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Genetic Engineering and Biotechnology Monitor

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A. POLICY, NEWS & OTHER EVENTS

United Nations and other organizations' news

WHO forms new division of tropical diseases control (CTD)

"Practical application and management" is how Dr. Jose Najera, Director of the Division of Tropical Diseases Control (CTD), sums up the essential responsibilities of the newly formed WHO division.

CTD was created, with effect from 9 January 1990, to strengthen tropical disease control activities and to improve co-ordination in the field. The new division was formed by a merger of the smaller technical divisions of Vector Biology and Control, the Malaria Action Programme, and the Parasitic Diseases Programme, so that their areas of responsibility could be re-prioritized and reapportioned.

The mandate of CTD, according to the WHO official announcement of the Division's creation, will be to "develop at global, regional and country levels strategies for the control of malaria, trypanosomiases and leishmaniases, schistosomiasis, leprosy and filariasis. Accordingly, the new Division of Tropical Diseases Control will evaluate, adapt and make available to the countries concerned existing or newly-developed control technologies and collaborate in drawing up practicable, manageable and sustainable strategies."

CTD consists of seven units - five for disease control (malaria, trypanosomiasis and leishmaniasis, schistosomiasis, leprosy, filariasis), one for training, and one for operational research. (Source: TDR News, No. 31, March 1990)

Regulatory issues

Forthcoming guidelines will set safety standards for r-DNA foods

By the end of 1990 a new set of scientific guidelines will answer some of the regulatory questions. The guidelines, "Biotechnologies and Food: Assuring the Safety of Foods Produced by Genetic Modification", are scheduled to be published in the July/August issue of Regulatory Toxicology and Pharmacology Journal.

They were drafted by the International Food Biotechnology Council (IFBC) - organized in 1989 to develop criteria and procedures to evaluate safety of foods produced through genetic modification. The guidelines were reviewed by 130 representatives of governments in 11 countries, as well as industrial scientific organizations, professional societies, public interest consumer groups and academics. It sets limits on tests required to assess the safety of foods derived from genetic engineering.

IFBC recommends that regulatory agencies and biotechnology companies consider three sources of information: knowledge of the genetic background and procedures of genetic modification, knowledge of the food's composition, and toxicological data. (Source: McGraw-Hill's Biotechnology Newswatch, 21 May, 1990)

General

Many biotechnology companies enter 1990s with sharply higher revenues

With the start of a new decade, the health of the biotechnology industry in the 1990s is a topic of much speculation. If the close of the past decade is any indication, the industry is moving slowly towards profitability. Revenues in 1989 were up sharply for many biotechnology companies, with increased product sales contributing more significantly to income. However, the industry as a whole is not yet showing a profit.

According to a 1989 survey of nearly 500 biotechnology companies by Ernst & Young, a San Francisco-based consulting firm, only about one fourth of biotechnology companies are reporting net profits. But more than 50 per cent of all companies are seeing some improvement in performance in terms of smaller losses or larger profits than in previous years.

Combined 1989 revenues totalled slightly more than $1.2 billion, an increase of 33 per cent over 1988. In addition, in 1989, these companies reported a combined loss of $175 million. Larger companies, including Amgen, Biogen, Collagen, and Genentech - with a few major products among them - saw the greatest increases in revenues and earnings. For some companies reporting a net income, 1989 marked the first year of profitability.

Sales account for about two thirds of revenues for those companies marketing products. Total sales reached nearly $600 million in 1989 for 20 of the 35 companies reporting product sales. This 53 per cent increase over 1988 sales is higher than the industry average of 33 per cent growth in sales from the survey by Ernst & Young, which determined that 74 per cent of all companies have product sales.

Contract research and collaborative R&D agreements provide the second most significant source of revenue for most companies. R&D spending averages 63 per cent of sales in the biotechnology industry. Biotechnology companies in the area of therapeutics and agriculture can easily have R&D expenses at levels of more than 100 per cent of sales. The norm for R&D spending in the pharmaceutical industry is 16 per cent of sales.

Analysts predict that the 1990s will bring an increased flow of major biotechnology products. Introducing at least one new, and often a first, product is the goal of most companies in the near future. As many companies approach the final stages of product development and preparation for marketing, expenses increase markedly and earnings can drop dramatically.

For most companies, sources of financing remain the major concern. According to the Ernst & Young survey, 45 per cent of all companies will need major financing of a few million dollars each by the end of 1990 and 30 per cent will need financing by the end of 1991. For some companies the problems are imminent: 53 per cent of small companies, 35 per cent of mid-size, and a few per cent of large companies will survive less than 12 months without immediate financing.

In general, companies seek support from three sources - public equity markets, R&D or manufacturing alliances with large companies, and mergers. Cash flow problems affected several companies in 1989 and are leading to what some believe are the first stages of consolidation in the industry.

Large pharmaceutical companies can use an acquisition of a smaller company as a means to obtain an established technology and enter the biotechnology arena.

Not all acquisitions or mergers have been among large pharmaceutical and smaller biotechnology companies

Unlike the acquisition of a biotech firm by a large, capital-rich pharmaceutical company, acquisition of one biotechnology company by another can strain finances and often requires betting on future prosperity.

Companies with successful product launches may become self-sustaining companies in the future and find public markets more willing to invest. A long-stated goal of biotechnology companies has been to operate as independent, vertically integrated biopharmaceutical firms. Most companies currently rely on manufacturing alliances to market their products.

However, in light of industry goals, companies will have to balance short-term cash returns with long-term commitments to outside companies. An increased number of strategic alliances throughout the 1990s, concludes Ernst & Young, may lead to a smoother consolidation of the biotechnology industry in the future. (Abstracted with permission from Chemical and Engineering News, 2 April 1990, pp. 9-11, by Ann M. Thayer. Copyright (1990) American Chemical Society)

AIDS epidemic moves south through Africa

AIDS has spread south from East Africa to Zimbabwe. At the start of May, the country's health ministry announced that Zimbabwe now had 7,375 confirmed cases of full-blown AIDS - three times the official total nine months before.

Truck drivers have helped to spread the disease through the continent. Three years ago, an unpublished survey of 300 bar girls living along the two main arterial routes between Zambia and Zimbabwe found that some 70 per cent were HIV-positive.

The level is similar to that for groups of prostitutes and bar girls tested in Uganda, Rwanda and Kenya at around the same period. Between 67 per cent and 90 per cent of them were found to have the virus.

Even more alarming are the figures for Zimbabwe's first-time blood donors, some 7 per cent of whom tested HIV-positive during the first months of 1990. Over half the donors were teenage high-school students, hardly any of whom were infected. Among the rest - the first-time donor adults, most of whom were factory workers - about 15 per cent were infected.

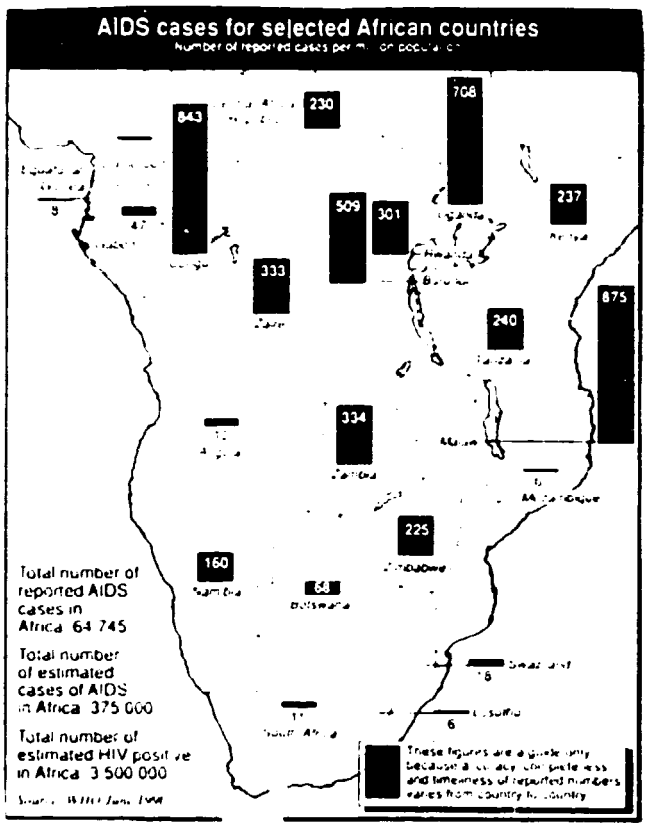
Each donor was first examined by a nurse, counselled, and then made to sign a form that sought to discourage donations from those who have had many sexual partners. This suggests that HIV-prevalence, at least among urban adults, may exceed 15 per cent.

Other statistics from around the region are just as alarming. A source in Zimbabwe's health service says that recent tests on adults in the Zambian capital, Lusaka, found 32 per cent to be infected. Extrapolations made by a consultant epidemiologist from Malawian survey data indicate that 17 per cent of sexually active adults in the country's rural areas, and 19 per cent of those in towns, have HIV. The long-running civil war has prevented widespread data collection in Mozambique, but last year 10 per cent of adults sampled at random in the Beira corridor, and 24 per cent of a small group of newly returned refugees, were discovered to be carrying the virus.

Such figures are ominously similar to those in Uganda, where a national survey carried out in late 1987 and early 1988 found that nearly 800,000 people (including 12 per cent of the rural adults in one region, and 29 per cent of the urban adults in another) were HIV-positive. Last year the Ugandan Government estimated that one million people, or 6 per cent of the total population, had already been infected with HIV.

The similarity ends here, however. Uganda currently reports 12,444 such cases - or nearly three times as many per capita as Zimbabwe. All this would suggest that HIV began to infect people in Uganda in large numbers some years before it did in Zimbabwe.

Many epidemiologists believe that the reason for HIV's rapid spread in southern Africa - both from country to country, and from town to countryside - is that the transport network is better developed than in East Africa, allowing both human beings and the human immunodeficiency virus to move about more easily. (Source: New Scientist, 7 July 1990)



Conference on medicinal plants

The International Conference of Experts of Developing Countries on Traditional Medicinal Plants was held in Arusha, Tanzania, from 19 to 23 February 1990. The experts had gathered because of growing concern in the South about their enormous wealth constituted in their genetic resources of medicinal plants.

Traditional medicine based on herbal remedies has always played a key role in the health systems of the South. The tropical areas of the South are the origins of more than two thirds of the world's plant species, at least 35,000 of which are estimated to have medicinal values. People in third world countries have learnt how to select, grow and use them. As a great part of Western medicine is based on medicinal plants - at least 7,000 medical compounds in the modern Western pharmacopeia are derived from plants - new biotechnologies will open new venues for the use of medicinal plants and people in the North disillusioned about their

medical system look for exotic alternatives, the South feels threatened by "unchecked profit-making interests". The current trend towards highly restrictive patenting of life forms adds to the threat. Already 25 per cent of the retail sales in the pharmaceutical trade are based upon medicinal plants. The estimated value of the South's germplasm for the pharmaceutical industry by the year 2000 ranges from $US 4.3 billion to $US 47 billion.

The experts from the South felt that time was ripe for action to defend their rights to their plants and their knowledge of them and guard against the 'monopolistic privatization drive of the transnational pharmaceutical companies'. Therefore South-South co-operation was needed in areas such as systematizing inventories on medicinal plant resources and the use of them; promoting their cultivation, processing, marketing and use in the South to improve the general health care; conservation of medicinal plants in situ as well as ex situ with special attention to endangered species; and in the areas of financial, institutional, technical and legal requirements.

Participants stressed the need to involve traditional healers in the academic processes and the information dissemination and to strengthen their position. Education on medicinal plants was necessary for lay people as well. The establishment of national lists of essential traditional herbal medicines corresponding to the prevailing disease patterns together with legislation to foster their use were considered important educational and political means to upgrade and consolidate the role of herbal medicines in the medical system.

The conference envisaged that co-operation between strengthened Southern research units would reduce dependence on the North. For this purpose, first of all research priorities within national and regional networks have to be defined. National surveys of medicinal plants initiated at sub-national (local) levels and geared towards the solution of the prevailing major health problems was felt such a priority. The resulting information should be collected in newly created data banks for detailed scientific as well as traditional and ethnobotanical information on medicinal plants. Participants were planning to liaise with organizations working in the area of medicinal plants and to draw on the expertise of international organizations such as WHO.

Participants were particularly concerned that persons and communities, including traditional practitioners, be appropriately rewarded for their innovative contributions to herbal medicines. As a consequence legal protection of discoveries and innovation was considered to be very important. It should go hand in hand with national policies on the distribution of the potential income from innovations, part of which should ensure popular access to herbal remedies at an affordable cost. (Source: African Diversity, Nos. , & 5, Dec 1990)

Keystone dialogue calls for $500 million fund

With the recent progress in FAO and other international fora as the background, the second session of the Keystone Dialogue Series on Plant Genetic Resources took place at the beginning of February in Madras, India. The Keystone Center (an American foundation) aims to bring together in their personal capacity key actors in the global genetic resources debate from industry, NGOs and intergovernmental institutions in order to reach consensus on specific points in off the record discussions. The first session of this Dialogue series took place in the United States in August 1988 and resulted in a consensus report that presented strong recommendations on several major issues in the genetic resources controversy, including the FAO debate, the Gene Fund, IBPGR and the role of NGOs.

The follow-up session in Madras brought together almost 50 individuals from a wide range of backgrounds including several gene bank directors (USA, Netherlands, India, Ethiopia, USSR), representatives from public research institutes, corporate officials (Ciba-Geigy, Pioneer Hi-Bred, KWS), people from different United Nations agencies (FAO, the United Nations Environment Programme, the United Nations Conference on Trade and Development), international agricultural research centres, and NGOs like ENDA, SEARICE, RAFI, GRAIN, WCC, etc. Through a long week, the participants tried to tackle a whole array of different issues relating to plant genetic resources conservation, without avoiding the most controversial ones. From the very beginning it became clear that most of the participants had come all the way to India with a strong desire to reach consensus. With so many of the antagonists gathered around the table, the discussions were intense, sometimes heated but also realistic. The outcome, achieved towards the end of the week, is an impressive 40-page consensus report that highlights several critical recommendations to help move the conservation of genetic resources forward.

Agreeing that discussions would part from the consensus already reached in the first Keystone round, three parallel working groups brainstormed throughout the week on what were considered the most important items: (1) an assessment of the current PGR system, (2) intellectual property protection, and (3) global co-ordination and funding.

Regarding the assessment of the current PGR systems, the Dialogue participants concluded that, in many countries, activities at the national level are badly organized and called for a strengthening of National Plant Genetic Resources Systems (NPGRS). Recognizing that many nations of the world may not be in a position to support full-fledged NPGRS, the Dialogue encourages activities at the regional level. As well, it was concluded that although numerous initiatives are springing up, a truly global system does not exist. The Madras Dialoguers agreed that this network could be organized, involving all organizations that hold genetic resources, "under agreements that safeguard the farmer's long-term interests in the context of the International Undertaking". The work of FAO in drawing up an ethical code of conduct for germplasm collectors was endorsed, while it was stressed that such a code should be based on the recognition of the contribution of farmers in providing genetic resources.

Perhaps the most interesting feature of the discussion on the assessment of the current PGR systems is the substantial attention the Dialogue participants dedicated to the important role of NGOs and communities at the grass roots level. Local varieties and wild plants are recognized not only as an important source of genetic diversity, but also as a crucial tool for viable agricultural development. According to the Dialogue participants, the work that farmers and communities carry out to improve local plant varieties is not sufficiently recognized and supported. Therefore financial and institutional assistance for these activities was recommended. Grant systems should be developed to support communities in this task, training on mass selection and other forms of genetic improvement should be provided, and NGO networks working in these areas strengthened.

Patents vs. genetic diversity

In the field of intellectual property rights (IPR) systems, the Keystone Dialogue consensus came forward with some remarkably strong language on their consequences for genetic resources conservation and utilization. For many years, NGOs have been pointing to the negative impacts that IPR systems such as plant breeders' rights and patents have on genetic diversity and plant breeding. For the same number of years, official circles and representatives from seed companies vigorously denied such impacts. Now, at the turn of the decade, this impressive gathering of government administrators, corporate representatives and NGO folk agreed in unison that "At the level of individual plant species of agronomic value, current IPR systems reinforce the tendency of plant breeding to decrease genetic diversity." Also, "The existing IPR systems are not considered generally useful in developing countries." Furthermore, "While stimulating the commercial development of new cultivars (...) these IPR systems restrict their availability and/or transferability for direct commercial exploitation without a licence." While the careful wording of the language used does not hide the hours of tedious negotiation that went into it, it also shows that a broad consensus is slowly building up on the impact of IPR systems on genetic diversity and the availability of genetic resources.

The Keystone Dialogue is, in particular, deeply concerned about the current GATT negotiations on the Trade Related Intellectual Property Rights (TRIPs). GATT negotiators from the USA and other Northern countries consider the lack of strong IPR systems in developing countries as an unfair trade practice. In parallel, industrialized countries are increasingly moving towards the patenting of genetic resources. The Keystone participants strongly felt that if the GATT deal goes through and includes the patenting of genetic resources, it will seriously clash with all international initiatives on genetic conservation, such as FAO's International Undertaking and UNEP's convention on biological diversity, both of which start from the fundamental principle of genetic resources being the "common heritage" of mankind.

Keystone consensus went so far as to declare that: "If some of the changes now proposed by some industrial nations to GATT and WIPO are successful, the only forms of human invention that will not be patentable will be those of informal inventors in developing countries. The twin dangers of expansion of the scope of formal patent rights on the one hand, and non-recognition of informal innovation systems on the other, will lead to a widening of the economic gap between industrialized and poor nations. A better common future for humankind will remain an illusion."

The final report urges GATT to get in touch with bodies such as FAO, IUCN, UNEP, UNESCO, UPOV, and WIPO, and asks governments involved in GATT to consult their national insitutions working in the field of biological diversity. "No decisions should be taken in GATT concerning the extension of IPR to plant genetic material without resolving these issues."

Money on the table!

The third working group discussion on global co-ordination and funding focused on recent FAO and UNEP activities, delved into farmers' rights, and came up with strong recommendations on getting the money on the table. It was noted with satisfaction that the FAO IBPGR controversy is becoming something of the past and the Dialogue participants called upon the players in the debate to urgently resolve the remaining differences and get on with it. With the intent to tone down the long-standing FAO controversy on the different categories of germplasm affected by the undertaking, the Dialogue participants stated that the whole debate boils down to trust. "Unfortunately, as is often the case, the technical problem, as real as it is, is subordinate to the political will for the nations involved." To lay down the path toward greater co-operation in this field, the group therefore agreed to clear definitions of germplasm categories.

