) has published a range of studies on Community policy for biotechnology covering: priorities and actions (January 1990), economic benefits and European competitiveness (June 1990), and creation of a Community task force and an advisory body (July 1990). Two other studies are covering bioinformatics in Europe: strategies for biotechnology information infrastrcuture. For further information/ copies contact: CEFIC, Av. Louise 250, B-1050 Brussels.

Long-range Nordic biotechnology research

The Nordic Fund for Technology and Industrial Development has produced an information booklet NR9/1990, in English, relating to biotechnology in five Nordic countries: Denmark, Norway, Sweden, Finland and Iceland.

The report covers the following areas of biotechnology: protein engineering; bioprocess engineering; plant cell research; thermophilic and psychrophilic micro-organisms; biotechnology for the food industries; and biotechnology and the environment.

The report estimates that more than 2,300 researchers are involved with biotechnology in the Nordic region, which has more than 150 biotechnology companies, employing an additional 2,800 researchers. The benefits of networking and collaborative projects aimed at strengthening the position and competitiveness of the Nordic industry are emphasized in the report. Further details are available from: Nordic Fund for Technology and Industrial Development, Nedre Vollgate 8, N-0158 Oslo 1, Norway. Tel.: (47) 2416480; Fax: (47) 2412225. New Scandinavian Technology No. 1, 1991 - covers medicine and biotechnology in English. Details are available from: New Scandinavian Technology, Box 5173, S-10244 Stockholm, Sweden.

International Symposium on the Biosafety Results of Field Tests of Genetically Modified Plants and Micro-organisms, 27-30 November 1990, Kiawah Island, South Carolina

This promptly produced report of an International Conference (mentioned in EBIS 1) must be of considerable interest and importance to everyone who is concerned that the regulations governing field release of GMOs should be on a sound scientific basis. The conference brought together leading researchers and administrators from many countries of the world. Their collective wisdom was brought to bear on how to evaluate the safety of the products of agricultural biotechnology.

The report is in five main sections covering:

1. Predicting field performance for plants and microbes;
2. Regulation of field release in France, the US and Japan;
3. Specific case studies of plants and microbes;
4. The future problems of large-scale field testing and commercialization;
5. Conclusions of the conference.

The conclusions cover emerging principles, some advice from the conference, points of consensus and a final message: "if we do not embrace the techniques of biotechnology, we will miss a tremendous opportunity for improvement in human health care, in our environment and in assuring a wholesome food supply. We will miss

the opportunity to make a better world for ourselves, our children, and our children's children."

The conference was attended for the Commission by Dr. Loannis Economidis, responsible within BRIDGE for safety research. US organizer David MacKenzie is one of several visitors contributing on this topic at the EC-US Task Force on Biotech Research, 15-16 July 1991. The report is obtainable at $10 from Agricultural Research Institute, 9650 Rockville Pike, Bethesda, MD 20814 7123, USA.

New UK Biotechnology Directory announced

The BioIndustry Association (BIA) and BioCommerce Data Ltd. have scheduled publication of the third edition of their popular directory of British biotechnology for September 1991. The UK Biotechnology Handbook 91/92 will provide full-page profiles of over 600 organizations including universities, venture capital providers, government agencies as well as over 400 companies. The book also includes eight in-depth review articles by eminent authors dealing with such topics as biotechnology for sustainable development, EC and DTI support, environmental release in the UK, public perception of biotechnology, joint venturing and strategic partnerships and the competitiveness of UK biotechnology.

BIA members are entitled to a 10 per cent discount on the price of £95. Advertising space is also available in this directory. For more information contact: BioCommerce Data Ltd., Prudential Buildings, 95 High Street, Slough, SL1 1DH, UK. Tel.: (0753) 511777; Fax: (0753) 512239.

BioTechnologie - das Jahr- und Adressbuch 90/91 hrsg. von Andreas Mietzsch, Braunschweig, Polyucom, 1990, 324 pages

Do you want to know what the research institute of Borstel is doing? Do you need the address of Gynkotek GmbH? Are you looking for a complete, reliable overview of German university institutes and companies having an interest in biotechnology? The Jahr- und Adressbuch published by the GBF and its information service BIKE offers all these services, covering not only the whole of Germany, but also Switzerland and Austria. The index helps you to find any organization by field or product group, including consultants, information brokers, and cell culture collections, provided you know the term you are looking for in German. And do not skip the well-written article "Gentechnik und Politik" by Ernst Ulrich von Weizäcker, director of the Institute for European Environmental Policy, in which he states that even though gene technology might be a high risk to biodiversity, we cannot do without it any more for resolving current and future problems of survival. For further details contact: Ingo Wahrendorf Polycom Verlagsgesellschaft mbH. Tel.: (49) 531 33 39 28; Fax: (49) 531 33 64 60.

New weed identification manual

The International Rice Research Institute (IRRI) has published a full-colour manual to identify seeds and seedlings of the most important rice weeds in South and South-East Asia. It was designed for easy and inexpensive translation and co-publication.