Another specific measure to move the FAO debate forward and ensure broader political support is the suggestion to create a Technical Advisory Committee to assist the FAO Commission in both priority setting and the management of the Gene Fund. Noting the initiatives of IUCN and UNEP to establish a convention on biological diversity, the group proposes to set up a Global Commission on Biological Diversity within the UN ambit, holding a broader mandate than the current FAO Commission, but drawing from already existing structures.

Clearest of all in the keystone session recommendations are the strong calls to get money on the table. The cornerstone of any funding mechanism, according to the Madras participants, is farmers' rights. "Local communities bear much of the burden of protecting germplasm and the rest of the world has an obligation to help them carry out this task and help them in utilizing the material. (...) We speak of 'compensation' because it implies a relationship with obligation. We agree on the concept of Farmers' Rights and we agree that contributions to a fund in recognition of these rights should not be voluntary." Accordingly, it was agreed that the compulsory fund must draw in new and substantial money, and the group is very firm on what "substantial" means: "It is not possible for us now to determine the real financial requirements for a fund for Plant Genetic Resources. (...) We have no doubt, however, that there is a great and genuine need for substantial additional financial resources. (...) A conservative estimate indicates that at least $US 500 million per annum should be available to begin to meet these urgent needs."

To make the provisions of the consenses reached in this second Keystone session fully operational and effective, the steering group decided to establish several working groups on the key issues for 1990. These working groups will also develop new areas for discussion for the Third Plenary Session, to be held in 1991.

The Keystone Dialogue is explicitly "informal, off-the-record and restricted to personal views". However, the recommendations of the Dialogue are generally highly regarded in policy making circles because of the unique composition of the group. The FAO, for example, already incorporated several of the recommendations of the first Keystone Dialogue in recent decisions. There is no doubt that this second session will have a similar, decisive impact in a broad range of circles. The report of this Dialogue is forceful, worded on intellectual property rights systems, farmers' rights and the Gene Fund. Hopefully, it should provide the so desperately needed impetus to knock a sense of urgency and realism into international negotiations, while at the same time not disregarding controversial issues. Further information is available from: the Keystone Center, P.O. Box 606, Keystone, CO 80435, USA. Tel: (1 303) 468.58.22. (Source: Seedling, Vol. 7, No. 1, February 1990)

European body promotes biomass

The European Association for Biomass (AEBIOM) has been formed in Brussels by several national organizations to promote the usage of biomass. The founding members consider that biomass represents a significant solution to the problem of diversification of outlets for European agricultural products.

Biomass - or vegetable or animal origin - can be used in energy production and industrial processes. The EC's two major imports, grain and seed products, offer various opportunities in this respect, says AEBIOM.

The association will co-ordinate the activities of existing national associations at the European level, and intervene on their behalf with European Community bodies such as the Parliament, Commission and Economic and Social Committee.

Mr. Souplet, a French senator, will be president of AEBIOM. According to Souplet, France, Italy, and Portugal have already approved projects for the non-food use of agricultural products, and the Federal Republic of Germany may soon join them. He estimates that biomass from 15 per cent of cultivated land may be sufficient to provide all the energy requirements of French agriculture.

"First research is to occur on "clean" biomass production to make sure that so-called agricultural production does not generate a new pollution as it makes possible to avoid." (Source: European Chemical News, 28 May 1990)

New environmental group

The new European Environmental Research Organization (EERO) soon will establish its headquarters on the campus of Wageningen Agricultural University. This reflects a major financial commitment to the new organization made by a consortium that includes Dutch government ministries, research agencies and institutes, RaboBank (Utrecht, the Netherlands), and the Universities of Wageningen and Utrecht. In addition to funding already announced from the German Volkswagen Foundation EERO will receive one million guilders (US$30,000) per year for at least five years from the consortium for its efforts in promoting environmental research. Further contributions are earmarked from the Swiss Department of Foreign Affairs and the Spanish Ministry of Education and Science.

EERO's choice of Wageningen is also based on the intellectual and material barriers to be gained from locating at an institute that already contains one of the largest concentrations of scientists in Europe working on issues related to environment and ecology. In addition to the 7,000 university scientists engaged in environmental problems, Wageningen is close to the National Institute of Public Health and Environmental Protection and 11 of the 17 research institutes of the Dutch Directorate for Agricultural Research. Alexander Zehnder, professor of microbiology at Wageningen Agricultural University, has now succeeded Kenneth Timmer as chairman of the EERO council. The vice-chairman is Ralf Hutter of the ETH Centrum (Zurich, Switzerland).

Modelled on the European Molecular Biology Organization (Heidelberg, Federal Republic of Germany), EERO will not fund research directly. The organization has set a budget of 2.5 million ECU's ($3 million) for the first five years of its work, supporting long- and short-term fellowships, advanced laboratory courses, and workshops. EERO soon will announce the appointment of its first executive secretary.

Ten areas highlighted for special attention are: the biotransformation of pollutants in nature, where their behaviour may not reflect that observed under laboratory conditions; and the parameters that determine whether a polluted ecosystem will return to its original state following the disappearance of the pollutant, or whether a qualitatively different population of organisms will establish itself. A third aim is to stimulate research and the spread of expertise on processes - biotechnological or otherwise - that can eliminate pollutants in waste waters, dump sites, and accidently contaminated environments. (Source: Bio/technology, Vol. 8, April 1990)

Preserving the present

The Centre for Genetic Resources and Heritage (CGRH), a library that will be filled with genetic material from rare or endangered Australian plants and animals, has been set up at the University of Queensland, but lack of federal government support is forcing the library to seek support from commercial interests in Australia and overseas.

CGRH, part of the University's Centre for Molecular Biology and Biotechnology, will be a "Genetic Louvre", in the words of director John Mattick. Collected material will be stored as cryogenically or desiccated cells and tissue, isolated DNA and cloned gene libraries. Other gene resource libraries have traditionally restricted themselves to collections of microbiological cultures and seed material. According to Daryl Edmondson, co-ordinator of the gene library, the CGRH is unique in that it will "actively collect data. Most other libraries simply collate their own collections." CGRH will collect cells or DNA from Australia's most threatened species, such as the false water rat, one of the country's rarest mammals, and the short-necked swamp tortoise. The university's large collection of bacteria, fungi, yeast, algae and viruses, accumulated over 25 years, will also be represented at the centre.

CGRH, at present supported by the university, is seeking help from private sources and has been in touch with corporations in Australia and Japan and scientific foundations in the United States. The project will not yield any visible benefit for two years, according to Mattick, but, if it is not done, "subsequent generations will say we had the technology to keep (DNA) cottonwool and still ask us, 'why didn't you?'" (Source: Nature, Vol. 345, 3 May 1990).

Biotechnology professionals urged to join ASTM Committee on Biotechnology

ASTM standards-writing Committee E-48 on Biotechnology invites all scientists, engineers, manufacturers, researchers, and representatives of government and academia who are interested in biotechnology to join the committee.

The scope of the committee extends from identification of biological materials to process validation (GMP). It also develops standards for the biomass industry involving wood materials, alcohol fuels, and anaerobic/aerobic digesters. E-48 is broken down into seven technical sub-committees: materials for biotechnology, characterization and identification of biological

system, unit processes and their control, environmental issues, biomass conversion systems, validation of biological processes, and terminology.

All interested individuals are invited to join the committee, and are welcome to attend the committee's meetings. The next meeting is [illegible] October - 1 November 1990, in San Antonio, Texas. For a free brochure outlining the benefits of joining Committee E-48, contact John Cowell, ASTM, 1916 Race Street, Philadelphia, PA 19103-1187, (215) 299-5496. For more information on the activities of Committee E-48, contact Committee Chairman Dr. Larry Eitel, Fear Siegler Measurement Controls Corp., [illegible] Inverness Drive, East Englewood, CO 80112, (Tel.: 303 [illegible]-[illegible]00).

Committee E-48 is one of [illegible] ASTM technical standards-writing committees. Organized in 1898, ASTM (American Society for Testing and Materials) is one of the largest voluntary standards development systems in the world. (Source: News Release, [illegible] July 1990)

What is the human genome project?

The goal of the Human Genome Programme is nothing less than a complete understanding of the genetic basis of Homo sapiens, including the genetic basis of disease.

The human genetic blueprint - the human genome - contains an estimated 100,000 genes, which encode information in DNA for making a human individual in the first place, and for maintaining the individual in his/her daily life. These genes are distributed among 23 pairs of chromosomes (22 pairs of so-called autosomes and a pair of sex chromosomes, X and Y). Each chromosome contains a long DNA molecule combined with various protein molecules, which determine the overall structure of the chromosome. The DNA molecule is composed of just four units, known as nucleotide bases, linked together in varying combinations of order like beads on a string. There is a total of 3 billion bases in the human genome.

Only 2 per cent of human genes have so far been pinpointed to specific chromosomal locations; and only a handful of some 4,000 genetic diseases are understood at the molecular level. The Human Genome Programme aims to locate the position of all these genes, and to read the genetic information encoded in them, including the aberrant information in disease genes. Several levels of attack are planned: first the genetic map, secondly, the physical map and thirdly, the complete DNA sequence.

The genetic map. By studying the inheritance patterns of certain characteristics [illegible] disease, physical traits and [illegible], genetic markers - geneticists are able to build up a picture of which genes are located close to which other genes. For instance, the genes for characteristics that are always inherited together must be located close to each other on the same chromosome. Genes for characteristics that are inherited together frequently, but not always, are probably located on the same chromosome, relatively close together. Co-inheritance of characteristics at levels no better than chance probably indicates that the genes are on different chromosomes. Extensive analysis of this sort produces a map that shows the general - but not absolute - location of the genes for these characteristics, as they occur on the chromosomes. Genetic mapping has long been an established activity among human geneticists, but is being boosted under the Human Genome Programme.

The physical map. [illegible] fragments of DNA can be [illegible] a physical map [illegible] of DNA [illegible] fragments of DNA [illegible] the fragments in some way, and then determining how the different pieces physically relate to each other [illegible] like assembling the pieces [illegible] put together, to get a picture [illegible] genome mapping of this sort [illegible] enterprise, and the goal [illegible] Programme is to have a complete physical map [illegible] within [illegible] years.

The sequence. A reading [illegible] of the [illegible] nucleotide bases that [illegible] the DNA [illegible] in the [illegible] chromosomes [illegible] the genome [illegible] sequence. In principle, every element of the genome - genes, control regions, [illegible] - will be visible and identifiable and the instructions they contain interpretable. Of all the parts of the Human Genome Programme, [illegible] the sequence is the greatest challenge, with a target date set at 2005.

In addition to work on the human genome, mapping and sequencing of a series of other genomes - from model organisms - will also be undertaken. The idea here is to provide a pool of comparative data against which human genome information can more effectively be interpreted. A crucial part of the entire programme is the development of new technology for the job, particularly sequencing, and devising ways of handling the huge quantity of data that will begin to flow from it. The boldest biological endeavour ever undertaken, the Human Genome Programme will cost about $3 billion over a period of 15 years. (Source: New Scientist, [illegible] 1990)

Human gene therapy

The chances of the first human gene therapy experiment winning approval improved when the US National Institutes of Health human gene therapy sub-committee [illegible], approved an experiment to treat adenosine deaminase (ADA) [illegible] [illegible]

[illegible]

[illegible] and [illegible] Anderson of the National Heart, Lung and Blood Institute [illegible]

[illegible]

[illegible] Blaese [illegible] ADA [illegible]

Blaese says he has already met and discussed the risks of treatment with the families of two ADA deficient children. (Source: Nature, Vol. [illegible])

Canine genome project

In a strategy modelled on the first phase of the human genome project, researchers are developing a genetic linkage map to help find the genes responsible for several hundred diseases in man's best friend.

The ultimate goal is a simple blood test a vet or breeder can use to determine whether a dog is carrying a gene for, say, hip dysplasia, blindness or copper toxicosis.

The project is being conducted by two human geneticists, George Brewer and Yilma Kurbasian-Gorkan of the University of Michigan, and three veterinarians, William Schall, George Padgett, and Ulreh Mostosky of Michigan State University. They have received a $270,000, 5-year grant - the largest ever for dog health research from the American Kennel Club, the Morris Animal Foundation, and the Orthopedic Foundation for Animals, Inc.

The first task is to find 300 DNA markers or "landmarks", spread around the chromosomes, for construction of a map with landmarks spaced every 10 million bases or so. It should then be possible to find the rough location of a disease gene by seeing whether it is inherited along with a marker. From there, developing a diagnostic test is relatively straightforward.

How many genes are ultimately detected this way will depend on research money, says Brewer, who estimates that, once the map is in hand, it will still cost about $20,000 to $40,000 to seek out each disease gene. (Extracted with permission from Science, Vol. 248, p. 1194, 8 June 1990. Copyright AAAS 1990)

B. COUNTRY NEWS

Australia

Genetic engineering regulation

The Australian Government is under pressure to introduce new laws to govern the regulation of genetic engineering after a public outcry over the sale for human consumption of 53 genetically altered pigs. The pigs had come from a research programme aimed at breeding "superpigs" through the introduction of extra copies of the gene for porcine growth hormone. They were sold for slaughter apparently without approval from any of the bodies regulating genetic engineering.

At present, guidelines on genetic engineering in Australia are issued by the Federal Government's Genetic Manipulation Advisory Committee (GMAC). Any organization seeking to release a genetically altered organism into the environment [illegible] seek advice from GMAC, although compliance with the guidelines is voluntary.

According to Anne Sears, project manager of the genetic manipulation section of the Victorian Law Reform Commission, GMAC has no powers of direct sanction should their guidelines be ignored. GMAC can, however, recommend the removal of federal funding and tax incentives from both the research group involved and the parent institution.

The Australian Conservation Foundation (ACF) is taking advantage of the questions raised by release of the pigs to push for a national uniform system of legal regulation. Phillip Toyne, director of ACF, said: "As companies increasingly seek to commercialize research results new laws are becoming even more necessary." The University of Adelaide also believes GMAC guidelines should be enshrined in legislation.

In a report released last year, the Victoria Law Reform Commission recommended legislation requiring mandatory notification of any proposed release of a genetically altered organism to GMAC and to any relevant state or federal body, such as the Department of Agriculture.

The commission also called for an environmental assessment before the release of any experimental organisms and the advertising of proposed releases "to ensure that interested people can obtain information and participate in decision-making before the proposal is approved". Australia's "superpigs" were the world's first transgenic animals with enhanced production characteristics. In a project run by Bob Seamark, reader in endocrinology at the University of Adelaide, transgenic pigs incorporating genes for porcine growth hormone grew as much as 15 per cent faster, with a 30 per cent better feed conversion rate. (Extracted from Nature, Vol. 345, 31 May 1990)

Gene "museum"

Queensland University's Centre for Molecular Biology and Biotechnology is to establish a Centre for Genetic Resources and Heritage (CGRH) to act as a kind of 'museum' of genetic material of Australia's indigenous flora and fauna.

The Centre's Director, Professor John Mattick, said that the Centre would collect and hold sample tissue from many endangered species of plants and animals to preserve their genotype in the DNA contained in the samples. The preserved DNA will act as a reference library, and also theoretically offers the potential to 'reactivate' the DNA of lost species by transferring it to the cells of a related species. Although the latter scenario is probably still some way off, the samples of DNA will be frozen and can be kept for many years.

Of more practical and immediate impact, the material collected will add to the University's already recognized collection of bacteria, viruses, yeasts, fungi and algae built up over the last 25 years, offering scientists access to a wide range of material for research and commercial development work.

Meanwhile, overseas, scientists at the University of California are reported to be trying to resurrect the fungus gnat, extinct for 40 million years, by implanting DNA from amber preserved tissue, and scientists in Russia are trying to

[illegible] (Source: Australian Journal of Biotechnology, Vol. [illegible], No. [illegible], [illegible])

Government policy [illegible]

Professor Ralph Slatyer, [illegible] the Prime Minister's Science [illegible], has [illegible] a programme of co-operative [illegible]. The government plans to establish [illegible] co-operative Research Centres in order to link the CSIRO, universities and research groups. Up to $100 million has been pledged, with the rest of the necessary funds to come from co-operating institutions. Fifteen centres are expected to be established in two years, with the remaining [illegible] over the next three years, creating employment for [illegible] scientists.

The centres will be on or near university campuses in order to enable post-graduate and young researchers to benefit from more experienced people in the field. It is hoped that the centres will help to attract companies to the new technology parks growing up around universities, and increase ties with industry. (Source: Australian Journal of Biotechnology, Vol. [illegible], No. [illegible], April 1990)

C-MIST

The first meeting of the Consultative Group on Marine Industries, Science and Technology was held in Canberra on 2[illegible] February 1990. Dr. Martin [illegible] was invited to be a member of this Consultative Group and attended on behalf of the ABA. The concept is that this Consultative Group work in conjunction with a committee of the Heads of Marine Agencies and provide advice to that body. Both these groups will work in conjunction with the Marine Section of the Department of Industry, Technology and Commerce. The first meeting was spent explaining progress following the McKinnon Study on the Marine Industries.

The aim of the Consultative Group will be to provide a wide representation by accessing industry bodies such as the ABA. It is likely that the Consultative Group will meet approximately twice a year. This, in itself, is not likely to contribute greatly to formation of policies on marine industries and marine science and technology. However, it will attempt to be effective by forming a series of working parties. It is proposed to establish the following working parties:

- Strategic Information for Marine Industries;
- Policy Co-ordination and Resolution of Marine Resource Conflicts;
- Innovation in the Marine Sector;
- Long- and Short-Term Training Requirements for Marine Industries;
- Aquaculture: Feasibility of a National Approach;
- Offshore Resources and Engineering.

The ABA Council has not yet considered whether it is appropriate for the ABA to continue to be represented on this Consultative Group. It would appear at this stage that it would be useful for the ABA to remain represented because areas such as aquaculture, fish feed and fish vaccines, as well as algal culture, are all part of biotechnology. The organization held a meeting in Melbourne on 1[illegible]-11 May 1990 entitled "Ocean, Australia 1990". This conference was of interest to everyone involved in the future of marine industries, science and

[illegible]

[illegible]

[illegible] Australian Trade Commission (AUSTRADE) [illegible] develop [illegible]

AUSTRADE [illegible] Australia's export [illegible] [illegible], fruit and [illegible] processed [illegible] [illegible], the early stage [illegible] and agricultural technology [illegible] export earnings.

Growth markets

Australia is [illegible] well placed [illegible] the growth markets of North and South-East Asia, North America and the Pacific region. [illegible] these fast growth markets, AUSTRADE, [illegible] with industry, has developed strategies [illegible] increase exports [illegible] pipeline.

[illegible] AUSTRADE [illegible] [illegible] aspects of [illegible] development and [illegible] key markets as a [illegible] and related technology.

The latest of these strategies - [illegible] processed food - was released in December [illegible]. The strategy was developed by AUSTRADE in [illegible] with 60 companies in the food industry and identifies factors that have [illegible] food exports, and details how AUSTRADE [illegible] work with industry [illegible].

[illegible]

AUSTRADE [illegible] industry [illegible] market.

Modernization programme

Australia's [illegible] industry has already [illegible] modernization programme [illegible] future investment.

Vegetable production [illegible] export investment opportunities [illegible] third of our vegetables are processed.

The agricultural systems strategy [illegible] major export earner which will build on Australia's

success in finding innovative solutions to problems encountered in farming in a wide range of conditions.

Such solutions are relevant to agricultural development in Asia, Africa and the Middle East.

AGRITEC

AGRITEC, the agribusiness industry group established jointly by industry groups and AUSTRADE in 1988 to promote the export of Australia's agricultural technology, has been closely involved in the development of the strategies. AGRITEC brings together some 40 companies representing a wide range of farm inputs including machinery, seeds and plants, chemicals, livestock, consultancy services, as well as research and education.

Together AUSTRADE and AGRITEC are developing an appropriate market entry programme. Priority markets include Africa, the Middle East, South-East Asia and, more recently, China and India.

At present, exports of Australian agricultural systems are exceeding $80 million a year and could top $300 million by 1991/92.

In a move designed to assist innovative producers, processors, manufacturers and marketers of rural-based products to exploit commercial opportunities, the Federal Government introduced an Innovative Agricultural Marketing Program (IAMP). Jointly run by AUSTRADE and the Department of Primary Industries and Energy, the IAMP currently provides $3 million a year for approved projects, with a special emphasis in export marketing and associated innovative production, processing and developmental activities. It aims to help innovative projects by providing seed money to supplement resources available from the private sector.

So far 146 projects have been funded by the Innovative Agricultural Marketing Program. These covered a wide and varied range of products, from the development of a special wrapping for oranges in non-refrigerated containers to special scoured wool blends as important replacements for the Australian carpet wool industry.

AUSTRADE believes that some of these new and innovative industries could earn Australia more than $804 million by year six of the programme. A survey of IAMP projects funded in 1986/87 and 1987/88 suggested that grant funds of $2.4 million have generated export sales of $8 million and import replacement of $7.1 million, a total of $15.5 million.

There is also a big market for further processing of traditional exports - meat, cereal, dairy, wool, cotton and hides and skins.

Meat

Australia has a livestock industry which includes 150 million sheep, 23 million cattle and 3 million pigs. Demand is growing for quality cuts of beef and lamb in packaged form for the catering, hotel and restaurant trades in Japan, South-East Asia, the Middle East and North America.

The production of meat and meat products accounts for 25 per cent of the food processing industry's turnover. About 50 per cent of this product is for export and, of this, nearly half is destined for the United States where further processing occurs. Opportunities exist for further processing to take place in Australia and for the development/manufacture of highly processed meats and products, particularly with a very low fat content.

Cereals

Australia is a major producer of quality white wheat and coarse grains. Cereal products currently produced in Australia include starches, gluten, bread, pasta, breakfast cereals and biscuits. Although more than 13 million tons of wheat are harvested each year, little is processed in Australia. Up to 75 per cent of this wheat is sent overseas in an unprocessed form.

Dairy products

The quality and availability of Australia's raw products, combined with competitive production and processing techniques, have been the major factors for the success of the nation's dairy industry.

While cheese is a major product of the dairy industry, taking some 30 per cent of manufacturing milk products, there are still major openings in the cheese industry for the development and export of specialist cheeses. Other new products are being developed to cater for the changing tastes of consumers.

Fisheries products

World trade in fish products has been steadily growing over the past few years and Australia, with a diverse range of seafood, is well placed to take an increasing share of this market. With the world facing increasing difficulties in sustaining ocean catch levels, aquaculture has an important role in supporting the seafood market.

Australia has the natural resource, a high level of expertise and the established infrastructure. To date there has been no extensive development in this sector. A strong research and technology base has been developed to support large and profitable fish farms.

Wool products

Good investment opportunities exist in Australia's wool processing industry, particularly in scouring, combing and the production of wool tops. Yarn and textile production also has potential. We are at the forefront of this technology and have many suitable locations for processing plants.

Cotton products

Significant export opportunities also exist in the cotton industry. While some of this cotton is already processed in Australia, real opportunities are in yarn spinning or the production of fabrics.

Hides and skins

Major opportunities exist in the traditional leather industry following a rationalization. Investment is required in modern, efficient plants, with the potential to convert into leather some of the $700 million of hides and skins that Australia exports each year.

AUSTRADE's message to rural producers is clear: the future of agribusiness export growth

lies through working with grower co-operative or other industry groups to invest in adding value to agricultural products. "Value adding" need not mean problematical outlays on complicated new systems or processes. It can simply be the establishment of quality assurance programmes, professional packaging and advanced transportation. In the areas of raw materials it could mean adding stages of treatment or further processing.

AUSTRADE emphasizes that agribusiness is not just the domain of multinational enterprises. An interest in agribusiness translates into being an interest in the complete marketing chain by any organization or group, no matter how small or large.

As the end of the twentieth century approaches, it is important that Australia's agribusiness sectors prepare themselves to capture market opportunities by becoming as efficient in the marketing of their agricultural products as they are in producing them. (Source: Australian Journal of Biotechnology, Vol. 4, No. 2, April 1990)

Austria

New PHB production process

The Austrian company, btf, has developed a new method for the production of poly-beta-hydroxybutyric acid (PHB). The process was described by the company, which is the biotechnology research unit of Austrian industries, at a recent workshop held in Spain.

The process uses a natural mutant of Alcaligenes latus, which is able to accumulate PHB in very high concentrations during the growth phase. The product is recovered using one extraction and one precipitation step, producing a technical grade product with purity greater than 99 per cent.

The company has the capacity to produce 0.5 ton/week of PHB in a 15,000-litre fermenter. It expects to be able to increase this to 1 ton/week without major design adaptations. (Source: European Chemical News, 2 July 1990)

Canada

The regulation of biotechnology in Canada

Over the past months, the National Biotechnology Advisory Committee has considered the factors which provide an appropriate regulatory climate for biotechnology. Current legislation applicable to biotechnology in Canada pertains to specific product categories, without regard to the process of production. These product categories include veterinary biologics, pest control products, foods, drugs, cosmetics and medical devices. Other products intended for use in the open environment, such as organisms for waste treatment or mineral leaching, or waste products from biotechnology processes that are unintentionally released to the environment, are not well covered by existing legislation. Research activities without a clearly defined end-product are not currently under legislative control.

Some products intended for open or semi-contained use in the environment and currently under development in Canada include hybrid canola (rapeseed) varieties, new ornamental and greenhouse plants produced by cell culture techniques, fish vaccines, interferon-based treatments for animal diseases, bioleaching agents for silver and gold recovery, and pulp and paper waste treatment agents. Bacterial inoculants for seeds and soil, and bacterial and viral pest control products, can be registered for use in Canada under existing legislation.

The processes used in biotechnology range from older techniques such as fermentation, and mutation with selective breeding, to newer techniques such as cell and protoplast fusion, and recombinant DNA methods. The new biotechnologies greatly extend the gene pool available for genetic recombination and, therefore, the range of functional characteristics which can be produced. While there is presently no reason to consider these new products any more hazardous than similar products of older technologies, novel processes may open new avenues of product contamination and require new approaches to quality control and product safety evaluation.

Wastes and by-products may also be process-dependent. Increased use of biological processes, even if the product is chemical, provides new opportunities for the introduction of process organisms into the environment during waste disposal. Such process organisms tend to be poor competitors in the open environment; nevertheless, existing environmental legislation in Canada may not provide for adequate surveillance and control over such releases. The proposed Canadian Environmental Protection Act is intended to correct this situation.

Existing Federal regulatory system

The document "Guidelines for the handling of recombinant DNA molecules and animal viruses and cells" was originally developed in 1977 by the Medical Research Council. These Guidelines specify appropriate levels of containment for micro-organisms, including viruses according to the taxonomy, the degree of pathogenicity, and the nature of the research. They were revised in 1979 and again in 1980, with progressive relaxation justified by continued safe experience and consistent with international experience. The MRC Guidelines clearly apply to laboratory research (culture quantities up to 10 l) and are not intended to address procedures for field trials, commercial scale production or open environmental release. Compliance with the Guidelines is required only by MRC and the Natural Sciences and Engineering Research Council funding applications. The Guidelines are not enforced by the granting councils, except by withholding of funds. The Guidelines are presently undergoing a further revision and they are expected to be available in the near future.

The major federal statutes applicable to products of biotechnology are administered by Health and Welfare Canada, Agriculture Canada and Environment Canada. The following are the major federal statutes applicable to the products of biotechnology:

The Food and Drugs Act is administered by the Health Protection Branch of Health and Welfare Canada. Compliance requires pre-market notification and testing of drugs, cosmetics and medical devices. Foods are not subject to pre-market notification requirements, although post market evaluation or voluntary pre-market review can be

undertaken. Drug manufacturing by novel biotechnological processes, including recombinant DNA methods, cell fusion, or cell culture, must comply with MRC Guidelines and Good Manufacturing Practice guidelines defined in the Food and Drugs Act, and drugs produced by these processes cannot be sold in Canada without a licence from Health and Welfare's Bureau of Biologics. Evaluation criteria give considerable attention to product purification and removal of extraneous substances or infectious agents.

The Quarantine Act, which is administered by the Health Protection Branch, Laboratory Centre for Disease Control, prohibits importation of infectious diseases. However, controls over importation and transportation of human pathogens are obscure, being dependent on other legislation such as the Animal Disease and Protection Act and the Transportation of Dangerous Goods Act (see below). The legislation is seldom used.

The Animal Disease and Protection Act is administered by Agriculture Canada. It prohibits importation, transportation or sale of veterinary biologics in Canada without a special permit. Permit conditions for transportation consist of documentation and safety requirements specified in Transport Canada's Transportation of Dangerous Goods Act. Licence conditions for sale include purity, potency, efficacy and safety requirements.

The Pest Control Products Act is administered by Agriculture Canada and it requires that all chemical and microbial/biological pest control products be registered prior to manufacture, sale or use in Canada. Registration guidelines for active ingredients and end-use chemical products, and guidelines for the Registration of Microbial/Biological Pesticides are available. General requirements include specifications, manufacturing methods, quality control methods, toxicology, residue data, environmental and non-target studies, environmental chemistry (fate or expression for microbials), efficacy and proper labelling.

The Food Production and Inspection Branch has released a "Guide to the regulation of agricultural products of biotechnology". In addition, a workshop to air the regulatory concerns of Canada's biotechnology industries and to allow the Regulatory Branch of Agriculture Canada to outline its policies for the review and regulation of agricultural products of Biotechnology was held in December 1988.

The Fertilizer Act, also administered by Agriculture Canada, regulates fertilizers and supplements offered for sale in terms of their safety, merit and value. Growth-promoting microbial products genetically engineered and otherwise) are defined as supplements and must comply with the standards, guarantees, safety and labelling requirements outlined in the regulations. Additional guidelines for environmental release and research exemptions are presently under consideration.

The Plant Quarantine Act, also administered by Agriculture Canada, prohibits importation of any pest organism capable of causing injury or damage to plants or plant products, or of any plant or other object that may carry a pest organism. The Act applies to pest organisms or plants produced by biotechnology, as well as to naturally occurring species. However, new expertise may be needed to evaluate capability of injury or damage by genetically engineered organisms.

Existing provincial regulatory system

The Canadian Provinces and Territories play a prominent role in regulation, sharing responsibility with the Federal Government for environmental protection, and having primary responsibility for occupational health. Occupational health legislation is the only type of regulatory instrument that could be used at present for control of research activities. Most research activities adhere closely to MRC Guidelines, although the guidelines are voluntary. Provincial environmental legislation is generally modelled after federal instruments, and usually lacks pre-manufacture notification requirements, or specific penalties for violation. Applicability to biotechnology products or wastes is uncertain, and may vary from province to province.

An analysis of the current situation: definitional and legal issues

The definition of terms within existing legislation needs to be periodically reviewed to determine which, if any, biotechnology products and processes are included, and to ensure that new products under development are subject to adequate control. For example, it may be appropriate to broaden the definition of "substances" under the Canadian Environmental Protection Act.

Legal issues which are likely to arise in relation to these definitions include the status of products containing killed organisms as either chemicals or biologicals. Both applicability of, and requirements under, existing legislation depend on this distinction. If sterilized products are classified as chemicals, it may be necessary to require demonstration of complete sterilization, or studies of DNA uptake by other organisms

Any special regulatory treatment of biotechnology products, such as recommended by the Canadian Environmental Law Research Foundation, will require precise definition of biotechnology in terms of process techniques such as recombinant DNA or cell fusion methods. Any distinction between organisms with and without foreign DNA would require a definition of "foreign". A precise definition of this term could be difficult to achieve in view of the genetic plasticity of micro-organisms in nature. Regulatory agencies do not consider special biotechnology legislation appropriate at this time.

Co-ordination and jurisdictional issues

With development of biotechnology products for open environmental use, some designed for environmental persistence, ecological impacts are a prime consideration. Ecological processes are global in nature; therefore, consistency in approach between jurisdictions is an essential element of effective regulatory control. Co-ordination between agencies at all levels, and between levels of government is necessary to ensure this consistency.

The federal Interdepartmental Committee on Biotechnology currently serves a co-ordinating function in Canada. However, monitoring of the international situation, maintenance of a data base

on international regulatory experience, and interdepartmental dialogue relative to jurisdictional overlap and adequacy of regulatory instruments will require increasing effort and human resources over the next decade. An independent, non-regulatory body with full-time staff is needed to fulfil this function, and also to communicate the soon-to-be-released guidelines entitled: "Biotech Regulations: Users' Guide", to industry.

Recent developments

Several analyses of the current regulatory system in Canada have been undertaken. The Henley Report to the Federal Interdepartmental Committee on Biotechnology, (FCB) in 1986 provides a comprehensive inventory of Federal and Provincial regulatory instruments and their applicability to biotechnology. Examples of jurisdictional inconsistency and weaknesses in environmental legislation are noted. The Beak Report, "Regulatory Policy Options for Canadian Biotechnology", prepared for MOSST in 1987 examines policy issues pertaining to biotechnology regulation in Canada and recommends establishment of a non-regulatory co-ordinating bod, with a national mandate.

The FCB Sub-Group on Safety and Regulations, reporting to the Federal Interdepartmental Committee, has reviewed the regulatory situation and in response has produced guidelines entitled: "Biotech Regulations: Users' Guide" to assist industry in coping with the maze of regulations. Individual federal agencies are also reviewing regulatory positions, instruments and responses in order that they will be able to deal effectively with new technological developments.

The Medical Research Council has established a sub-committee, jointly with Health and Welfare, reporting to the MRC's Standing Committee on Ethics in Experimentation, for review of MRC Guidelines with respect to new developments in biotechnology. Health and Welfare has established a Branch Biotechnology Committee within the Health Protection Branch to examine all aspects of biotechnology that impinge on Branch activities, including reviews of Federal health protection legislation. Agriculture Canada has identified the need for an advisory panel on biotechnology to review regulatory responses related to veterinary biologics.

Environment Canada's new Canadian Environmental Protection Act (CEPA) has been approved by Parliament. The Act is intended to have very wide applicability and is a "cradle to grave" piece of legislation, covering safety in the research, production, use and disposal of products. Its application in the field of biotechnology is still inadequate. Consultations have been held nation-wide with interested Canadians and specific proposals have been developed to deal with inadequacies of the Act in respect to biotechnology.

Provincial agencies are also in the process of reviewing their regulatory positions pertaining to biotechnology. For example, Ontario and Alberta have established interdepartmental committees to study their respective regulatory regimes and Manitoba is actively consulting with industry. The Provinces are supportive of consistent national action and look to the Federal Government to provide scientific information and criteria to aid in setting policies.

The international dimension

Canada has been very active in the Organization for Economic Co-operation and Development (OECD) work on safety and regulations and is supportive of the OECD proposals for the international harmonization of regulations related to biotechnology. The 1987 Canada-OECD Joint Workshop on National Policies and Priorities in Biotechnology, held in Toronto, highlighted the importance of public confidence in the regulation of biotechnology, and supported the creation of an international data base for regulatory and risk assessment criteria and information.

The World Health Organization (WHO) recently held an international meeting to discuss potential health impacts of biotechnology, and adopted several general risk assessment considerations, including potential for adverse effects, probability of organisms escaping, and safety of products and handling methods. A battery of specific product tests was suggested, including tests for pathogenicity, allergenicity and/or photosensitivity, hypersensitivity, toxicity, carcinogenicity, mutagenicity and/or teratogenicity. These tests are currently used for human health assessment of drugs and pesticides in Canada. Occupational health recommendations included routine worker surveillance and monitoring, and documentation of safety, containment and organism identification procedures. (Source: Annual Report of the National Biotechnology Advisory Committee, 1987-1988)

Life sciences technology park planned for Ottawa

Begun in the early 1980s as an idea from an Ottawa-Carleton report on biotechnology, the Ottawa Life Sciences Technology Park (OLSTP) is coming to fruition.

The research and technology business park will provide a home to start-up companies and more established firms who use biotechnology and life sciences to produce products and services for health care and other markets. One of the main objectives of the new venture is to develop close working relationships between university and clinical researchers, and private industry. The life science park will provide a commercial outlet for applied and developmental research in the region.

The business plan supports financing from private and public sources. The park will require about $15 million over six years before becoming self-financing.

OLSTP founders have already been approached by companies with an interest in locating in the park. Some key development areas would be in health care products such as pharmaceuticals and drugs, nutritional supplements, immunological products and microelectronic medical devices.

Officially incorporated in October 1989, the OLSTP formed a Board of Directors comprised of its founders, governments and industry. The OLSTP has ensured that 50 per cent of its Board was selected from the private sector. This was an important objective to ensure the industry perspective to successfully commercialize technology developed in the laboratory.

The technology park is planned for lands adjacent to the Ottawa Health Science Centre. The park will be a geographically focused collection of enterprises that creates an atmosphere conducive to the development of new products. It will be located among existing medical and university facilities in a campus-like environment covering over 200 acres.

Metro Ottawa also offers a concentration of life sciences technology sources in a number of public sector laboratories.

The OLSTP has been structured to meet the needs of its tenants including access to technology, financing and business expertise, all in a world-class research park.