The manual, Seeds and Seedlings of Weeds of Rice in South and Southeast Asia, by Dr. Robert L. Zimdahl, Rosario T. Lubigan, Dr. Keith Moody, and Maxima O. Mabbayad.

The manual describes the most important rice weeds in tropical South and South-East Asia, where most of the world's rice is grown.

Meanwhile, IRRI has released a 1989 edition of the catalogue of all publications and educational materials published by 22 International Agricultural Research Centres: Publications of the International Agricultural Research and Development Centres.

The 730-page catalogue is probably the world's largest compilation of titles on agricultural science for development.

Included is a 182-page keyword index to help the reader locate all publications in certain fields (i.e. cytogenetics, insect resistance, maize).

The catalogue may also be available soon on computer disk.

IRRI published the catalogue on behalf of all centres, and is handling its distribution. For further details contact Southeast Asian Weed Information Centre, P.O. Box 17, Bogor 106001, Indonesia, Telex: 48299 BIOTRO IA.

Biotechnology: EEC policy on the eve of 1993

Recent developments suggest that the European Community is beginning to make the political choices needed to fulfil biotechnology's potential. On 12 April 1990, the member States adopted two Directives which go a long way towards establishing a regulatory framework for the biotechnology industry. To help in the task of keeping abreast of developments, the European Study Service has published a 400-page study, Biotechnology: EEC Policy on the Eve of 1993, priced at 11,800 BF (including postage and packing). Further details are available from: European Study Service, 43 Avenue Paola, B-1330 Rixensart, Belgium or on +32 2 653 90 19. Fax: +32 2 652 03 02.

Shattering: Food, Politics, and the Loss of Genetic Diversity by Cary Fowler and Pat Mooney. Published by the University of Arizona Press, 258 pages; $12.95 paper, $24.95 cloth

For over 10 years, senior Rural Advancement Foundation International (RAFI) staff members Cary Fowler and Pat Mooney have worked to educate the public and international policy makers about one of the world's more serious, but little-known environmental catastrophes: the loss of genetic diversity in agriculture.

Fowler and Mooney's new book, Shattering: Food, Politics, and the Loss of Genetic Diversity, describes an environmental crisis which sets the

stage for widespread hunger. At stake is the integrity, future and control of the first link in the food chain: the seed. Written for the lay reader, Shattering brilliantly describes the struggle for control of seeds, as nations and companies now vie for access to and benefits from the world's plant genetic resources.

Industrialized agriculture promotes uniformity in food crops. More than 7,000 US apple varieties once grew in American orchards; 6,000 of them are now extinct. Every broccoli variety offered through seed catalogues in 1900 has now disappeared. As international agri-chemical corporations absorb seed companies - there have been nearly 1,000 takeovers since 1970 - the trend toward uniformity accelerates. And, as third world agriculture is transformed to meet the needs of international business interests, the gene pools of humanity's most basic food crops are threatened.

There is far more at stake than the historic and culinary interest of heirloom varieties. Without the genetic diversity from which farmers traditionally breed for resistance to pests and diseases, crops are more susceptible to the spread of pestilence. Tragedies like the Irish potato famine may be thought of today as ancient history; yet the US corn blight of 1970 shows that the high-tech monocultures of today's agribusiness are a breeding ground for disaster. Shattering reviews the development of genetic diversity over 10,000 years of human agriculture, then exposes the political and economic forces which have accelerated genetic erosion in our lifetime. The possibility of catastrophe is real; this book shows that it may not be too late to avert it.

Trees of Life-Protecting Tropical Forests and their Biological Wealth by Kenton Miller and Laura Tangley, World Resources Institute, Beacon Press, Washington, D.C., April 1991, 224 pages, $US 9.95

This is the second in the World Resources Institute Guides to the Environment series for general readers, written to dispel confusion about complex scientific and environmental problems. Trees of Life surveys current and historical assaults on the world's tropical forests and examines the costs and consequences in human, economic and ecological terms. It offers hard-hitting recommendations for revamping government policies in both developing and industrialized countries to halt deforestation and shows what individuals can do. This publication can be ordered from WRI Publications, Box 4852, Hampden Station, Baltimore, MD 21211, USA.

The Least Developed Countries. A Statistical Profile - 1990 (TD/B/1288)

This Statistical Profile presents in one sheet key indicators of development on the 42 least developed countries (LDCs) as a group and individually. The statistical information provided is grouped under four main headings, viz. major economic indicators, social indicators, demographic indicators, and aid/debt indicators. For a number of key indicators, comparisons are made between LDCs individually and as a group, on the one hand, and the average for other developing countries and for the developed market-economy countries, on the other. This publication can be obtained from UNCTAD.

Vaccines enter a new era: More new products, more adult users

More than 400 different vaccine programmes are currently in various stages of development, according to Frost & Sullivan's new 380-page study The US Market and Development Activities for Vaccines (No. A2370).

The programmes identified cover a wide range of viral, bacterial and related infectious diseases - from syphilis to malaria, from leprosy to typhoid. The study finds 19 different programmes under way to develop herpes vaccines, with more than 45 concentrating on AIDS.

Frost & Sullivan expects some of the new vaccines to come onto the market as early as 1993, but most not until after 1995. Yet, even now, vaccines represent one of the faster growing sectors of the whole infectious disease therapeutics market-place. The study estimates that the total US market for vaccine products grew from $315.1 million in 1985 to $670 million in 1990. The forecast is for a $1.25 billion market in 1995. By the year 2000, that could be a $2.6 billion market.

The study analyses both child and adult vaccines. Product sales are expanding in both groups. In the child vaccine segment, for example, a new vaccine was introduced in the mid-1980s for haemophilus influenzae type B - a form of influenza affecting about one in 200 US children under age five and a common cause of bacterial meningitis and a number of other conditions.

Sales of the vaccine rose from $5 million in 1985 to $70 million in 1990, and the vaccine has been improved. The study forecasts sales of $120 million in 1995. Sales of combination vaccines for measles, mumps and rubella were also $70 million in 1990 and are forecast to reach $121 million in 1995. (This is in addition to sales of single vaccines.) Overall, the child vaccine segment is expected to grow from $325 million in 1990 to $495 million in 1995.

The adult vaccine segment totalled an estimated $345 million in 1990 sales, forecast to reach $455 million in 1995. That forecast, the Frost & Sullivan study notes, could be too conservative. Sales of the hepatitis B vaccine make up 38 per cent of the adult vaccine segment - and consideration is now being given to broad-scale vaccination of the entire population with the hepatitis B vaccine.

The vaccines market in general is shifting from concentration on children to the targeting of adults. Many recent vaccines have targeted the elderly, for example pneumonal vaccines. Many of the vaccines expected to come on the market in the mid-1990s (a gonorrhoea vaccine, various herpes vaccines, and others) will be adult vaccine products.

In addition, more and more adults who may not have been properly vaccinated for childhood diseases are now being vaccinated. Details of the

report, priced at $3,500.00, from: Customer Service, Frost & Sullivan Ltd., Sullivan House, 4 Grosvenor Gardens, London SW1W 0DH. Tel.: 071 730 3438. In the USA, Frost & Sullivan Inc. is at 106 Fulton Street, New York, NY 10038, USA. Tel.: +1 (212) 233-1080. (Source: Biotechnology Bulletin, Vol. 10, No. 3, April 1991)

Environmental biotechnology proceedings

The growing awareness of environmental problems provided the stimulus for the 4th International Symposium on Biotechnology, Interbiotech 90, held in Bratislava, Czechoslovakia, to look at the relationship between biotechnology and the environment. The 436-page proceedings, priced at $180.00, are now available from Elsevier.

The papers are mainly devoted to the contribution of biotechnology in solving environmental problems, including biological waste water treatment, utilization of municipal sewage sludge, detoxification of polluted soil and the utilization of lignocellulosic waste. There is also some consideration of possible dangers in such cases as the release of rDNA organisms into the environment. Further details are available from: Elsevier Science Publishers, P.O. Box 211, 1000 AE Amsterdam, the Netherlands.

US FDA and EPA regulations on disk

Interpharm Press has published the complete texts of the entire US Code of Federal Register covering regulations of the Food and Drug Administration (FDA) and the Environmental Protection Agency (EPA) on computer disk. Users of Regs-on-Disk can access the regulations with search times of 2-3 seconds.

System requirements include IBM PCs, true compatibles and most MS DOS computers, 448 K memory, DOS 2.0 or higher. In addition, a 20 Mb hard disk is recommended. US prices are $298 for the FDA disk and $498 for the EPA disk. For further information contact: Interpharm Press, 1358 Busch Parkway, Buffalo Grove, IL, 60089, USA. Tel.: +1 (708)459-8480; Fax: +1 (708)459-5644.

World-wide use of PCR to reach $1.1 billion by 2001, says TMG

Markets for products utilizing polymerase chain reaction (PCR) will reach $345 million world-wide by 1996, and grow to over $1.1 billion by 2001, according to a report entitled The Impact of PCR on Human and Veterinary Diagnostics - a Worldwide Market Study, published by the Technology Management Group (TMG). Most of this will be for human diagnostic applications.

Since its introduction in 1985 and commercialization in 1987, PCR has been rapidly adopted in almost all areas of DNA analysis. The PCR process is controlled by Cetus under a series of patents and has been licensed to Hoffman-La Roche for human diagnostic applications and to a number of companies in the veterinary diagnostics field.

PCR can be applied in nearly every application in which duplication or amplification of DNA is useful. In addition to diagnostics for viral, genetic and bacterial diseases, applications of PCR include the identification of human tissue, as in tissue typing for organ transplants, criminal identification and forensic uses. Determination of desirable genetic characteristics can also utilize PCR in plant and animal breeding.

Industrial quality assurance and quality control applications are also expected. In addition, PCR may play a role in the production of therapeutic proteins and in anti-sense agents. A large number of research applications are expected to develop. The report profiles 77 companies and 116 other organizations involved in PCR work. Further details of the report, priced at $1,495, from: Technology Management Group, 25 Science Haven Park, Connecticut 06511, USA. Tel.: +1 (203) 786 5445; Fax: +1 (203) 786 5449.