For more information on the Ottawa Life Sciences Technology Park, visit the OCEDCO booth (B,C) at the ABC meeting in Toronto or call Hugh B. Anderson at (613) 733-6870. (Source: Bioscope, Vol. 3, No. 2, Summer 1990)

Costa Rica

Biotechnology in Costa Rica

Guidelines for biotechnology research at about 60 public and private institutes in Costa Rica are presented in the "Programa Nacional de Ciencia y Technologia 1986-1990". Primary objectives include: stimulation of tropical agriculture, especially basic foodstuffs, generation of foreign currency and job creation, medical applications and alleviation of dependence on export of primary products.

Priority areas in the research programme can be divided into three areas: agriculture, stock-breeding and health. In agriculture the use of in vitro propagation techniques gets most attention. Biological and biotechnological control of plant diseases and pests also ranks high as well as nitrogen and phosphor fixation. In stock-breeding most attention goes to clonal and micromanipulation as well as transplantation and freezing of embryos. Health research concentrates on diagnostical systems.

The lack of scientific trained people in Costa Rica in the field of biotechnology is relatively small compared to other countries in the region. Staff at post-graduate level is available at the Centre of Cellular and Molecular Biology at the Universidad de Costa Rica and the Centre for Research and Education in Tropical Agronomy (CATIE).

Research at National Institutes and Universities

The Agronomy Department of the Ministry of Agriculture and Livestock is co-ordinating six national research programmes on: rice, corn and sorghum, grain and legumes, vegetables, fruits and sugar. Next to these programmes the Ministry has initiated its own programme on the production of potateseeds through tissue culture and diagnostics of blue tongue disease.

The Research Centre for Molecular Biology (CIBCM) has a wide experience in molecular biology and diagnosis of viruses of plants and animals. Research furthermore concentrates on: virus resistance of beans, expression of viral proteins on bacteria, cloning of families of Brucella and molecular biology of Rhizobium.

The National University, Heredia, works on clonal and micropropagation, freezing and transplantation of cow embryos. Studies are carried out on: vescular and stomatitus virus in Costa Rica, induced mutations of rice beans and palms for breeding purposes, and characterization of mycorrhizae associated with forestry species.

Research at the Research Centre of Cellular Biology (CIA) covers biochemistry, (cyto)genetics, immunology, and cellular, nuclear and molecular research. Special attention is paid to selection of Rhizobium phaseolus strains, biological fixation of nitrogen in legumes and biological control of Monilia in coca, of Black Sigotoka in bananas and Pseudomonas. (Source: Biotechnology and Development Monitor, No. 2, March 1990)

Centre for Research and Education in Tropical Agronomy (CATIE), Turrialba

An important programme at CATIE is the Tropical Crops Improvement Programme. This programme concentrates on three perennial crops of major importance for the region: coffee, cocoa and Musaceas (plantain and cooking banana), as well as on promising crops such as: cassava, sweet potato, coco and true yam, taro and some others of local importance.

In co-operation with the Inter-American Institute of Agricultural Sciences (IICA), coffee research is done through using somatic embryogenesis and microstakes for the multiplication of superior genotypes.

Tissue culture methods are used for the genetic improvement of cacao by developing haploid plants, micropropagation and embryogenesis as well as simple methods of in vitro conservation. DNA research is still not within reach although advances in tissue culture methods permit the use of micropropagation for cloning desirable genotypes.

With respect to plantain, tissue culture techniques are used for somaclonal variation and micropropagation for breeding principally on disease resistance. The International Network for the Improvement of Banana and Plantain (INIBAP) has part of its germplasm collection stored at CATIE. In the near future the material will be stored in vitro.

As there is some risk involved in the maintenance of field collections, in vitro collection is also the main target for research in promising tropical crops. In vitro culture with coffee is applied; experiments on the isolation and cultivation of protoplasts and on the regeneration of plantlets are in progress.

The strategy of CATIE is to develop technological packages and to be able to multiply superior germplasm through tissue culture. For this reason collaboration has been sought with commercial enterprises. Recently CATIE started co-operative programmes with Monsanto on embryo transplantation of cow embryos for improving milk quality in tropical areas.

CATIE is considered as the most important centre in agricultural education in the Central American isthmus and the Caribbean. Each year CATIE trains over 250 students on tropical crop improvement. Further information available from the Centre for Research and Education in Tropical Agronomy (CATIE), Turrialba, Costa Rica. Phone: (506) 566431, Telex: 8005 CATIE. (Contact: Dr. V. Villalobos.) (Source: Biotechnology and Development Monitor, No. 2, March 1990)

European Community

Biosafety R&D proposals sought by EC

A formal call for proposals has been issued (OJ-C118/22 of 12 May 1990) for research proposals in the area of "safety assessment associated with the release of genetically engineered organisms into the environment". This call, which is part of the BRIDGE Programme, is for two types of projects:

N Projects (i.e. basic research aimed at extension of scientific knowledge) deal with aspects of assessment of the safety of release of genetically engineered organisms into the environment, e.g. monitoring, control and assessment techniques, gene behaviour and organism survival; and novel gene constructions to prevent survival of GMOs, or to ease their destruction in the environment;

T Project (i.e. large-scale co-ordinated research aimed at removal of bottlenecks to technical progress in specific areas). This project covers "High resolution automated microbial identification for environmental impact studies". It deals with development of new techniques for analysis of taxonomically important cellular components, their automation, and their application to monitor the impact of new introductions to the environment.

As in other BRIDGE areas, project proposals must be multinational and preferably involve relevant industrial or agri-business interests.

The information pack containing call for proposals and application form is available from: Commission of the European Communities, DG XII-F/2 BRIDGE, 200 Rue de la Loi, B-1049 Brussels. Fax: (322) 235 53 65. (Source: Irish Biotech News, Issue No. 26, July 1990)

BRIDGE Programme update

The final selection of projects to be funded under the EEC BRIDGE Programme has now been made From the original 403 proposals for funding 63 N-Projects will be funded, and in addition, around 150 EEC laboratories will also be involved in five T-Projects on lipases, lactic acid bacteria, plant cell regeneration, yeast genome sequencing, and mapping of the Arabidopsis genome.

Several further BRIDGE T-Projects are planned to begin over the next 18 months. The call for BioSafety projects has already been made, while a T-Project on animal cell biotechnology will be launched later this year.

In addition to research funding, funds for training and research-stays by Ph.Ds and M.Scs in laboratories in other EEC countries are continually available. (Source: Irish Biotech News, Issue No. 26, July 1990)

EC Human Genome Analysis Programme adopted

The Human Genome Analysis Programme, HGAP (1990-1992) was finally approved on 29 June 1990 and has a budget of ECU 15 million which will be allocated to some 20 European laboratories.

The complete list of genome research projects currently being funded by various EEC sources is as follows:

Title	EEC Programme	No. of labs	Periods of execution	EC Funding (million ECUs*)
Sequencing of the chromosome III from yeast	BAP	35	89-90	2.635
Sequencing of the yeast genome	BRIDGE	31	91-93	5.060
Molecular identification of new plant genes (Arabidopsis genome)	BRIDGE	27	91-93	3.000
Establishment of a complete map and strategic approach to the sequencing of the Bacillus subtilis genome	SCIENCE	5	89-91	0.750
A complete physical map of Drosophila melanogaster genome	SCIENCE	3	88-93	0.872
Functional and structural analysis of the mouse genome	SCIENCE	3	89-92	1.278
Development of a genetic and physical map of the Porcine genome	BRIDGE	11	91-93	1.200
Physical map of Human genome	HGAP	20	90-92	15.000

* $US 1.18.

Further details on the Human Genome Analysis Programme is available from Dr. Bronwen Loder, DG XII/F6, Commission of the European Communities, 200 Rue de la Loi, B-1049 Brussels. Phone: (322) 236 3193 or 235 0749. (Source: Irish Biotech News, Issue No. 20, July 1990)

New EC R&D programmes in preparation

The approval by the Council of Ministers of the Third EC Framework Programme (1990-1994) in April 1990 has provided the funding (ECU 5,700 million) and general guidelines for the preparation of 15 specific R&D programmes. Many of these have a relevance to some aspect of biotechnology. Those of most direct interest, however, are the following:

Research area	Funding (million ECU)
Biotechnology	164
Agriculture and agro-industry	433
Biomedical and health care	134

The remaining programmes cover Information, Communications, Energy, Nuclear and other industrial technologies. There is also a "Human Capital and Mobility" programme which will provide funds for student and employee training and exchange programmes.

Detailed R&D programmes in each of the above areas are now being prepared by the Commission, with advice from various representative committees. These programmes will be based on the strategic goals set out in the Third Framework Programme (1990-94). The strategic guidelines for the biotechnology-related programmes are:

Biotechnology: The "aim is to reinforce basic biological knowledge as the common and integrated foundation needed for applications in agriculture, industry, health, nutrition and the environment". Priority areas will include protein and gene structures and function, gene expression and control, genome analysis and conservation, immunology, neurobiology and receptors, and other topics.

Agricultural and agro-industrial research: The objective is to help achieve a balance between agricultural and aquacultural production, and consumer and industrial needs. To this end the Agricultural Programme should aim at enhancing competitiveness of agri-business, and at upgrading and diversification of agri-products. In the field of agri-food research, topics will include food nutrition, toxicology and hygiene, and new technologies for food processing.

Biomedical and health research: The main focus is on new approaches to tackling economically and socially significant diseases (in particular, cancer, AIDS, cardiovascular disease, mental illness, aging and workplace health problems). Human genome analysis and early screening for risk factors will also be included.

The R&D programmes based on the above guidelines will be in preparation over the next months. Calls for proposals will be made when the process of consultation and agreement has been finalized. This is likely to be in early 1991. (Source: Irish Biotech News, Issue No. 26, July 1990)

European Environment Agency

The EC Council of Ministers responsible for the environment resumed examination of the proposal to establish a European Environment Agency and a European Environment Monitoring and Information Network at its meeting of 22-23 March 1990.

The Council accepted the bulk of the amendments proposed by the Commission following the comments of the European Parliament. Two leading scientists, particularly well qualified in the field of environmental protection, will be appointed to the Management Board of the Agency.

The Council recalled that the seat of the Agency was a matter for a decision by the General Affairs Council. The Regulation to establish the Agency will be decided when the decision on the seat has been taken. (Source: BIO/Technica Journal No. , 1990)

EC directives on modified organisms

In its meeting in March 1990 the EC Council of Ministers responsible for the environment approved the substance of the proposals for EC Directives on:

The contained use of genetically modified micro organisms; and

The deliberate release to the environment of genetically modified organisms.

The purpose of the first Directive is to adopt measures to control the contained use of genetically modified micro-organisms. It makes provision for notification of operations, the application of containment measures specific to the type of micro-organism and to the characteristics of the operation, as well as measures relating to accidents and waste management.

The purpose of the second Directive is to ensure the completely safe use to the environment of genetically modified organisms. It establishes a procedure for notification and case-by-case approval, for which the procedures differ depending on whether the organisms are being released for R&D purposes or in products which are placed on the market. (Source: BIO/Technica Journal No. 2, 1990)

EC biotechnology directives are to be implemented in next 18 months

Europe has formally adopted two key EC directives to regulate biotechnology within the EC. Member States now have 18 months to introduce the directives, which regulate the contained use of genetically modified organisms and their deliberate release into the environment. (Source: Manufacturing Chemist, May 1990)

EC to fund R&D projects for ICI biopolymers

The EC is to provide funds for two research projects involving ICI's biopolymers. The first, aimed at introducing genes for production of ICI's biopolymers into crop plants, is to receive a grant under the EC's ECLAIR initiative, established to promote pan-European research.

The polymers, tradenamed PHB-V in the US and Biopol outside that market, have previously been produced by the bacterium Alcaligenes eutrophus. The advantages of the gene being expressed by a crop plant rather than a bacterium are ease of growing and harvesting, plus the sustainability of the parent plant (compared with the need to destroy bacteria to extract the plastic).

The three-year project will involve staff from ICI Biological Products, ICI Seeds, the University of Hull and the Belgian universities of Ghent and Gottingen. The project will cost ECU 3.5 million ($4.6 million) of which the ECLAIR programme will provide ECU 1.7 million.

The second project is to be carried out jointly with the Federal Republic of Germany's engineering company Krupp, with funds from the EC's BRIDGE programme. This aims to develop biopolymers with improved composition specifications. Features of particular interest are the improvements of barrier properties, such as alcohol resistance, which would be particularly useful in containers.

This project will also last three years, at a cost of ECU 2.4 million, half of which is to be provided by the EC, and the remainder shared equally between ICI and Krupp. (Source: European Chemical News, 2 July 1990)

EUREKA environmental push

The European EUREKA programme has increased its commitment to developing environmental protection technologies. Earlier this month, 37 projects costing ECU 253 million ($309 million) were approved in this sector, along with 54 other projects, giving a total investment of ECU 964 million. Other sectors covered include biotechnology (nine projects, ECU 96 million), new materials (five projects, ECU 36 million), and energy (two projects, ECU 27 million).

A total of 20 US organizations will participate in 13 of the 91 new projects, bringing the country's total involvement to 186 organizations and 45 projects.

To date, no East European countries have applied to join the EUREKA initiative, which aims encourage pan-European collaboration on high-technology R&D. Moves to encourage their participation are planned, however. The current membership of EUREKA comprises 12 EC member States, six EFTA countries and Turkey.

Since its launch five years ago, the programme has initiated 386 projects with a total budget of ECU 7.8 billion. Around one third of this sum is provided by governments; the remainder comes from the private sector. France participates in the largest number of projects, at 163, followed by Italy (137) and the Federal Republic of Germany (129). (Source: European Chemical News, 11 June 1990)

Germany

Gene law gets the go-ahead

The framework law on genetic engineering has been passed by the upper house of parliament, the Bundesrat, and became effective on 1 July 1990.

The legislation passed on the last working day before the elections in North Rhine-Westphalia and the Lower Saxony shifted the parliamentary majority in favour of the Social Democrats. Critics of the law have accused the Christian Democrat-Liberal government of "whipping" the legislation through parliament before the elections.

Both the chemical industry association, the VCI, and the chemical employees union, IG Chemie-Papier-Keramik, have expressed satisfaction over the passing of the legislation. (Source: European Chemical News, 21 May 1990)

Gene law impact analysed

Under the new German Genetic Technology Law well-known genetically engineered products such as Genentech's tissue plasminogen activator (t-PA), Amgen's erythropoietin (EPO) or Biogen's interleukin-2 (IL-2) could be manufactured without disclosure of production plans or the necessity to hold a public hearing. This is one of the conclusions of a study on Health Care Biotechnology in the Federal Republic of Germany, carried out by RauCon Bioinformatics & Consulting GmbH.

According to RauCon, the production processes used by these companies to produce such products would be classified under safety level 1, because they use harmless organisms. This implies that the competent authorities would be obliged to approve their production processes within three months after submission, provided that normal safety standards are met.

RauCon warns, however, that it is still uncertain to what extent other laws could interfere with the Genetic Technology Law - which came into force on 1 July. Environmental laws (e.g. regulating the erection and operation of chemical synthesis plants) could interfere with the law if a genetic engineering plant needs a chemical step to transform the recombinant product into its final form.

Moreover, RauCon sees a conflict potential arising from the EC Council Directive on the contained use of recombinant micro-organisms, adopted on 23 April. Overall, however, the study concludes that the new law has restored the basis for Germany's competitive position in pharmaceutical biotechnology. Details from: Dr. Norbert Sax, RauCon Bioinformatics & Consulting GmbH, P.O. Box 1064, D-6507 Ingelheim, Federal Republic of Germany. (Source: Biotechnology Bulletin, Vol. 3, No. 5, June 1990)

France

Technology helps firms meet biotechnology challenge

New applications for enzymes and ferments in the pharmaceutical and food industries are being discovered as technology, in genetic engineering and enzymology advances. Doris Jebland, on behalf of the European Chemical News, examines how French companies are expanding their operations, and pinpoints the factors that go together to produce a successful biotechnology business.

Enzymes and ferments for agro-food and pharmaceuticals are undergoing deep changes, spurred by constant technological innovation applications. Progress in genetic engineering and enzymology is generating new uses and developing new potential applications for micro-organisms and enzymes in the biotechnology industry.

An example is the French cheese industry, which is increasingly applying direct insemination through lyophilized or frozen concentrated ferments. Numerous projects are reaching advanced stages of development and the jump to industrial applications and commercial development will depend on appropriate legislation for genetically engineered products. It will also depend on whether new technologies add real gain to manufacturing processes.

In a study of how enzyme and ferment producers, more particularly in France, are adapting to this changing environment, the Paris-based consultant Precepta points to the vital role R&D is assuming in successful growth strategy to launch new products and to diversify into new client areas such as pollution control, agriculture and food additives. In order to trim costs and select the most appropriate technology, manufacturing processes must also be mastered. In addition, marketing strategies are evolving towards supplier/client partnerships. In a climate of growing competition, other moves, such as increased internationalization or external growth operations, tend to reduce the number of players involved.

The enzymes and ferments industry can be divided into four main groups of activities: industrial enzymes, bakery yeasts, lactic ferments (yeasts, bacteria and moulds) and miscellaneous ferments (acetic, malolactic and so on).

Ideally, belonging to a group brings a scientific or financial bonus. In France, most companies belong to a group that is either specialized or diversified in chemicals, pharmaceuticals or food.

Some companies are linked to a single client in the food business; some cater for several clients, mainly in food, while others are geared to a large number of client sectors both in food and other areas.

But for all of them, growth is linked to sustained demand of traditional clients and to the rate at which new technologies will enter industrial applications.

It envisages client demand exceeds a 5 per cent annual growth rate, and is all organized by legislation favourable to genetically engineered products. It is quite likely, new players will enter the trade, especially those specializing in genetic and enzymatic engineering. The would either act as intermediaries between the enzyme and ferments producers and the user companies, or as direct competitors of established companies offering "turnkey enzymatic or ferment systems" rather than products.

Such competition, believes Precepta, would mainly involve industrial enzymes, and companies like Unilever Brocades and Novo Nordisk Bio Industries, seek to associate, or even buy up, these competitors.

The trend has already started with Novo acquiring the US-based Zymo-Genetics, which specialises in genetic engineering, in 1988. Gist and Novo will seek to consolidate their positions through their high technological potential and reputations in their respective sectors.

Other companies will diversify by enlarging their range of products. Those laboratories geared to the dairy sector could diversify into rennin, animal food, environmental protection or ensilage.

If industrial applications of new technologies develop more slowly because of adverse legislation, several trends could emerge, believes Precepta. External growth operations may continue to develop at the current brisk rate; the internationalization of companies may increase; there may be a tendency to widen the product range to increase attractiveness to traditional clients; and there may be further diversification towards new sectors in order to increase sales.