Proceedings of the European Workshop on Law and Genetic Engineering

The graphic symbol chosen for the European Workshop on Law and Genetic Engineering, which took place in Hamburg on 14 and 15 December 1989, a paragraph symbol in the form of a DNA sequence or, vice versa, a DNA sequence in the form of a paragraph symbol, reflects the two aspects the Workshop was focused on: genetic engineering on the one hand and its regulation by law on the other. The Workshop was co-organized by the Landesverband Bürgerinitiativen Unweltschutz of North-Rhine- Westphalia and the Heinrick-Böll-Stiftung.

During the last decade, genetic engineering has increasingly become a relevant topic not only for authorities but also for legislators at the European level as well as national level.

Whereas both parliaments and governments for a long time hesitated to regulate genetic engineering research and its application, the situation has undergone dramatic changes within a very short time.

The speed at which directives and regulations are being passed presently seems to conform itself to that of the developments in the genetic engineering research:

- At the European level directives concerning the contained use and the deliberate release of genetically engineered organisms have recently been passed;
- In the Netherlands similar regulations have been passed;
- In the Federal Republic of Germany the Government has prepared a Genetic Engineering Bill;
- In Belgium a rDNA Committee has been set up recently.

These proceedings aim at providing the reader with a comprehensive view on the scientific background of genetic engineering and legislation within the EEC. The proceedings of the Workshop may be obtained for about 10 ECU from the BBU Verlag, Prinz Albert Str. 43, D-5300 Bonn 1, Germany.

G. SPECIAL ARTICLE

Perspectives on the diagnosis of parasitic diseases in the tropics

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Abstract

Recent progress in the diagnosis of tropical parasitic diseases is reviewed, with emphasis on the potential of new technologies. Unsolved diagnostic questions are highlighted. Sustainable breakthroughs in the development of diagnostic tools can only be achieved by an integrated approach involving health workers and managers, researchers and specialists from industry. Although the technical development of a tool is central, more emphasis should be laid on identifying diagnostic necessities, defining precise diagnostic objectives and guaranteeing dependable validation, which must include the validation of the test in the setting in which it will ultimately be used.

Introduction

The major cause of morbidity and mortality in tropical developing countries is the high prevalence of infectious diseases. Besides the plethora of microbes causing gastrointestinal and respiratory infections, there are major diseases of parasitic origin caused by pathogenic protozoa and helminths. Table 1 summarizes the major infections of developing countries in tropical and subtropical Africa, Asia and Latin America. Two major programmes of the World Health Organization (WHO) are focused on the control of acute respiratory infections and diarrhoeal diseases with the central objective of reducing severity and mortality. The main objective of these programmes is the improvement of acute case management; diagnosis does not have high priority. In the developing world, specific diagnostic exploration is often impossible. A febrile patient will be automatically treated for malaria before other pathogens are taken into consideration. In many health centres and small hospitals in rural areas, laboratory facilities are rather limited owing to lack of trained personnel, adequate equipment or sufficient operating funds. In contrast, in major cities, the diagnostic laboratory potential is very often no different from that of industrialized countries.

The field of diagnostics has made enormous progress in the last decade, primarily as a result of advances in biotechnology. Recombinant DNA and hybridoma technologies as well as peptide chemistry allow the production of highly specific reagents for the diagnosis of infectious diseases. The Polymerase-Chain-Reaction (PCR) with its phenomenal power of amplifying very small amounts of specific DNAs, boosts sensitivity to levels beyond imagination. New "generations" of test kits for viral hepatitis or HIV infections etc. testify to the rapid development of diagnostics. If they can be produced in conjunction with an appropriate robust and simple test design, and at a low cost, such techniques could make their way to the rural health centres or hospitals. An example is the new "dipstick" test for antibodies to HIV developed by the Programmme for Appropriate Technology in Health (PATH) in Seattle.

Before highlighting recent advances and open questions on the diagnosis of some tropical diseases, I should like to express my views on some basic prerequisites for the development of diagnostic tools. While reviewing the literature, I often get the impression that many tests have been developed with no very precise idea of what purpose they will serve, and in what kind of environment they will be used. Validation is often hampered by the fact that ill-defined specimens ("accidently" found in a freezer) have been analysed. It should be self-evident that diagnostic goal(s) have to be clearly defined and an appropriate technique carefully chosen before a costly test development is started. Only a precise definition of the diagnostic goal(s) allows a relevant validation.

For most acute viral or bacterial diseases, the major diagnostic aims are either to detect present infection or to analyse the immune status. For many parasitic diseases diagnostic issues are more complex. This stems from two factors. Firstly, the patient often has a lifelong history of contact with the disease. Secondly, each disease has a wide clinical spectrum ranging from states of latent infection or asymptomatic carriers to acute or chronic pathology, including life-threatening conditions. Relevant diagnostic questions associated with individual cases might be related to identifying the stage of infection, assessing morbidity, identifying subjects who are at risk of developing severe morbidity, assessing the parasite load (as in helminth infections) and so on. Diagnostic issues are different depending on the purpose for which they are required. For example, for public health purposes, diagnostic tools are used to facilitate effective treatment, whereas an epidemiologist uses them to quantitate transmission or assess the impact of control measures on incidence, prevalence, overall morbidity, or transmission.