Currently, the world industrial enzymes market is around FF 3.5 billion ($625 million) with the US the largest sector. The world market for milk auxiliaries is around FF 1.32 billion. (Source: European Chemical News, 4 June 1990)

India

Indian National Working Group on Patent Laws

In August 1988 the Indian National Working Group on Patent Laws was established in New Delhi in response to pressure exerted upon India to introduce substantial changes into the Indian Patents Act of 1970. The group comprises representatives of a cross section of NGOs including professional associations, trade unions, health and consumer organizations and even industry representatives.

The group campaigns for a patent system best suited for India. Forging a national alliance, mobilizing public opinion on India's and international patent issues, organizing various studies on aspects of the patent system in India and elsewhere and convening a number of relevant seminars and conferences are some of the campaign tactics. As a result the group has already been able to generate awareness of the issues at stake. In the December 1989 National Conference of scientists on Science, Technology and Patents organized by the Group, for instance, eminent scientists from all over the country unanimously passed a resolution against any changes to the Indian Patent Act designed to fall in line with Northern viewpoints and against patent protection in the area of biotechnology, urging the Indian Government to withstand pressures to change its patent law and take a strong stand in GATT.

The Group as well as the Third World Patent Convention encouraged similar initiatives in all third world countries in order to influence their governments to present at international fora such as GATT a strong unanimous front against Northern pressures towards a uniform patent system which would be of great disadvantage to the South. (Source: African Diversity, No. 2 & 3, June 1990)

Indonesia

Biotechnology in Indonesia

Through support of a stable research network, the Indonesian Government aims at stimulating industrial applications of biotechnology. The Ministry of Science and Technology therefore has created the National Committee of Biotechnology which now designs policy and programmes. With the help of foreign know-how and finance, the Government intends to "leapfrog" into the field of biotechnology. Priority areas of Government in biotechnology are: the development of new clones, disease-free plants and cell-line purification, plant multiplication and the development of hybrid plants via embryo culture and cell fusion.

Through the Second Universities Development Project for Indonesia, financed by the World Bank ($US 260 million), bilateral programmes with different industrialized countries have been set up. Other important Government-financed initiatives are the Indonesian Institute of Science (better known as the LIPI centres: Lembaga Ilmu Pengetahuan Indonesia), and the Inter-University Centres (IUC).

Two research institutes under LIPI concentrate on both agricultural and pharmaceutical products with a high added value. At the Centre for Research in Biotechnology (CRI-LIPI) in Bogor, a great diversity of biotechnology research is applied to plants and animals varying from fermentation and enzyme technology to microbial and genetic engineering. At the Research and Development Centre for Applied Chemistry (RDCAC-LIPI) at Bandung, research is focused on the development of industrial processes chemicals, food and feed. LIPI has proposed the establishment of a large centre of research on all aspects of biotechnology in Cibinong (near Jakarta).

The IUC consists of three centres which concentrate on biotechnology in the field of agriculture (Bogor Institute of Agriculture, IPB), pharmaceutics (University of Yogyakarta, UGM), as well as industrial applications of biotechnology, (Bandung Institute of Technology, ITB). Plant tissue culture of forest species is applied at the Regional Centre for Tropical Biology, at Bogor (SEAMEO BIOTROP).

While industrial application of modern biotechnology is not common in Indonesia, more traditional applications, mainly based on fermentation, are widely in use. Fermentation is used in the small-scale production of tempeh, soy sauce and tauco (soy beans), or on (pressed peanut cake), tape (cassava or glutinous rice). Currently, there are more than 40,000 tempeh manufacturers in Indonesia. Industrial applications are in the manufacture of molasses, brewing of beer, production of citric acid from solid cassava waste and monosodium glutamate production, using molasses as substrate. Research is in progress to improve the traditional fermentation processes. Research and Development Centre for Biotechnology-LIPI. (Contact: Dr. Susono Sonono) Jl.Ir.H. Juanda 18 Bogor 16122, Indonesia. Phone: (0)251-322108, Fax: (0)251-328177. (Source: Biotechnology and Development Monitor, No. 3, June 1990)

Ireland

Irish National Centre for Bioinformatics

The Irish National Centre for Bioinformatics at the Genetics Department of Trinity College Dublin is a national facility for DNA and protein sequence analysis. The Centre maintains the GenBank/EMBL DNA sequence data library; the current version, Release 64, contains over 30 million bases in more than 43,000 entries.

The Centre can provide homology search and sequence alignment services, and advice on evolutionary analyses. There is a wide range of sequence analysis software available, including the Staden package.

Multiple sequence alignment is achieved using the CLUSTAL Program software designed and developed by Dr. Des Higgins and Dr. Paul Sharp, researchers at the Centre. CLUSTAL was developed as the first package capable of performing multiple alignment on the type of microcomputer available to most laboratories, and has been widely distributed in response to requests from researchers around the world. CLUSTAL is also available on a mainframe, and can perform alignments of up to 100 sequences of maximum length around 400 residues.

The Centre can be accessed remotely by researchers in Irish colleges through HEANET.

Details from: Dr. Paul Sharp, Department of Genetics, Trinity College, Dublin 2. Telephone: (01) 772941, ext. 1035. Fax: (01) 798558. Electronic mail to incbi@vaxl.tcd.ie. (Source: Irish Biotech News, Issue No. 26, July 1990)

Ireland's salmon-vaccine trials tread water, awaiting lab results

Outdoor trials on the first genetically engineered vaccine for furunculosis, a deadly salmon disease, are being held up by Ireland's Recombinant DNA Committee.

Researchers at Trinity College developed the salmon-targeting vaccine by genetically engineering the furunculosis bacterium, Aeromonas salmonicida, to inactivate the aroA gene involved in the aromati. biosynthetic pathway for folic-acid production. The altered organism will not multiply in the salmon, yet it will elicit an immune response. BRI is also testing a variation of the vaccine with two inactivated genes as a safeguard. The vaccine is designed to be administered by injection into young fish.

BRI has filed a patent jointly with Trinity College and is seeking industrial partners for licensing in Canada, Scotland, Ireland and Norway. The agency's marketing manager hopes to have the vaccine available within a year, but there are no predictions about cost, which will be set by the licensors.

Furunculosis, which slowly destroys the salmon's internal organs, can cost fish farmers up to 20 per cent of their stock. (Extracted from McGraw Hill's Biotechnology Newswatch, 7 May 1990)

Italy

Advanced laboratory planned

A large Italian biotechnology laboratory that can operate in all the various sectors of basic research, not only for the health and pharmaceutical sector, has been on the experts' agenda for many years. For example, three years ago the Ministry of Research's biotechnology committee revealed that a good number of biotechnology centres exist in Italy. However, wide-ranging measures need to be taken as soon as possible for the many uncovered areas that still remain. A laboratory of this kind will be opened in Genoa in September 1991. The laboratory will be linked to the National Institute for Cancer Research (IST), which is currently one of the most important Italian centres of biotechnology studies for therapeutic applications.

Some figures provide an idea of what is planned for the new advanced biotechnology centre: 350 research workers (some of whom are being recruited internationally) and laboratories for cellular biology, molecular biology, genetics, immunology and biochemistry. The architectural design includes four towers. The first three (already under construction) for research activities, an auditorium for training purposes, and a fourth tower for industrial liaison activities such as market research, centres for the industrial application of prototypes resulting from research activities, and possibly offices of outside firms.

The centre obtained two packages of public financing from the FIO (Investment and Employment Fund) for 35.8 billion lire in 1987 and another 25.5 billion lire in 1989. The funding was sufficient for the particularly sophisticated architectural work and for the equipment. The University of Genoa, FILSE (Liguria's regional financial group), Genova Ricerche, and the Gaslini Institute will also become members of the consortium along with the IST.

The new laboratory, however, will also be a direct continuation of the biotechnology research already under way at the IST. In fact, in its 10 years of existence, the Genoa institute, with its 220 research scientists and 15 laboratories, has seen a rapid growth in biotechnology in its laboratories. Projects such as artificial skin (in vitro cultivation of human epithelial tissue), monoclonal antibody (probes and tumour killers) production and "programming", and immunological systems studies (also of interest in AIDS research) are carried out in five laboratories and are, in fact, areas of research that involve studies of the DNA and cells.

The new biotechnology centre will have a multiplying effect on these activities and will provide all the equipment capable of producing monoclonal antibodies, which can link themselves to T-lymphocytes (human cancer killing cells) and direct them in the task of immunity elimination.

This is the project strategy and its development status to date. It will also be of strategic importance for the Ministry of Health, which for some time has worked on a rather delicate project of defining regulations for, and developing centres of, biotechnological validation. In all industrialized countries, biotechnology is an activity that is subject to control and testing by government bodies with regard to both product safety and research projects.

In the coming years biotechnological production will increase in Italy. However, the establishment of accredited laboratories for product validation still remains an unresolved problem. The Genoa centre, with its extensive basic research capacity, will carry out fundamental associated functions.

The Genoa centre will be established to provide a greater in-depth study also in the field of marine biotechnology, an area with a vast potential but

which also requires a profound knowledge of the environmental implications involved. (Extracted from Il Sole 24 Ore, 6 February 1990)

Bioelectronics research programme

Recently the Ministry of Universities and Research set out to devise a perfect procedure to enable its transfer from biological to electronic hardware. Such an ambitious programme (National Bioelectronics Programme) calls for extremely high-level statistical and biophysical research and requires the establishment of interdisciplinary groups of highly interactive researchers. Industry is also expected to be actively involved in this research programme.

A decidedly revolutionary idea underlies the programme: exploiting the self-organizing capabilities of biological structures as well as the transmission modes of protein signals to develop biochips that can self-assemble by using an initial instruction code, as happens in nature with cellular physiology. The long-term programme is even more challenging: "improving" the properties of natural proteins. In other words, the programme sets out to improve the biological materials that have been obtained phylogenetically over hundreds of thousands of years.

An eight-year ministerial research project had never existed before. Neural chips and sensors that are 10,000 times smaller than VLSI (very large-scale integration) networks will be produced during the first three-year stage. The aim is to understand the relationship between the primary and the tertiary structure of proteins (space conformation) by using "bottom-to-top" procedures to characterize the three-dimensional structure of molecules (through nuclear magnetic resonance and X-ray crystallography) from a biophysical standpoint and by using computer-modelling techniques. Only with an understanding of these relationships can one artificially modify molecular properties in a profitable manner.

Almost 100 billion lire will be earmarked for the first three-year stage of the national bioelectronics programme, 10.2 billion of which is intended for the cultural and professional training of researchers and research technicians. CIPI (Interministerial Committee for the Co-ordination of Industrial Policy) has already approved the overall funding for the following five-year period. If the programme covers basic research activities with an unpredictable outcome and therefore without certainty of industrial applications, the long-term goal of the proposed research on proteins is also their long-term extensive use in bioelectronics. In the near future this will involve the specific area of protein engineering (biotechnological) and the production of VLSI neural chips and sensors with immediate economic as well as scientific interest and with a considerable impact on all industrial areas.

The two research stages with different durations are not only designed to allow for the monitoring of the work after a 36-month period but also to reduce the risks, or better, to make it possible to correct the programme while in progress. The activities to be carried out during the second five-year stage will depend heavily on the research findings of the first three years.

Electronic, neural and submicron areas

Theme 1: Silicon neural circuits and architectures for sensors and learning systems.

The Italian company SGS-Thomson is already carrying out research in this area. Its VLSI research laboratory in Agrate is one of its most prestigious advanced centres. In view of its future integration with traditional electronics, neural electronics offers a solution to problems calling for analog computing procedures (image, sound pattern, echo, movement, recognition, etc.).

SGS-Thomson is carrying out research on architectures that can emulate the animal brain. The goal is to implement synapses (the transmission of nerve impulses) in a thoroughly tested material such as silicon. At the same time, however, the knowledge that in 10 years it will be necessary to launch itself into composite materials or biochips is orienting the company's philosophy towards a completely new perspective for Italian industry: medium- to long-term research. SGS-Thomson is in fact a member of CIREF (together with Automa, Donegani, Elsag and Sorin), an association that aims at fully developing the bioelectronics sector.

Theme 2: Identification and simulation of industrial applications that can be optimized using neural architectures.

Theme 3: Amorphous silicon for reconfigurable structures.

This line of research aims at developing technologies for the production of silicon as an amorphous material and possibly elements of inorganic semiconducting material of the III-V group, to be used individually and/or jointly.

Protein engineering

Theme 4: The identification and characterization of proteins with electron transport and sensorial properties. The best known examples are molecules involved in cell respiration, cytochromes.

The research objective centres on the use of biophysical technologies. These include X-ray diffraction, Fourier transformation with bidimensional nuclear magnetic resonance (2Dtfnmr), recombinant DNA technologies, as well as the development of computerized "molecular modelling" techniques, integrated into an expert system to determine the three-dimensional structure of proteins. The use of 2Dtfnmr proves extremely interesting, as this technique (destined, in fact, to replace X-ray crystallography, at least in biomolecules) permits a structural analysis of the proteins within the aqueous medium.

Theme 5: The identification and functional characterization of proteins involved in chemical oxidation-reduction reactions with a view to improving their functional properties.

Theme 6: The identification and functional characterization of proteins (produced by immunological cells) featuring antibody properties, in view of their prospective use as active components for electronic molecular recognition devices.

Theme 7: The identification and functional characterization of synthetic receptor proteins.

First-generation bioelectronics

Theme 8: Technologies and equipment for the construction of orderly layers designed for the production of electronic devices with a molecular function.

The goal of this research is to develop electronic devices with molecular functions by studying the characteristics of orderly molecular structures arranged in films, through the use of high-resolution techniques such as tunnel-effect and atom-powered microscopes. In other words, this research is designed to develop construction methods of orderly biopolymer layers through self-organizing techniques. In order to obtain extremely stable polymers, researchers will use molecules derived from the micro-organisms capable of surviving at 97° C that were recently isolated on the slopes of Vesuvius (archaebacteria that can survive in extreme temperatures). (Extracted from Media Duemila, March 1990)

Japan

MITI's "Supercell" project

Japan's Ministry of International Trade and Industry (MITI) has announced plans to start a "supercell" research project beginning in the next fiscal year. The concept is to utilize the maximum capabilities of cells by controlling expression at the chromosomal level. The "supercell" project is to establish a basis for controlling cellular activities, not only by enhancing target substance production, but also by suppressing other functions in order to minimize by-product formation. MITI plans to classify this 10-year project as a next generation project, with funds totalling $100 million. (Source: BIO/Technica Journal No. 2, 1990)

Japanese protein system design project

Japan's Agency of Industrial Science and Technology (AIST) has started a 10-year research project "molecular assemblies for functional protein system" aimed at understanding how proteins assemble and function in a highly co-ordinated fashion in vivo, as well as developing technology for applying the mechanism. This project is part of the Research and Development Project of Basic Technology for future Industries. The agency has invited companies to join in order to set up a research association. The total budget will amount to ¥ 10 billion; the start-up funding is ¥ 151 million in fiscal year 1989. (Source: BIO/Technica Journal No. 2, 1990)

Work on genome

Japan's celebrated fifth-generation computer will go to work deciphering the human genome under an agreement reached between the Japanese Government and the Argonne National Laboratories in the United States.

Researchers from the two countries will work together to program a prototype computer called the multi-PSI to match items in the huge library of genetic sequences collected by scientists trying to map the human genome.

The Japanese computer is the first tangible fruit of a 10-year project launched by the country's powerful ministry of International Trade and Industry in 1982 to develop a computer capable of processing knowledge rather than numbers. The project is not yet close to achieving this goal, but has made advances in building computers consisting of many different processors operating simultaneously.

Under last week's agreement, the Japanese institute will instal terminals at Argonne through which American researchers will communicate with a multi-PSI in Tokyo. (Source: New Scientist, 3 June 1990)

Deep-sea research facility

Japan's Science and Technology Agency plans to initiate a three-year research programme on the biology of deep-sea life. It plans to establish research facilities in 1990.

The planned facilities consist of a high-pressure transportation system for submarine-gathered samples, as well as a laboratory in the submarine itself where microbes can be isolated and cultured. (Source: Bio/Technology, Vol. 8, April 1990)

Kenya

Biotechnology conference

A week-long National Conference on Plant and Animal Biotechnology in Nairobi drew 300 scientists from around the world. Convened with support from the US Agency for International Development (USAID) at the end of February 1990, the meeting was both warned and encouraged by the prospects for the new technologies in agriculture.

The possibility that Africa's export crops might be lost to biotechnology factory farming in industrialized countries became a major concern among delegates. Delegates were also disturbed that USAID officials were pressing African States to allow field trials of genetically altered organisms that might not be allowed in the regulatory systems in the North. Such was the concern that the Minister for Research, Science and Technology made a public pledge on the conference's second day stating that Kenya would not become a testing ground for dangerous new biotechnology products.
Dr. Calestous Juma, Director of the African Centre for Technology Studies (ACTS), advised scientists that USAID is encouraging Third World countries in Asia and Latin America to undertake similar testing roles for private American firms. (Source: African Diversity, No. 2 & 3, June 1990)

The Netherlands

The Netherlands as a base for biotechnology

Dutch sales of biotechnology products probably now amount to around $6 billion a year. The Netherlands Industrial and Agricultural Biotechnology Association, the industry's two-year-old trade association, further estimates that this represents around 7 per cent of the world market of perhaps $90 billion. Biotechnology activity is expected to grow over the next few years at an annual rate of 8 per cent, with the fastest growth likely in fine chemicals, plant breeding and environmental biotechnology.

The number of companies now involved in the new biotechnology in the Netherland, has now climbed to 150, 40 per cent more than there were just five years ago. Most of these companies, like Holland Biotechnology of Leiden, are engaged in medical diagnostics or in plant biotechnology. On a larger scale, the fermentation company Gist-Brocades has cornered around 30 per cent of the world market in baker's yeast and a quarter of the global market for penicillin. Another Dutch company, CCA Biochem, produces over half the world's supply of lactic acid. DSM, AKZO and Shell are all active in the biotechnology area. There are 10 or 12 new

recombinant DNA products was being carried out in the Netherlands. One reason for the strong growth has been a concerted effort [illegible] by the government, the Dutch [illegible] and industry to promote the [illegible] [illegible] 150 million guilders ($[illegible] million) a year.

The Dutch preoccupation with environmental problems could also help the biotechnology industry in a number of ways. For example, the country has a manure-mountain problem. One way to reduce it would be to improve the conversion of feeds. The use of enzymes could mean each animal needs less feed and made better use of it, producing less manure. Taiwan and Hong Kong, along with other small countries facing the same problem, have been showing considerable interest in the Dutch solutions. Environmental engineering also offers opportunities for biotechnology, says [illegible] – the Dutch Suppliers of Environment Equipment & Technology. Anaerobic and aerobic sanitation, mechanical pre-separation, ventilation equipment, membrane technology and physical-chemical techniques are just some of the technologies that can be applied to the task. Gist-Brocades and Paques together supply [illegible] per cent of the expertise used in anaerobic industrial waste water treatment facilities world-wide. Dutch companies are also working on anaerobic and aerobic solutions for dealing with soil decontamination. (Source: Biotechnology Bulletin, Vol. [illegible], No. [illegible], May 1990)

Dutch regulations now in force

On 1 March the Netherlands became the second European country – after Denmark – to have in place a framework for regulating the environmental use of genetically engineered organisms. Under a new subsection of the 1985 Chemical Substances Act – the Order for Genetically Modified Organisms – it is an offence to use genetically modified organisms in the environment in an experimental or commercial setting without a permit from the Ministry of the Environment. The order should facilitate field trials by authorizing them on a national basis (previously, permission granted under the near century-old Nuisance Act only applied locally); using such organisms under containment will continue to be dealt with under the Nuisance Act.

The new rules are very closely aligned with the European Commission's directive on environmental use and could be seen as implementing the directive in advance. (When the Directorate receives approval from the Council of Ministers the EEC member States will have 18 months in which to enact it at a national level.)

The new Dutch legislation differs from Denmark's 1986 Gene Technology Act in one important respect: there is no requirement for manufacturers to demonstrate "usefulness" or "social need" for genetically modified organisms.

By using the existing legal framework of the 1985 Act, genetically engineered organisms will be subject to essentially the same procedures as their non-genetically engineered peers – albeit with different guidelines for providing information.

Unexpectedly, the order maintains the requirement of notifying the public of the nature and precise location of intentional introductions. Similar to the recent UK proposals coming out of the Royal Commission on Environmental Pollution, advertisements must be placed in one national and two local papers.

Following the sabotage last August of a plot of genetically engineered potatoes developed at the [illegible] research station, Wageningen, the Netherlands and at Plant Genetic Systems, Ghent, Belgium, there had been calls to relax the existing safety requirements.

Despite the general welcome given the new policy, the Dutch are reserving the right to introduce specific laws for gene technology. The new order calls for a draft law on the environmental use of genetically engineered organisms to come before Parliament by 1 March 1992, although it would probably not be enacted for several years after that. Whether that draft will demand Parliamentary consideration may depend largely on the next two years' experience. (Extracted from Bio/Technology, [illegible], April 1990)

Romania

[illegible] in the Romanian [illegible]

A new report from the Romanian Government suggests that efforts by it and foreign organizations are failing to stop the spread of AIDS in Romania. The report reveals that there were [illegible] cases of clinical AIDS in Romania as at 1 May, far more than the earlier estimates of 700 cases.

Even the new figure may be a drastic underestimate of the true situation. It is not known how many people are infected with HIV, the virus that causes AIDS.

Most alarming, 42% of the cases were found in children less than 13 years old. Of these [illegible] are under four. The now discontinued practice of giving 'microtransfusions' of blood to malnourished infants, many of them orphans, is thought to be behind the explosive spread of AIDS.

The blood supply, and the needles and syringes used, were contaminated by the AIDS virus. In a random nation-wide sample of blood taken from children in orphanages, nearly 10 per cent of the children tested positive for HIV, although the World Health Organization (WHO) warns that this number might be high because of double reporting.

Testing of blood donors (there are an estimated 600,000 in Romania annually) and of blood already stored in blood banks is not being carried out systematically, partly because of a shortage of testing equipment.

Foreign relief organizations have delivered modern test equipment as well as thousands of sterile syringes and needles for injections and transfusions. The French organization Medecins du Monde alone has provided three ELISA (enzyme-linked immunosorbent assay) readers and thousands of test kits to laboratories in Bucharest for AIDS testing. But the Health Ministry has begun testing blood only in Bucharest and the three hard-hit eastern cities of Constanta, Iasi and Giurgiu. At least 20-25 laboratories including readers and kits will be required before blood screening can be comprehensive. (Source: Nature, Vol. 345, 3 May 1990)

Singapore

Singapore invests in biotechnology

Singapore is to embark on a $60 million plan to boost its position in biotechnology. The Government has unveiled a number of projects intended to

develop technology, manpower and infrastructure for its biotechnology industry.

The Singapore Economic Development Board (EDB) said that the move would involve the creation of a new venture capital company, Singapore Bio-Innovations, with a $20 million investment fund, and the setting up of tertiary level centres for training and research. Scholarships will be introduced to increase the pool of biotechnology expertise.

The three centres will be based in the National University of Singapore (NUS), one in the chemical engineering department and one attached to the botany, zoology and biological sciences departments. The third, for applied food sciences, will be a link between NUS and the Singapore Institute of Standards and Industrial Research (SISIR). (Source: European Chemical News, 28 May 1990)

Sudan

Genetic Engineering & Biotechnology Unit in the Sudan

At the end of March 1990 a UNIDO expert visited the Genetic Engineering & Biotechnology Unit of the National Council for Research (NCR) of the Sudan based in Khartoum, various research centres at Sudanese universities and a number of scientists of NCR and universities to give advice on the Sudan's biotechnology programme. The consultation aimed at improving the existing capabilities through training programmes, seminars, visits to biotechnology and genetic engineering laboratories and other information sources; establishing a National laboratory; augmenting equipment and facilities in existing laboratories and linking the Sudan's research groups with groups in other African countries and institutions outside Africa. An overall African biotechnology programme planned by UNIDO has not yet materialized due to funding problems. (Source: African Diversity, No. 2 & 3, June 1990)

Sweden

Swedish permit to cultivate manipulated plants

The growing of plants changed with the aid of gene technology will in the future require a special permit, according to a decision by the Swedish Government. Permits will be issued by the National Board of Agriculture after consultation with the Delegation for rDNA questions and the National Environment Protection Board. The Board of Agriculture is to make a risk assessment before any permit can be issued. (Source: BIO/Technica Journal No. 2, 1990)

Swedish Bioscientific Research Centre

A new research centre for biosciences was inaugurated in February 1990 near Stockholm. Called NOVUM and located adjacent to Huddinge University Hospital and the southern campus of the Karolinska Institute, the centre is the largest R&D venture in the fields of biotechnology and medical technology in Northern Europe.

NOVUM is designed to promote cross-fertilization of ideas, while also promoting commercial interests. NOVUM research centre will be part of a large research village and some of its institutions will be included in a planned university for the Södertörn region. Among the NOVUM partners are the Centre for Biotechnology (CBT) of the Karolinska Institute. (Source: BIO Technica Journal No. 2, 1990)

United Kingdom

Genetic dispute around the letter and the law

The UK Government will meet most of the Royal Commission on Environmental Pollution's concerns over the regulation of the release of genetically manipulated organisms (GMOs). Most of the issues recently brought up by the Commission are, however, more fit for regulations rather than legislation under the Government's new environment bill.

The Government had met 98 per cent of the Commission's concerns, while some form of compromise on further disagreement would be found.

The issue of a specific consent for the release of each new GMO has been the subject of a persistent exchange of letters between the chairman of the Commission, Lord Lewis, and Chris Patten, the Secretary of State for the Environment.

The Commission believes that the state of knowledge on GMOs is such that a consent should be required for each new release.

The new European Community directive on deliberate releases, one of two biotechnology directives shortly to be adopted by the EC, also clearly states that a consent should be obtained before the release of each new GMO. The only exceptions to this rule are organisms obtained through certain techniques of genetic modification which have conventionally been used in a number of applications and have a long safety record. (Extracted from Chemistry and Industry, 7 May 1990)

Deliberate releases so far

Genetically manipulated organisms have so far been released into the environment at eight centres in the UK. They are: Rothamsted Experimental Station at Harpenden, Institute for Plant Science Research in Cambridge, Scottish Crops Research Institute at Invergowrie and Pentlandfield, Shell Research Ltd. at Sittingbourne, British Fermentation Products Ltd./Gist Brocades in Felixstowe and Nickerson International Seeds Ltd. in Cambridge. The Government is currently considering notifications from three more centres. (Source: Chemistry & Industry, 21 May 1990)

Government rethinks stand over altered organisms

The Government has bowed to pressure over its "green" bill and will now consider giving the public access to information on proposed releases of genetically modified organisms into the environment. This U-turn came as the Environment Protection Bill completed its committee stage in the House of Lords.

Legislation over genetically modified organisms has proved to be one of the most contentious areas of the bill. An anomaly in the legislation means that the treatment of products of genetic engineering is misaligned with proposals for handling other potential threats to the environment, such as toxic waste and other pollutants. While the legislation requires information on these to be made public, this does not apply to genetically altered organisms.

Environmentalists argue that this omission is a serious flaw in the bill, and they have been campaigning for the legislation to state exactly the information to be made public. This, the environmentalists argue, would increase public confidence in the safety of releases of genetically modified organisms outside. It is too important, they say, to be left to the regulations that flesh out the bill after it gains royal assent.

The Lords who argued for an amendment on this issue insisted that the public has a right to know what is going on, and that it would also be in the best interests of the biotechnology industry.

The Government has also agreed to consider an amendment which would recognize the formation of an advisory committee to monitor any proposed releases - the Advisory Committee on Releases to the Environment (ACRE). This, too, had been left to the regulations, and environmentalists feared that the environment minister might choose not to make public the advice of the committee, or perhaps might change its status, without having to seek parliamentary approval.

Further Government amendments to the bill could emerge later when the legislation reaches its report stage in the House of Lords. It will then return to the House of Commons for final scrutiny before becoming law by the end of 1990. (Extracted from New Scientist, 14 July 1990)

Crop protection aid

The British Technology Group has reached an agreement with Rothamsted Experimental Station in the UK to fund a crop protection research programme, aimed at developing "environmentally friendly" pest control agents. BTG will fund a team of scientists at a cost of £200,000/year.

Under the agreement, BTG will have first refusal on rights to any chemical inventions relating to crop protection which originate at Rothamsted over a five-year period. BTG will be responsible for licensing any acquired technology to the agrochemical industry.

Research will initially be targeted at developing insecticides, semiochemicals, phloem-mobile compounds and miticides.

In the insecticide sector, new pyrethrin analogues with activity against resistant pests will be investigated. The programme will also look at analogues which are harmless to fish, which would be suitable for use against insect pests of rice. Various plants will be analysed as potential sources of new products. New analogues of insect neuropeptides will also be tested.

Further research is planned into phloem-mobile fungicides and other products, which, when sprayed on to a plant's leaves, migrate into new plant tissue and into the roots to control soil-borne pathogens and other pests. (Source: European Chemical News, 18 June 1990)

Britain fails to harvest full fruits of biotechnology

Skills shortages, uncertainty about patenting, and a lack of openness with the public are holding British industry back from fully making the most of biotechnology. The findings emerge in a report called Developments in Biotechnology, published by the Government's Advisory Council on Science and Technology. The ACOST reviewed scientific and policy factors that have affected the development of biotechnology over the past decade, and which will govern industrial exploitation in future.

Estimates of the value of the market for biotechnology vary enormously. One, from the Organisation for Economic Co-operation and Development, says the world market could be worth between $9 billion and $100 billion by the year 2000.

If the UK is to win a share in this market, the Council believes that the European Commission must clarify its patenting policy for biotechnology products, such as genetically modified plants and animals.

Industrialists are worried about discrepancies in patent law between Europe and the US. In the US, for example, industry can patent a life form, such as a genetically altered mouse. In Europe, patents cannot be granted on new varieties of plants or animals.

Patent law in the US and Europe differs in other important ways, too. In the US, once scientific results are published, there is still a year in which to apply for a patent. In Europe, one must apply for a patent before publishing. This affects academics, who are under great pressure to publish.

The Council also believes that public debate about biotechnology and, in particular, genetically modified organisms, is essential. To date, this has not happened.

The report draws attention to shortages of skilled people working on plant molecular biology, biochemical engineering and downstream processing. (Extracted from New Scientist, 23 June 1990)

Aquatic biochemistry at the University of Stirling, Scotland

Aquatic biochemistry at the University of Stirling is organized under the auspices of the Natural Environmental Research Council (NERC) of the UK and is housed in the Department of Biological Sciences. Stirling University is only 22 years old and proud of its innovative teaching programmes. The NERC unit is housed in modern laboratories and has a scientific complement of about 20 personnel. Six of these, including the Director, Professor John R. Sargent, are at a senior level. Established in 1986, the unit was formed from the Institute of Marine Biochemistry at Aberdeen. The research of the unit is directed towards improving our knowledge of the natural aquatic environment, both fresh water and marine, so that predictive information can be obtained. All the research in the unit is at the molecular or cellular level and is focused in two general areas - lipid structure and function, and molecular toxicology. The toxicology and lipid groups appear to be unique in that they are highly committed to both molecular and field programmes.

Lipid structure and function

Much of the work of this section of the NERC unit centres around polyunsaturated fatty acids (PUFAs) - molecules that originate in the phytoplankton but are essential dietary components of higher organisms such as zooplankton, including larval fishes. The research carried out is heavily experimental, but does have field components.

notably a collaboration with scientist, in Spitsbergen, Norway. A further facet of this concentration on lipids is their use as biomarkers in dissecting marine symbioses and food webs. The latter is particularly important locally since sea lochs in Scotland support a large salmon aquaculture effort and salmonids have an absolute requirement for (N-3)PUFAs. Currently, these essential nutrients are supplied from fish meal, a situation in which, according to Professor Sargent, salmon are merely increasing the value of an existing product! Professor Sargent's group is researching other sources of these valuable molecules for both fish and human nutrition. To this end, they have analysed the fatty composition of several microalgal species and researched the means by which the physiological status of the cells influences the results. Until now, their findings have shown that as cells become older, i.e., when they divide less frequently, the fatty acids of their lipids become more saturated, shorter in chain length, and are found largely in wax esters or triglycerides. Functional roles for the highly unsaturated species of these molecules are also being followed, especially at the transmembrane-signalling level. The group is a source of information on the lipids of many marine organisms.

Molecular toxicology

A second interest of the NERC unit is that followed by Dr. Steven George. He is conducting basic studies of biochemical systems responsible for the detoxification of organic and metal pollutants. The information obtained is expected to aid in the design of molecular probes able to detect levels of pollutant in the environment below those needed to cause lethal effects. Measurement of primary, sublethal, pollutant response, which precedes the development of overt pathology, can serve as an early warning of potential environmental impact. For instance, levels of toxicants that influence behaviour are far lower than those that are needed for mortality. In many cases, pollutant detoxification systems are inducible by sublethal levels of the chemical. Thus, if the products of the induction can be detected, a mechanism to gauge environmental stress can be developed. This is the research strategy that this group has adopted. In the case of the induction of mixed-function oxidases that add -OH groups to aromatic rings, for instance, the situation is complicated by the fact that several forms of the enzyme system (including the cytochrome P-450 moiety) are constitutive in fish liver cells. However, only some of these isoforms are able to increase their levels in response to various pollutants. This, in turn, provides a means of differentiating between the stress-related and the normal mixed-function oxidases. Although mixed-function oxidases can be regarded primarily as detoxification systems, in some organisms they are responsible for activating xenobiotics, i.e., they convert relatively innocuous components into extremely toxic ones. This facet of their activity makes them particularly appropriate indicators. Dr. George favours a quantitative immunological (Western Blot) approach rather than using enzymological assays to detect the P-450 system in livers from stressed fish.

Certain heavy metals, as well as organic materials, find their way into our environment and present us with a pollution problem. As in organic pollution, certain specific proteins are induced in organisms by metal exposure. Thus, measurement in tissues of these macromolecules, which are collectively known as metallothioneins, provides a sensitive indicator of stress. For instance, exposure of fish to zinc [illegible] in a 20- to 30-fold increase in hepatic metallothioneins. Many [illegible] concentrations, days, or even [illegible] on the metal burden of an animal [illegible] recent metal exposure. What is required [illegible] assay, for the induced heavy-metal burden [illegible] In the laboratory, assays based on a [illegible] method, reaction on radioactive cadmium binding are used. The antibody, which was prepared from [illegible] cross-reacts with metallothioneins from other fish species. This is not surprising since the gene for metallothionein is highly conserved. The assay has been used to show that zinc injections cause a 10- to 20-fold increase in hepatic metallothioneins in marine flatfish. Since the Zn binding protein has a half-life of about 30 days, this assay was capable of detecting exposures in the recent past indicating that care was necessary in interpreting assays from fish obtained from the field.

Since environmental pollution is rarely of one type, it is important to examine the effects of multiple stresses on an organism. The group has examined the activities of both mixed function oxidases (organic pollution indicators) and metallothionein levels (for heavy metal exposure) in salmon from control rivers and rivers where fish are known to be jaundiced. They found that even in fish that showed no obvious pathology, there were elevated P-450 and metallothionein levels. Work in this laboratory continues to dissect the toxic interactions in situations such as this. A major problem in this area is the influence of enzymes induced by concurrent heavy-metal exposure on mixed function oxidases systems. By virtue of this, the group is developing new procedures that will be helpful in working with multiple pollutant exposures and the interactions they engender. The first of these is a fish cell culture system (trained to replace use of whole fish, and another is an RNA probe for metallothionein. (Source: European Science News, March 1990)

United States of America

To allay public fears, states plan regulation first, then education

On 1 July, North Carolina's "Genetically Engineered Organisms Act" goes into effect. Its stated goals are "to allow the unencumbered development of biotechnology". The law, which is designed to be "minimally burdensome, and to meet with federal regulations", provides North Carolina's biotechnology community with a single, central system that can assure the public regarding the safety of releases and commercial uses covered by the law. A key component of North Carolina's legislation is public involvement and an education program designed to instill confidence.

At present, a total of 22 states are considering similar legislation, but a new "biotechnology bill" recently drafted by the House subcommittee on Investigations and Oversight, would block such initiatives. (Source: McGraw-Hill's Biotechnology Newswatch, 3 June 1990)

Deliberate release

Plans by researchers at Auburn University (Auburn, AL) to genetically test engineered [illegible] outdoor ponds will have "no significant impact on the quality of the human environment", according to a US Department of Agriculture (USDA) review. Critics disagree with the preliminary conclusions of this formal environmental assessment (EA), the first

of its kind to be issued by USDA's Cooperative State Research Service (CSRS). Thus, the tests initially proposed in early 1989 and reviewed and revised extensively, since then could well be facing further delays - possibly court-imposed.