It is obvious that one single diagnostic test cannot answer all those questions. The prime test parameters, sensitivity and specificity, must be carefully adapted to optimize the predictive value for either a positive or a negative test result. One should not forget that predictive values are dependent on prevalence. This means that the threshold value of a quantitative test must be chosen according to the level of prevalence but also to the purpose that the test is to serve. For example, for HIV diagnosis maximal specificity (excluding false-positive results) is a high priority for the diagnosis of individual cases. On the other hand, one would aim at a high predictive value for a negative result, accepting false-positives, for screening blood products for transfusion. For some diagnostic issues a strategy combining a sensitive screening test to be followed by a more specific confirmatory test might be an acceptable solution.

Highlights on advances and problems in the diagnosis of some tropical diseases

1. Malaria

Specific diagnosis of malaria is usually achieved by microscopic examination of a blood specimen. However, the detection of a malaria case might be a time-consuming and costly exercise, especially in areas with a low level of transmission. For an experienced microscopist 10 to 20 parasites per μl blood are considered to be the detection limit when analysing a thick blood film. For public health purposes - e.g. to assess the impact of control measures - a more efficient method would be of great advantage. During the last decade, alternative diagnostic

approaches have been developed using three techniques, namely DNA probes, antigen detection and quantitative buffy coat (QBC) analysis.

Most DNA probes for Plasmodium falciparum (either genetic probes or synthetic oligonucleotides) detect a family of 21 base-pair tandem repeats, which comprise about 10 per cent of the genome (for review see 1). With the most sensitive procedures, using isotope-labelling and long exposure times, the sensitivity, claimed for parasites obtained from in vitro cultures, was 20 to 50 parasites per µl. However, using blood samples from infected individuals sensitivity was considerably lower (approx. 200 to 1,000 parasites µl. A comparative study of four hybridization assays with different probes and procedures (part of a vaccination trial) confirmed that all of them were less sensitive than microscopic examination of thick blood films or in vitro cultivation. (2) In fact, the DNA probes had a disappointing sensitivity of only 5 to 28 per cent compared to culture and 13 to 40 per cent compared to thick films. The application of DNA hybridization as an alternative diagnostic method for malaria is thus still in its initial phase. Further improvements, especially of sample preparation and of the detection system may increase sensitivity.

A second alternative approach to the diagnosis of malaria is the immunological detection of red blood cell-associated antigens or soluble antigens in the serum. Two test principles have been used so far. In the first, a competitive radio-immunoassay, malaria antigens (in blood lysates) were used to bind polyclonal (3) or monoclonal antibodies (4) and thus inhibit the subsequent binding of these antibodies to antigens bound to a solid phase. The results of preliminary attempts to use this method were far from satisfying. The sensitivity was much too low (several thousand parasites µl). A much better sensitivity was reported by a different technique, an immunoradiometric assay (IRMA). (5) An excellent correlation was reported between IRMA binding activity and parasitaemia for in vitro cultured parasites. However, this correlation was less satisfactory when blood samples from patients were analysed. A major problem is the interpretation of antigen-positive results from microscopically-negative individuals. One explanation is the persistence of antigen from an infection that has been treated. Antigens could be detected by IRMA as long as two weeks after the disappearance of parasitaemia. This could cause confusion and lead to false diagnosis of other febrile illnesses. In addition, considering the common practice of self-medication for malaria in endemic areas, parasite antigen detection in human blood might not be a satisfactory alternative to conventional microscopy in prevalence surveys.

Antigen detection assays have proven their merits for detecting infective mosquitoes. (6) Two-site immmunoenzymatic methods using monoclonal antibodies against the repetitive epitope of the P. falciparum circumsporozoite antigen are now reliable and applicable tools in the field measuring impact of control on transmission or giving valid answers to entomological questions. (7)

An effective method for the rapid detection of acute infections - where the lengthy procedure of DNA hybridization and present antigen detection assays are inappropriate - was recently developed by Becton-Dickinson (Franklin Lakes, N.J.). The clever principle of this QBC technique, staining parasitic DNA with acridine-orange and concentrating infected red blood cells by centrifugation, is based on a modified microhaematocrit tube. Infected red blood cells can be easily detected in a 1-2 mm broad band using fluorescence microscopy. High sensitivity is to be expected since a larger blood sample can be rapidly examined (55 µl vs about 0.4 µl equivalent to 200 fields of a thick-film preparation). In a first field evaluation, the QBC method appeared to be at least eight times as sensitive as conventional microscopy, detecting an additional 10 per cent of infections not diagnosed by conventional microscopy. (8) In our experience with imported malaria cases QBC has proved to be as sensitive as classical microscopy, (9) and in a holoendemic area we confirmed a slightly higher sensitivity of QBC. The great advantage is the remarkable time gain for microscopic reading; the test needs about one compared with 10 to 15 minutes for thick films. This is especially important if there are many negative samples to be screened. For dependable species diagnosis, however, blood has to be re-examined by conventionally stained blood films.