The carp in question contain an engineered version of a trout growth hormone gene that makes the fish grow more rapidly than usual. The outdoor pond experiments will determine whether the gene affects the reproductive capacity of brood carp, whether offspring inherit the engineered gene, and how it affects their survival, growth rate, and behaviour. The proposed experiment calls for distribution a total of 50,000 fry (young carp at least 0.5 cm long) into 10 specially designed 0.1-acre ponds. The numbers of fish will eventually be reduced, with the remainder allowed to grow for about one year, until just before they reach sexual maturity. (Extracted from Bio/Technology, Vol. 8, April 1990)

Drugs in the pipeline

The Pharmaceutical Manufacturers Association (PMA, Washington) says 104 genetically engineered medicines are in human clinical tests or at the Food and Drug Administration for review, an increase of 23 medicines in development since PMA's 1989 survey. The numbers include 59 genetically engineered cancer therapies. The survey also shows an increasing number of biotechnology drugs are nearing development completion. According to PMA, clinical trials have been completed for 18 medicines now awaiting FDA approval; an additional 15 are in the final stage of clinical testing. In last year's survey, only eight drugs had completed clinical trials. PMA says monoclonal antibodies make up the largest category, with 37 medicines in development - up from 23 in 1989. PMA also releases its analysis of biotechnology patents issued in the US. The numbers indicate that in 1989 US corporations accounted for 47 per cent of pharmaceutical or health-care patents involving genetic engineering - up 10 per cent since 1986. The analysis also shows a record 1,949 US biotechnology patents were issued in 1989, an increase of nearly 60 per cent from 1986, according to PMA. Of these patents, 20 per cent involved genetic engineering techniques and nearly half of those were in the pharmaceutical or health-care field. The number of health-care patents using genetic engineering, however, has dropped 11 per cent since 1987, says PMA. (Source: Chemical Week, 16 May 1990)

Texans try for the customized cow

Cattle that produce lean beef containing less saturated fat, cows that produce milk better suited to human infants, and cows that produce pharmaceuticals are each one step closer to reality at a ranch near Houston in Texas. Four genetically engineered calves, born over the past 15 months, are the first transgenic bovines created by researchers in the US.

A team of scientists including Bert O'Malley, a biologist at the Baylor College of Medicine in Houston, and Ken Bondioli of Granada BioSciences, a subsidiary of the Granada Corporation, a cattle breeding and food company, developed the modified calves.

The first transformed calf, born in March 1989, contains a human oestrogen receptor gene that the scientists hoped would accelerate growth by causing the cow to use its own oestrogen more efficiently. However, the calf has as yet grown no faster than other calves. Two other calves, born in September 1989 and March this year, have an extra cop, of a bovine gene that produces "insulin-like growth factor". The scientists expect the extra growth factor will help to generate more muscle tissue, and therefore enhance meat production.

In December 1989, the fourth calf, a female, was born with an extra copy of the gene that produces bovine growth hormone. Biotechnology and drug companies produce this same hormone in bacteria. They hope to sell it to dairy farmers who will increase milk production by injecting it into cows. These plans have ignited a major controversy in both Europe and the US. Some scientists say the hormones harm the cows.

The Texan researchers, who hope that their genetically engineered cow will show higher milk production, may be able to circumvent the consumers' complaints. (Source: New Scientist, 23 June 1990)

C. RESEARCH

Research on human genes

Brain cells cultured

For the first time, scientists have succeeded in culturing brain cells - a breakthrough that could lead to treatments for a range of neural disorders, including epilepsy, Parkinson's and Alzheimer's diseases. Until this announcement, it had been thought impossible to cause neurons to reproduce like cells of other organs. Cerebral cortical tissue obtained from an 18-month-old girl undergoing hemispherectomy because of intractable seizures, were plated in medium containing serum. After 21 days all cells had died, except for two small foci of growth, which were cloned and designated HCN-1 and HCN-4. Subsequently, these cells have been passaged more than 20 times in the course of 19 months, with no significant changes in morphology or growth characteristics. Dr. Solomon Snyder of Johns Hopkins University, one of the successful team, said they had achieved "one of the major goals of all brain research".

It is felt that with the use of genetic engineering techniques it would be possible to insert adapted genes into cultured brain cells and then implant them into patients to correct imbalances caused by such diseases as Parkinson's and Alzheimer's. Details from: Dr. Solomon Snyder, Department of Neuroscience, Pharmacology and Molecular Sciences, and Department of Psychiatry and Behavioral Sciences, Johns Hopkins University, School of Medicine, Baltimore, MD 21205, USA. (Source: Biotechnology Bulletin, Vol. 3, No. 1, May 1990)

Method developed to examine egg cells for genetic defects

A researcher at the School of Medicine, Tufts University, has developed a technology for isolating egg cells likely to produce embryos without genetic damage stemming from too few or too many chromosomes. Eggs with the correct number of chromosomes and solid protein scaffolding (spindles) holding the chromosomes in place are more likely to result in successful pregnancies. Previous methods for examining eggs rendered them non-viable, but the Tufts method uses a low-energy light source, a video camera and computer enhancement to produce detailed pictures of the chromosomes and spindle without damaging the eggs. The technique has been

successful with rodent egg cells and will be tested on human egg cells. The technology may lead to practical methods for increasing the success rate of human in vitro fertilizations. (Extracted from Discover, April 1990)

Genetic key improves cancer drug's action

A gene that causes resistance to anticancer drugs in tumour cells, could be used to help patients withstand the side-effects from higher and potentially more effective doses of chemotherapy, claims Dr. Michael Gottesman, chief of the cell biology laboratory at the US National Cancer Institute.

Speaking at the recent Bristol-Myers Squibb symposium on cancer research in Tokyo, Gottesman suggested this gene could be introduced into the bone marrow of a patient undergoing chemotherapy to enable it to resist the destructive effects of high-dose anticancer drugs.

The gene encodes a protein "pump" (p-glycoprotein) on the surface of malignant cells. This pump appears to expell a sufficient quantity of the anticancer drug to allow resistance to build up in cancer cells. In order to circumvent the action of the pump, very high doses of chemotherapy are administered. This kills the cells before resistance can develop, but also destroys the bone marrow necessary to maintain the immune system.

To discover whether bone marrow can be made resistant to chemotherapy, Gottesman and his colleagues created a transgenic mouse with pump protein in bone marrow, by inserting the human pump gene into the mouse DNA.

Experimental results with anticancer drugs showed that the transgenic mice did not lose white blood cells (indicating bone marrow damage) when given chemotherapy. Conversely, in mice that could not express the pump protein in bone marrow cells, a significant loss of white blood cells was observed.

Other scientists are attempting to develop drugs that will inhibit the expression of the pump. The aim is to make tumours that produce the pump more vulnerable to drugs. At the same meeting Dr. Takashi Tsuruo, chief of cancer chemotherapy at the Japanese Foundation for Cancer Research in Tokyo, described a genetically engineered "guided missile" that inhibits the action of this pump.

Tsuruo has designed a monoclonal antibody (Mab) specific to the pump protein that attacks the pump-expressing cells in the same way as the body's immune system.

In laboratory tests, Tsuruo found that the pump antibodies prevented tumour development in mice that had been inoculated with human ovarian cancer cells. In addition, the Mabs appeared to treat mice that had already developed tumours. Other experiments showed the antibodies destroyed several other kinds of multidrug-resistant cancer cells grown in the laboratory.

From these results, Tsuruo concludes that anti-pump Mabs may be able to rid patients of many kinds of cancer cells with accumulations of the drug-resisting pump. He envisages its use after chemotherapy to "mop-up" drug-resistant cancer cells.

Tsuruo believes that his Mabs, in contrast to others, bind to the outside of cells, blocking the ability of the pump to eject the anticancer drug through the cell membrane and enabling the anticancer drug to remain within the cell long enough to kill it.

The next step in bringing this therapy to patients is preclinical trials on ovarian cancers and tumours, scheduled to begin later this year in conjunction with the NCI. The goal is to determine whether there are adverse side effects with these Mabs in humans.

To produce an antibody that specifically recognizes the pump protein, Tsuruo repeatedly inoculated a mouse with human drug-resistant tumour cells. This caused the mouse to develop an immune response and the antibodies were isolated. Tsuruo then developed a hybrid antibody that is essentially human, but contains the portions that recognize pump protein from the mouse's antibody.

Because Mabs are specific, in this case to the pump protein, it is anticipated that they could be used as a diagnostic tool to determine whether a particular cancer will resist chemotherapy. This situation may permit physicians to decide upon the most appropriate treatment strategy. (Source: European Chemical News, 4 June 1990)

New approach to bone marrow transplants

Research in treating some genetically-caused blood disease involves a new approach to bone marrow transplants. A technique by researchers at the University of California at San Francisco avoids rejection problems that have occurred in earlier methods of marrow transplants. The new approach involves removing donor bone-marrow tissue from a monkey foetus that has been aborted early and has not yet generated cells that would initiate an immune reaction. The marrow tissue then is implanted in a foetus carrying a genetic defect before the recipient foetus's immune system has developed to the point of rejecting the implant. The research has involved monkeys, but may be used with humans. The procedure has been described to women at risk of having babies with sickle-cell anaemia. (Extracted from The Economist, 26 March 1990)

Fatty genes

How fat or thin you are is mostly a matter of genetics, according to two studies published last week in the New England Journal of Medicine.

Researchers from Laval University of Quebec confined 12 pairs of male identical twins aged between 19 and 27 years to a dormitory for 100 days and over-fed them with identical meals. The difference in weight gained was about three times as great between pairs of twins as within pairs.

A second study recorded the difference in weight between identical and fraternal twins reared apart or together. Identical twins reared apart had similar weights, the researchers found, despite variations in their diet. However, the authors concluded that although 70 per cent of the difference in weight between individuals is due to genetic factors, about 30 per cent is due to environment. (Source: New Scientist, 7 June 1990)

A new type of genetic disease

Genetic diseases are usually caused by defects in a cell's proteins. Now a team of biologists in the US has discovered the first genetic disease that is caused by a defect in the machinery that a cell

uses to manufacture proteins. It has also identified a mutation that causes a form of epilepsy.

The results of the team, based at Emory University in Atlanta, Georgia, are especially interesting because the molecular defect they have identified is not located in nuclear DNA, as is usual. Instead, it is located in DNA in the mitochondria, the discrete structures, or organelles, within cells that produce energy. There are several thousand mitochondria in a cell, and each carries its own genetic material in the form of a circular DNA molecule with 16,569 nucleotide base pairs.

According to Wallace, mitochondrial DNA has a unique pattern of inheritance and replication. For this reason, he says, the diseases caused by mutations will not look like normal genetic diseases.

In particular, Wallace and his colleagues have been studying the disease complex known as MERRF - myoclonic epilepsy and ragged-red fibre disease. People suffering from the disease experience sudden, brief muscular spasms (myoclonic epilepsy) and progressive degeneration in a range of nerve and muscle tissues, as well as kidney and liver damage. All the symptoms result when the ability of mitochondria to deliver energy to the tissues is reduced.

In order to pinpoint the genetic defect unequivocally, the Atlanta team sequenced the mitochondrial DNA of several MERRF patients, together with a range of controls. The molecular defect turned out to be a mutation in the gene that encodes for a transfer RNA molecule, the one whose job it is to carry around the amino acid lysine.

In other words, it looked as if there was no problem with any specific type of protein, but with the production of all proteins; and the bigger the protein, the worse the problem. The mutant transfer RNA molecule in MERRF apparently is unable to adequately perform its role.

In most genetic diseases - those that are caused by mutations in nuclear genes - the picture is relatively simple. A person either has the mutation and the disease, or they do not. And the symptoms depend rather clearly on which gene is affected. There are often varying degrees of severity of such diseases, depending on a number of circumstances in the genetic background. But overall the link between genetic mutation and the clinical picture is rather direct. With mitochondria, however, it is very different.

For a start, because the principal job of mitochondria is to generate energy, most defect will affect energy-related systems. However, because some tissues have higher energy demands than others, their response to exactly the same mutation will be different. The central nervous system is most voracious in its energy demands, with other nervous tissue following, then muscle, kidney and liver.

The pattern of a disease caused by a mitochondrial defect will, therefore, depend on just how severe the defect is. Different degrees of severity of the condition will depend on what proportion of the thousands of mitochondria in each cell carry the mutation.

A mild condition may affect only the central nervous sytem, while a severe condition will involve all nervous tissue, skeletal muscle, heart muscle, kidney, and liver. Remember, this spectrum of disease patterns would be the result of the very same mutation, just at different degrees of severity.

But the picture is complicated still further by another aspect of the natural history of mitochondria. At the time of fertilization of an egg, only one set of nuclear chromosomes comes from the mother and one set from the father. However, each egg contains several thousand mitochondria, each with its own mini-chromosome. It is, therefore, likely that only some of the mitochondrial chromosomes will contain defective DNA, in the case of a diseased mother. During embryological development tissue types differentiate and body structures form, incorporating descendants of the original stock of mitochondria.

It is possible that each different tissue type will contain normal and defective mitochonria in exactly the same proportion in which they arrived in the mother's egg, say 50:50. If this is the case, all tissues will suffer the same degree of defect in the energy-producing system. However, it is also possible that, because of chance distribution of normal and defective mitochondria in the fertilized egg, the mitochondria in some tissues will be mostly normal. In this case, some tissue types will suffer a severe inadequacy in energy production while others will be almost normal.

Clearly, the clinical picture in these two cases would be very different, simply because of the different distribution of defective and normal mitochondria types among different tissues of the body. The actual molecular defect in the two cases, again, is identical. (Source: New Scientist, 30 June 1990)

New genes for ailing hearts

If all goes well, the first attempt to perform true gene therapy on a human patient will take place later this year. But at most, only a handful of children will be eligible for that particular therapy, which aims to treat a severe hereditary immunodeficiency. Meanwhile molecular biologists have been taking the first tentative steps towards devising gene therapies that can help the millions of people who suffer from cardiovascular diseases.

At a symposium on "Vascular Biology and Medicine: The Next Frontier", James Wilson of the Howard Hughes Medical Institute at the University of Michigan School of Medicine in Ann Arbor reported that he and his colleagues have used gene therapy to lower blood cholesterol, albeit temporarily, in Watanabe rabbits. Because of a genetic defect, the cells of this strain of rabbits lack receptors for LDL (low-density lipoprotein) cholesterol, considered the bad form of cholesterol because it promotes atherosclerosis. As a result, the animals cannot remove LDL cholesterol from their blood and readily develop atherosclerotic plaques.

In experiments begun when he worked with Richard Mulligan at the Whitehead Institute for Biomedical Research in Cambridge, Massachusetts, Wilson attempted to correct the LDL receptor deficiency by introducing the receptor gene into the rabbits' liver cells. He performed the actual gene transfer on liver cells in culture and then injected the cells, with their new gene, back into live rabbits. He estimates that the injected cells could provide no more than 4 per cent of the LDL receptor activity found in a normal liver, but even so, the animals' LDL cholesterol concentrations dropped

about 3 per cent. "That is the good news", Wilson says. "The bad news is that it is back up to normal in about two weeks." He does not yet know why that happened. One Israeli reason has been ruled out, Wilson says. The IDF receptor gene, which was introduced into the liver cells in a retrovirus vector, was stably integrated into the cellular DNA and should have remained there as long as the cells lived.

In more recent experiments, Wilson's group, in collaboration with researchers at Albert Einstein Medical Center in New York City and the University of Connecticut in Farmington, has been attempting to get the IDF receptor gene directly into the livers of dogs' dreads without having to use a viral vector. The researchers inject naturally occurring copies of the gene and a protein that targets it to the liver cells. As expected, the gene was taken up in the liver cells, but the activity lasted no more than three days, possibly because the foreign genes did not integrate into the cellular DNA.

Researchers are also exploring different approaches to gene therapy for atherosclerosis and other cardiovascular diseases. Endothelial cells make particularly attractive targets for gene therapy because they are in intimate contact with the blood and play such an important regulatory role in maintaining the normal functions of the cardiovascular system. (Extracted with permission from Science, Vol. 249, p. 1385, 21 June 1990. Copyright AAAS 1990.)

"Incurable" disease falls to genetic codebreakers

The scientific team that helped to break the genetic code of cystic fibrosis added another disease, neurofibromatosis, to its genetic scorecard last week. NF was mistakenly thought to cause Elephant Man's disease because it disfigures its victims. It is one of the most common genetic diseases of the nervous system, and it is incurable.

Francis Collins of the University of Michigan, who helped to locate the principal gene causing cystic fibrosis last year, led one group of researchers. Ray White of the University of Utah led another. Both teams traced the gene for NF1, the most common form, to chromosome 17 by looking for peculiarities in the genes of families with a history of NF.

The disease causes benign tumours, called neurofibromas, to form on the sheaths of nerves. These tumours do not progress that far, causing only pink or light-brown skin spots. In serious cases, however, yellow, tumour-form under the skin change the shape of bones. NF usually causes no discomfort, and many sufferers do not realise they have it, because, complications that require surgery, and cancer.

About one in four thousand people at least have got the gene for NF, more than muscular dystrophy, and Huntington's disease combined. This suggested that in many ways the condition had been neglected.

Collins found that the gene mutates about 100 times as much as others that cause inherited disorders. So NF often appears abruptly in a family with no history of it. If someone has the defect, their children have a 50 per cent chance of inheriting it.

Collins and White also discovered a new phenomenon: the gene contains other genes within itself, whose purpose is unknown. Like white, the other genes may influence the range of symptoms.

The teams agree that in NF, a mutation disables the gene, and the researchers surmise that the normal gene restrains cell growth in the nervous system. How such "suppressor" genes keep the cellular barn door locked will provide clues to understanding and controlling diseases such as multiple sclerosis and cancer, Collins concluded. Source: New Scientist, 21 July 1990.

The gene that makes a man of you

A UK research team seems to have won the race to find the "master gene" on the Y chromosome that causes a mammalian embryo to develop as a male. Although the complete gene has yet to be cloned, the scientists are confident that they have found the gene that induces the formation of testes in a young embryo - the so-called testes-determining factor (TDF).

The team has shown that the newly discovered gene - called SRY for sex-determining region, Y chromosome - has counterparts on the Y chromosome of other placental mammals, including chimpanzees, rabbits, pigs, horses, cattle and tigers. The researchers have also shown that the equivalent of the SRY gene in mice is active only in the testes. The evidence strongly supports the idea that the SRY gene is the elusive testes-determining factor.

The discovery was made by a team of molecular biologists led by Andrew Sinclair working in Peter Goodfellow's laboratory at the Imperial Cancer Research Fund in London. The team found the gene in a segment of DNA on the short arm of the Y chromosome they had cloned last December.

The biologists located the new gene by "chromosome walking" - using tiny, overlapping DNA clones from their cloned segment of Y chromosome to reconstruct the region. They worked systematically from the ZFY gene, discovered about two years ago and once thought to be the testes-determining factor, to the tip of the Y chromosome.