2. Amoebiasis

It is estimated that approximately 10 per cent of the world's population are infected by Entamoeba histolytica and that in some developing countries invasive amoebiasis is among the 10 leading causes of death. (10) Imperfect diagnostic tests limit our perception of the magnitude and severity of this disease. The two major problems concerning diagnosis are to find more efficient methods to detect an intestinal infection, and simpler ways to distinguish pathogenic and non-pathogenic forms (isolates). Even using concentration methods for microscopical detection, a reliable diagnosis needs repeated stool examinations. From our own data using the "SAF"-method, (11) which involves fixation and concentration of the parasites, we calculated - from analyses on multiple specimens - that at least four stool specimens are needed to guarantee a predictive value for a negative result of 0.99. (9) If only one false-negative out of 1,000 stool specimens is acceptable, one would have to analyse 10 stool samples from each patient.

Since it is evident that dependable stool examinations are strenuous, time-consuming, expensive and rely on a high level of microscopic skills, alternative diagnostic approaches were attempted. The first development of an ELISA test to detect stool antigens was described in 1978. (12) Using a commercial immunozyme test kit (Millipore Corp., Bedford, Mass.) conflicting results were reported with regard to sensitivity and specificity. This test depended on polyclonal antibodies, but more recent attempts utilized monoclonal antibodies for antigen capture. (13) Unfortunately the excretion of antigens, like that of trophozoites or cysts, is irregular and it is therefore still necessary to analyse multiple stool specimens to reach an acceptable level of sensitivity (own results).

Recently, first results using a DNA hybridization technique as an alternative to microscopy were reported. (14) The diagnostic clones, detecting highly-repeated parasite DNA sequences, reacted specifically with as few as 800 amoebae, but did not distinguish between

pathogenic and non-pathogenic zymodemes of E. histolytica. Further investigations with multiple sampling of individuals are needed to determine reliable predictive values.

When it comes to the analysis of (potential) virulence of an isolate, the current "gold standard" is the zymodeme analysis introduced by Sargeaunt and co-workers (for review see 15). The isoenzyme profiles obtained after electrophoresis allow the distinction of virulent and avirulent E. histolytica isolates. However, this technique is too time-consuming for most diagnostic laboratories. New ways of distinguishing E. histolytica possessing pathogenic and nonpathogenic zymodemes were opened by using either genomic DNA (16) or cDNA probes. (17) Preliminary results indicate that pathogenic isolates of E. histolytica are genetically distinct from nonpathogenic isolates. In addition to their diagnostic use, these probes could serve as tools to investigate the molecular basis of pathogenicity.

Serology is an important tool to aid in the diagnosis of suspected extraintestinal involvement or cases of bloody diarrhoea or chronic colitis. A wide range of methods, ranging from the very simple (e.g. Latex agglutination) to the rather sophisticated (time-resolved fluoro-immunoassay), were evaluated (for review see 18). For all of them, the major dilemma is to interpret a positive serological finding in an endemic area. This is related to the fact that antibodies due to past infections persist and that antibody titers can be low in the early stages of liver abscess formation. A solution to this might be the choice of (an) appropriate diagnostic antigen(s) - produced by recombinant DNA technique or as synthetic peptide(s) - in combination with class- or subclass-specific antibody detection of an early immune response after invasion. In view of the high mortality due to invasive amoebiasis, the development of a robust and reliable immune assay (e.g. dipstick or dot blot test) seems to be an urgent priority.

3. Intestinal nematodiasis

The detection of intestinal infections due to nematodes is still in the field of classical microscopical techniques. Since morbidity is related to worm burden, the quantitative assessment of egg counts is relevant. Recent studies have clearly demonstrated the impact of nematode infections on health, growth and physical fitness. Programmes for the control of nematodiasis are now being actively reassessed by WHO, the World Bank, UNESCO and UNICEF. However, there is no consensus on whether diagnostic screening before treatment is a required component of such programmes. The issue of mass treatment versus diagnostic screening has recently been discussed. (19) The central question still remains unanswered: Is it acceptable to treat individuals without knowing their infection status? Apart from the economic issue - a screening component increases programme cost by a factor of 2 to 6 - diagnostic screening is laborious and requires trained technicians and laboratory equipment. Diagnostic screening would therefore only be possible if simpler diagnostic tools were available. For severe hookworm infections, haematocrit values have been shown to be a possible indicator.

A negative consequence of any diagnostic screening, which often seems to be ignored, is that a significant proportion of infected individuals remain untreated, since the level of compliance with stool sampling is reported to be of the order of 50 to 70 per cent. (19) If one opts for diagnostic screening (to be in concordance with good medical practice) one ought to add an educational component to the control programme in order to enhance compliance. This problem illustrates the fact that the diagnosis of infectious diseases includes more than technical laboratory aspects. A diagnostic procedure has to find its place in a given health system, and has to be accepted by the health personnel and the population concerned.

4. Filariasis and onchocerciasis

There are major limitations to the parasitological diagnosis of tissue-dwelling nematodes. Infections remain parasitologically unidentified during the long prepatent period (until adult worms produce microfilariae) and in light and occult infections, as well as in individuals with an acquired immunity to circulating microfilariae. In addition, the periodicity of certain blood microfilariae necessitates the sampling of blood at night, which presents a significant obstacle for epidemiological studies. The replacement of night-blood by an alternative method is one of the defined diagnostic goals of the Tropical Diseases Programme (TDR) of WHO. For one possible approach, the detection of circulating antigens, a variety of immunological methods have been utilized, with polyclonal or monoclonal antibodies as reagents. To take the example of a monoclonal antibody-based immunoradiometric assay (IRMA), evaluations have clearly shown an association of patent infection with detection of the target epitope, and a good correlation between levels of serum antigen and blood microfilarial counts. (20) However, circulating antigens could also be detected in amicrofilaraemic subjects with acute symptoms of lymphatic filariasis, as well as in about half of the asymptomatic amicrofilaraemic individuals. Similar findings were also reported using other test systems.

The interpretation of a positive antigen test for an amicrofilaraemic individual is rather difficult. Does it mean that we are detecting a latent infection, or is antigen detection in "endemic controls" a sign for active immunity? From what has been said and in view of the possible interference with host antibodies, detection of circulating antigens seems not to be the appropriate approach to replace microfilarial blood counts, but it could be used to follow the effect of filaricidal drug administration, as was shown in a study in Papua New Guinea. (21)

Specific DNA probes were produced to diagnose Brugia malayi. A method to detect microfilariae in blood specimens has been developed. (22) There are ongoing efforts to adapt this technique for field application.

For onchocerciasis, major advances can be reported on two diagnostic issues, which are especially relevant for the Onchocerciasis Control Programme (OCP) in West Africa. The first is related to the differentiation of the savannah and forest forms of Onchocerca volvulus using specific

DNA probes. (23) These forms differ in the symptoms produced: The savannah form more often leads to blindness. This differentiation is therefore relevant with regard to identifying the potential pathogenicity of parasites carried by vectors invading the control area. The second issue is investigating the recrudescence of transmission in the control area, where an early indicator for reinfection is an urgent need. It has been shown that in early infections specific antibody detection is more sensitive than parasitological examination of skin snips. (24) The old problem of the poor specificity of serological tests can be overcome by using recombinant antigens selected for high specificity. (25, 26, 27, 28) Owing to individual variations in the immune response, a mixture of several recombinant antigens will increase sensitivity. For that purpose a collaborative study, including candidate antigens from several laboratories, has been organized within the TDR programme with the aim of developing a reliable field test.

5. Schistosomiasis

Morbidity in chronic schistosomal infections is mainly related to the magnitude of egg production, which is a function of the number of adult worms. I like to restrict discussions on that aspect taking the case of urinary schistosomiasis. The identification of heavily infected individuals is therefore an important diagnostic issue, in order to prevent morbidity by timely drug treatment. The standard diagnostic procedure is the urine filtration technique, which produces quantitative egg counts. However, multiple daily samplings of infected individuals revealed extreme fluctuations of the egg output over time, (29) and even in heavy infections egg-negative results were not infrequently observed. Analysis on a single day detected only 44 per cent of heavily infected children. A single urine examination is therefore not a reliable indicator for measuring the actual worm load. Repeated urine examinations require an excessive amount of work even for a single patient, and are certainly not realistic for public health purposes.

When community diagnosis (identifiying villages for which urinary schistosomiasis is a major health problem) is the diagnostic aim, diagnostic tools simpler than urine filtration have to be available. Reagent strips to test urine for blood or protein have been evaluated. (30) Both indicators have a high sensitivity for detecting egg-positive urine specimens but specificity was not optimal, especially for proteinuria. Results from two different endemic areas showed significant variations, which shows that locally defined criteria for the interpretation of test results are necessary. In a recent study in Tanzania, testing for microhaematuria was found to be a reliable indicator (93 per cent sensitivity and 92 per cent specificity) for heavy infections. (29)

An interesting approach is the immunological detection of parasite antigens in the urine. Especially the groups of Drs. Deelder and de Jonge (University of Leiden, The Netherlands) have put much effort in the development of antigen detecting assays over the last ten years. The detection of the "circulating anodic antigen" (CAA) in the urine by a monoclonal antibody-based two-site immunoenzyme assay had a sensitivity of 97 per cent. (31) If further validation attests adequate specificity and a simpler test format can be designed, such a test could become an interesting candidate for public health purposes. Preliminary studies point to an additional possible use of this antigen-detection assay to monitor the efficacy of chemotherapy. (32)

A completely different approach to measure morbidity in schistosomiasis is the use of ultrasound. (33) Various studies have shown that this is an efficient technique that is applicable and acceptable in the field at the community level.

A completely different approach, which may prove valuable for public health purposes, is the use of questionnaires based on the disease-perception of members of the community. In a study of urinary schistosomiasis a questionnaire administered to teachers and schoolchildren was tested as a diagnostic tool. (34) In comparison to urine filtration, this cost-effective way of screening revealed a sensitivity of 100 per cent and a astonishingly high specificity of 87 per cent for schools with a high infection rate. Using this approach of rapid assessment with key informants combined with selective reagent stick testing (performed by instructed teachers in schools identified by the questionnaire), the distribution of S. haematobium in a rural district with over 300,000 people could be mapped within a period of four months at a total cost of less than 1 US cent per inhabitant. (34) Currently this diagnostic approach is validated for schistosomiasis in different African countries.

Perspectives on future developments

The enormous potential of new technologies is being very efficiently exploited for the diagnosis of diseases that are of concern for the industrialized world. Although recent advances in the diagnosis of tropical diseases are discernable, only a few real breakthroughs have resulted in diagnostic tools that are appropriate for widespread routine use. The development of a diagnostic test is a rather complex and costly process (major stages are listed in table 2). For each step, the definition of precise objectives is needed; this requires the multidisciplinary collaboration of various specialists. Too often, researchers are not fully aware of the problems of developing countries with respect to urgent diagnostic needs and appropriate techniques. On the other hand, field workers have insufficient knowledge about new diagnostic possibilities. Field research networks were recently incorporated into the TDR programme to recruit more scientists for field-related research. Operational programmes, known as FIELDLINCS, have been initiated to improve interactions between researchers, managers and health workers from health ministries and national disease control programmes.

Training of scientists from developing countries, and the development of research capacities there, are important components of programmes of the World Health Organization (WHO), the United Nations Industrial Development Organization (UNIDO) and others. In the field of biotechnology, the International Centre for Genetic Engineering and Biotechnology, a major UNIDO project, fulfils this role. Goal-oriented research in diagnostics has to include test developers and test users from the beginning in order to ban costly mistakes and further, due to

ignorance of diagnostic needs, imprecise diagnostic objectives, inappropriate techniques or irrelevant validation. A dependable validation is a prerequisite for the production of a test kit. Such a validation has to include evaluating the test with defined specimens (e.g. from serum banks) to validate technical specifications. However, this is not enough; it is vital also to prove the appropriateness of the method under "real-life" conditions outside the developer's laboratory. For its inclusion in a health system or control programme the applicability of the method and its acceptability has to be tested.

The final step is the production of a diagnostic test kit. For this, a partner from the industry has to be found. However, the decline in the interest of industry in the industrialized world in parasitic diseases is a major obstacle. Making profits from diagnostic tools is apparently the driving force for test development. The aim of the newly established Product Development Unit within the TDR programme is to accelerate the development of high priority products, and to stimulate collaboration with partners from the industry. In the future, partners may be more easiliy found in the developing world, as a result of the programmes mentioned above.

I am confident that a goal-oriented, multidisciplinary approach, initiated and steered by international collaboration, will produce more and more appropriate diagnostic methods for large-scale use. When such methods are available, they will be able to make a major contribution to achieving the ultimate goal of improving health in the tropics.

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Table 1

Estimates of prevalence and mortality of major infections in Africa, Asia and Latin America (1977-78)

	Infections/y	Mortality/y
Diarrhoeas	4,000,000,000	75,000,000
Respiratory infections	unknown	4,000,000
Tuberculosis	1,000,000,000	400,000
Parasitic infections:	**Prevalence**	**Mortality/y**
Malaria	800,000,000	1,200,000
Amoebiasis	400,000,000	30,000
Ascariasis	900,000,000	20,000
Hookworms	800,000,000	55,000
Trichuriasis	500,000,000	low
Filariasis	250,000,000	low
Schistosomiasis	200,000,000	750,000

Estimates from WHO (cf. K. S. Warren (1990). Rev. Infect. Dis. 12, 142).

Table 2

Steps in the development of a diagnostic test

	Objectives	Remarks
A.	**Identify diagnostic necessities** **(a) For communities** To assess prevalence, morbidity etc. (to implement or to monitor control measures) **(b) For individuals** To diagnose acute cases, identify individuals at risk to develop disease, assess immune status etc. (to treat or to prevent disease)	(a) Besides public health data include grade of disease perception by the population
B.	**Define precise diagnostic objective(s)** Set specifications related to (a) Predictive values (b) Technical level (c) Standards of performance (e.g. accuracy, precision, reproducibility)	(a) Consider level of prevalence (b) Dependent on test "environment" (health post, health centre, reference laboratory)
**	**DECISION about step C & D**	
C.	**Develop diagnostic method** (a) Produce reagents (b) Establish appropriate technique	Requires defined clinical samples (need for specimen-banks)
D.	**Validate diagnostic test** (a) Related to fixed specifications (b) Appropriateness in authentic environment (applicability, acceptance, efficiency)	(a) Compare with current "gold" standard (b) As component of the health system
**	**DECISION about step E**	
E.	**Produce diagnostic test kit** (including quality control)	Preferably at local level (in endemic area)
F.	**Apply test**	With careful monitoring and feedback