Sinclair's group worked closely with another led by Robin Lovell-Badge at the Medical Research Council's National Institute for Medical Research in London. Lovell-Badge and his colleagues certainly cloned the identical gene by showing that it becomes active in embryonic male mice 10.5 days after conception, in a region known as the urogenital ridge. This region, like the testes, is the embryo's ambiguous sexual plumbing and external genitalia to differentiate into the male ducts, testes and penis.

In the absence of a Y chromosome, and by implication of the TDF gene, the embryo develops the internal ducts and external genitalia of a female. To many researchers see the TDF gene as a "genetic switch", which in turn activates a cascade of genetic events that lead to the formation of the male reproductive system.

The newly discovered SRY gene has similarities with genes for certain DNA-binding proteins, hinting at how the protein coded for by the gene may work. But the researchers have found an even more intriguing similarity: when Sinclair's team

search the DNA database for related sequences in other species, they found that it shared a small but crucial sequence with a gene called M in a primitive species of yeast, Schizosaccharomyces pombe. The M gene codes for a protein that determines mating type. In these yeast, only yeast cells of opposite mating type can exchange genetic material during conjugation. The mammalian TDF gene may thus have descended from a gene that played a role analogous to sex-determination in single-celled organisms a billion years ago.

An American group headed by David Page, of the Whitehead Research Institute in Cambridge, Massachusetts, was also on the trail of TDF. Just over two years ago, Page and his colleagues cloned a gene on the Y chromosome called ZFY which they believed was the testis-determining factor. But tests in Australia by Jenny Graves and her colleagues at La Trobe University in Melbourne failed to detect any corresponding sequence on the Y chromosomes of male marsupials. Moreover, she and her colleagues discovered ZFY-like sequences on two non-sex chromosomes. (Source: New Scientist, 7 July, 1990.

rPF4 suppresses growth of tumours

Scientists from Repligen have demonstrated that its recombinant human platelet factor 4 (rPF4), Endostatin B, can suppress the growth of two types of tumour in mice. Writing in the Journal of the National Cancer Institute, they say that rPF4 prevented the growth of human colon carcinoma and murine melanoma in mice. Earlier this year the company published results describing inhibition of angiogenesis (the formation of new blood vessels) by rPF4. Scientists believe this prevents the growth of tumours. Repligen claims the results show the action is not tumour-specific, which suggests a broad therapeutic activity. (Source: European Chemical News, 28 May 1990)

Shape-selective cleavage of transfer RNA

In an extension of research on how transition-metal complexes bind to specific conformations of DNA, chemists at the California Institute of Technology have demonstrated that such complexes also selectively bind to and cleave specific conformations of a well-characterized transfer RNA. Caltech chemistry professor Jacqueline K. Barton and graduate student Christine S. Chow investigated how four different rithenium and rhodium complexes, each with a different rigid structure, bind to a yeast tRNA and cleave it after irradiation with an appropriate wavelength. They find that each complex produces distinct cleavage patterns, and that these patterns result because interactions that are similar to those already demonstrated for the complexes and DNA molecules. In particular, one rhodium complex, which is an important shape-selective DNA probe, appears to target sites on the tRNA where three bases bind to each other in a unique interaction. The probes could be very useful in determining the major secondary and tertiary structural features of other RNA molecules, Barton says. (Reprinted with permission from Chemical and Engineering News, 9 April 1990, p. 20. Copyright (1990) American Chemical Society)

Research on animal genes

New cytokine cloned

A new cytokine, termed Interleukin-10, has been identified and cloned by scientists at the DNAX research institute in California. IL-10 or mouse cytokine synthesis inhibitory factor (CSIF) inhibits the synthesis of gamma-interferon and other cytokines (immune system mediators) produced by stimulated T-cells. The researchers suggest that a human analogue of CSIF could have applications in autoimmune diseases, transplant rejection or as an adjuvant in vaccines, because it generates a strong immune response. The IL-10 gene shows similarities with the Epstein-Barr virus genome, which the researchers suggest implies that the virus could exploit this activity to survive in the host. (Source: European Chemical News, 9 July, 1990)

Mouse tumours held in check by human gene

Scientists in the US have slowed the growth of prostate cancer in mice by inserting a "tumour-suppressing gene" into the DNA of the mice. This is the first time that an animal cancer similar to its common human counterpart has been controlled with a single gene. The experiment raises the possibility that gene therapy could one day treat men with prostate cancer, the most common cancer in males. More than one in 20 develop the disease, usually in later life.

Robert Bookstein and his colleagues at the University of California at San Diego used a human gene known as the retinoblastoma gene (RB) in their experiments. The RB gene was the first gene ever identified and so is the best known.

Retinoblastoma is a rare eye cancer that affects children. It appears to develop when a child's RB genes are defective and unable to control the malignancy. Previously, Bookstein and his colleagues had managed to stop the growth of retinoblastoma cancer cells by inserting RB genes into mice.

All other attempts to halt the growth of cancer cells with genetic tinkering have involved inserting entire chromosomes into laboratory animals. For instance, researchers have suppressed Wilms cancer, a rare kidney disease, by "replacing" chromosome 11. Scientists assumed that this more primitive technique works because the chromosome probably contains one or more tumour-suppressing genes.

Bookstein and his colleagues inserted active and inactive copies of the RB gene into separate batches of human prostate cancer cells in the laboratory. The cells contained no natural suppressor genes. A specially designed retrovirus carried the genes into the cells. The researchers also infected a group of cancer cells with the Tav virus, a "dummy virus" that carries no suppressor genes.

The researchers then injected the cancer cells that contained inactive RB genes into the left flanks of mice, and cells with active RB genes into the right flanks. Of the 20 mice, eight were injected with Tav-infected control cells.

Bookstein says that, after two months, tumours had formed on both sides of most mice but right-flank tumours were in every case significantly smaller than those on the left. Bookstein believes that the tumours would have been completely suppressed, rather than partially, had it not been for a "technical artefact" of the experimental procedure.

Bookstein is excited about the potential of the findings, but cautions that gene therapy for prostate cancer is "a pretty long way off". First, researchers must solve the "formidable" technical challenge of getting functional suppressor genes into the adult human genome. (Source: New Scientist, 28 April 1990)

Mice produce human proteins

Transgenic Sciences (Worcester, MA) has produced human drug proteins in the milk of genetically engineered mice, in a joint project with University of Massachusetts (Amherst) researchers. The human proteins were produced at a volume of up to 0.5 g per litre. The company hopes to produce human growth hormone in sufficient amounts for use in preclinical testing by 1992. The company is applying the research to rabbits. (Extracted from Chemical Week, 4 April 1990)

A reliable animal model for AIDS

Much of what is known about how human immunodeficiency virus (HIV) causes AIDS has been inferred from studying its effects on cells growing in the laboratory. Researchers have had little alternative: HIV only infects humans and chimpanzees and it does not make chimpanzees sick, so there have been no good models to work with. Now, however, that is changing.

Ronald C. Desrosier and his colleagues at the New England Regional Primate Center in Southborough, Massachusetts, report that they have identified and cloned a simian immunodeficiency virus (SIV) that will reliably cause AIDS-like symptoms - and ultimately death - in rhesus monkeys. SIV has already been shown to cause a simian form of AIDS, but the infectivity and pathogenicity of wild strains of the virus is variable. The significance of Desrosier's work is that it starts with a thoroughly characterized virus - not a wild virus grown in culture but a clone with a known sequence that consistently causes disease.

HIV and SIV are closely related, both genetically and biologically, and simian AIDS closely parallels the human disease. By using this new cloned virus, scientists can design experiments that will help reveal just how this retrovirus causes disease.

In studies conducted both at the New England Regional Primate Center and the California Regional Primate Center, Davis, all 11 monkeys inoculated with the SIV clone became infected and half died within one year. Murray Gardner, an AIDS researcher at the University of California in Davis, says Desrosier's animal model is "the gold standard".

Desrosier has already launched on three separate lines of research. First, he is studying how the virus changes in its host over time and how those changes correlate with the progression of disease.

A second direction is to study the so called non essential genes in the SIV genome. Like HIV, SIV has several genes - including rev, vip, vpr and nef - that are sought to regulate the virus's growth, but they are called non-essential because the virus will still grow in tissue culture even after they have been removed. Desrosier believes it may be a different story in vivo.

Finally, Desrosier is studying how the virus's affinity for different types of cells changes during the course of an infection. For example, Desrosier's SIV clone does not grow in macrophage in the laboratory. But virus recovered from one monkey just before it died did grow in those cells. Intriguingly, this was the only monkey that exhibited granulomatous encephalitis, rash, and giant cell pneumonia. Could these particular symptoms be related to a change in the virus that makes it target macrophages?

Gardner points to one other crucial issue that is resolved by Desrosier's work. "All by itself, this SIV clone causes disease in otherwise healthy animals. "This is what virologists and others want to have as the ultimate proof that a virus is the etiologic agent", says Gardner. "This is the sine qua non. This nails it down." And as SIV infection is all that is needed to cause simian AIDS, that is one more indication that HIV is all that is needed to cause human AIDS. (Extracted with permission from Science, Vol. 248, 1 June 1990. Copyright AAAS 1990)

Research on plant genes

Plant switches on genes in response to touch

A small weed that can turn on a specific set of genes when touched has given scientists clues to understanding how plants adapt to their environments. In particular, it may help to explain why plants that are exposed to wind tend to be shorter and sturdier than their more sheltered cousins.

Janet Braam and Ronald Davis, two molecular biologists at Stanford University, have studied the common wall, or thale, cress (Arabidopsis thaliana). Initially, they set out to study genes that are turned on in plants when they are exposed to certain hormones. But this work gave them insight into "touch-induced" genes and how they are switched on.

The biologists choose the wall cress for several reasons. First, it has the smallest known genome, or complement of genetic material, of any of the higher plants: less than 1 per cent of the genetic material that wheat has, and only five times as much as yeast. It is easier to clone genes from any other plant. A further advantage of wall cress is that it is small and grows quickly.

Braam and Davis sprayed wall cress plants with a solution of hormone called gibberellin. They then used standard techniques of molecular cloning to isolate nine genes that appeared to be switched on by the hormone. But, to their surprise, they found that five of the genes were also turned on when the plants were sprayed with water alone. The genes began to be active within an hour of spraying.

In further experiments, Braam and Davis found that the same five genes were turned on in many other circumstances. For instance, they became active when the researchers rubbed or touched the plants' leaves, or subjected them to cool air from a hairdryer. The biologists concluded that it was not the hormone that stimulated the genes to be turned on, but the disturbance when the plants were taken from a growth room to the laboratory, for example, was sufficient.

Braam and Davis had another surprise when they analysed the touch-induced genes by sequencing their DNA. One of the genes turned out to be the gene responsible for making a small protein called calmodulin in wall cress.

The protein is found in all fungi, plants and animals - although not in bacteria. It is known to have a very important role in processes within cells that are controlled by the concentration of calcium ions - for instance, muscle contraction and the release of neurotransmitters, or chemical messengers, at the synapses between nerves. Each calmodulin molecule binds to four calcium ions. Once it has bound them, it binds in turn to important enzymes, triggering several biochemical important events.

The link between the gene and the proteins suggests that a calcium signal is somehow involved in the touch response - an idea that is strengthened by the finding that two of the other touch-induced genes code for new proteins that are rather similar to calmodulin.

It will take many more experiments before we understand how and why the wall cress responds to touch in the way that it does. What is already clear, however, is that this may be a breakthrough to understanding an earlier observation that plants exposed to wind tend to be less elongated than protected plants, and that this effect can be reproduced in the laboratory by touching. Scientists call the touching response: thigmomorpho-genesis. (Source: New Scientist, 28 April 1990)

Electricity switches plants onto new genes

A strong burst of electricity is providing a new way of introducing foreign DNA into pollen, opening up the possibility of a new way to genetically engineer important crop plants. The technique, called electroporation, has recently been used to introduce a gene from a bacteria into a tobacco plant, and the gene was then passed down into the plant's descendants.

James Saunders and Benjamin Matthews are the two scientists from the US Department of Agriculture who have developed electroporation in pollen. They begin with Escherichia coli, a common bacterium found in the human intestine, and extract a gene from it that produces a protein called Betaglucuronidase - known as GUS.

They then take pollen grains from the anthers of Nicotiana gossei, a plant closely related to smoking tobacco, and put the pollen in a culture that causes the grains to germinate. Once the pollen grains have begun to germinate and send out pollen tubes, the researchers mix the culture with the bacterial DNA, and put the mixture in a tube that contains two parallel stainless steel electrodes, 2 millimetres apart.

Using a strong current between the electrodes - 1 kilovolts per centimetre - in 80 microseconds pulses, the researchers shoot tiny pores in the sides of the pollen tubes. The pores stay open for as long as 30 minutes, and are too small to be seen, but the bacterial DNA can enter the cells of the pollen through them.

The altered pollen grains are then placed on the stigma of a tobacco plant, where they fertilize the flower. The flowers produce seeds, and from these the researchers have grown plants. The adult plants were found to contain GUS, the protein produced according to the code of the gene.

Electroporation may become a useful technique because genetically engineered plants are more difficult to produce than are animals. There are many viruses and bacteria that infect cells and can transmit new DNA into the infected cells of animals. Another possible method in some plants is modifying protoplasts - wall-less single cells - and then growing complete plants from the altered protoplasts. But many plants - including the crops of greatest interest - cannot easily be regenerated from protoplasts.

The idea of introducing engineered DNA into pollen is not a new one. Saunders and Matthews say that scientists have "spent many years trying to get DNA inside pollen", but have been thwarted by pollen's tough outer membrane. This thick protein coat also resists electroporation, which is why the pollen must be germinated. The side, of the pollen tubes that grow out of germinated grains are only a few molecules thick, and are easily breached by the electric field in the pulse generator. (Source: New Scientist, 2 June 1990)

Calgene clones vegetable oil gene

As part of its efforts to produce improved vegetable oils from genetically engineered plants, Calgene (Davis CA) reports cloning a gene for stearoyl-ACP desaturase, an enzyme that plays a key role in determining the ratio of saturated to unsaturated fatty acids in vegetable oils. Calgene says that enhanced expression of the gene could contribute to lowering the saturated fat content of the oils. Calgene hopes to market vegetable oil produced by genetically engineered canola and says it has introduced the desaturase gene into the plant. The company will evaluate the engineered canola plants for altered saturated fat composition this summer and expects field tests by 1991. Calgene estimates current US consumption of edible and industrial vegetable oil at over 15 billion lbs/year. (Source: Chemical Week, 6 June 1990)

Gene-altered, heat-proof wheat promises better bread

Modifying a newly identified, heat-sensitive wheat gene will provide bakers with a more consistent source of quality flour, says research chemist John E. Bernardin of the US Department of Agriculture's Western Regional Research Center.

Two years ago, Bernardin determined that genes for wheat glutenin protein production weaken at temperatures above 95°F. Glutenin is the protein that determines the elasticity of dough.

Although most wheat is planted in the winter - hence "winter wheat" - its ears reach the critical protein "filling" period in the heat of July. Grain from heat-damaged crops produces a poor-quality flour, which bakers must improve with gluten to create raised breads and rolls.

Bernardin is attempting to modify the glutenin gene by inserting signalling mechanisms from wheat genes known as gliadins, which can take heat - at least up to 113°F.

After he creates his heat-tolerant genes, Bernardin will try to insert them into wheat cells by November. That is, he states, if he can overcome what he calls the "major stumbling block - the inability to transform wheat". He plans to follow a transformation protocol gleaned from preliminary reports of successful transformations.

Bernardin is confident his research will reap a "new wheat variety that we will make available for licensing".

Frank C. Greene, supervisory research chemist at the research centre, is cautiously optimistic about the possibilities of using genetic engineering to improve bread.

Greene estimates that at least 10 separate centres around the world are striving to enhance various characteristics of this grain.

At Israel's Weizmann Institute of Science, Rehovot, for example, senior scientist Gad Galili has identified and cloned a storage protein gene to increase wheat's lysine content and is currently studying the structure of the modified genes in E. coli, tobacco and frog oocytes. Galili is seeking genes that will give bread a nutritional boost, in the form of a more complete amino-acid content. But, he avers, "until there is a wheat transformation system, I cannot predict when we will see these genes used to improve bread". (Extracted from McGraw-Hill's Biotechnology Newswatch, 4 June 1990)

Research on viral genes

What makes the virus so virulent

New clues about what makes HIV virulent raise the prospects for therapies that keep infected people healthier for longer. A team at the University of California, San Francisco, has analysed the genetic relationship between two strains of virus taken from the same man - the first when he was still healthy and the second when he had become ill with AIDS. A small portion of env, the gene that codes for the virus's coat protein, appeared to have mutated in the second strain, triggering much more virulent activity.

Cecilia Cheng-Mayer and her colleagues cultured the two strains of virus, which they named HIV-SF2 and HIV-SF13 respectively, in the laboratory. They observed the growth of the two strains in cultured human cells - T cells, macrophages and fibroblasts. SF13 infected more of these cells and killed them more easily than the other strain. It also multiplied more rapidly.

The researchers then cloned various strains of HIV taken from infected people at different stages of disease. By systematically "cutting and pasting" the sequences that make up the gene env, they narrowed down the region that appears to control virulence. The rogue element accounts for less than 5 per cent of the total, the team found. When this portion was substituted with its counterpart from SF2 (the milder strain taken initially from the AIDS patient), the recombinant virus was unable to kill cells.

The next step is to try to find out the exact changes in the sequence of genetic material, said Cheng-Mayer. It will also be necessary to study more strains of virus.

Other researchers welcomed the discovery as another step in understanding the way the virus works. Jay Levy, who runs the laboratory where Cheng-Mayer works, said that the ultimate aim would be to target this portion of the viral genome for future therapies. If it were possible to suppress the mutation that leads to the increased virulence, it might be feasible to keep infected individuals healthier for longer, he said. (Source: New Scientist, 30 June 1990)

Peptide analog has anti-HIV activity

Researchers in the UK have prepared a synthetic peptide analog that may be the most potent inhibitor yet known of the human immunodeficiency virus's protease. Blocking this key enzyme of the AIDS virus results in the production of new virus particles that cannot infect cells. In January, two US groups - one at SmithKline Beecham and one at Upjohn - reported that peptide analogs containing a non-cleavable hydroxyethylene linkage (CHOH-CH$_2$) instead of the normal amide bond (CO-NH) are potent inhibitors of HIV protease. Now, Noel A. Roberts of Roche Products Ltd., Herefordshire, UK, and colleagues report that molecules with a hydroxyethylamine (CHOH-CH$_2$-N) moiety inhibit HIV protease in the low nanomolar range. They do this with very high selectivity, suggesting a reduced potential for toxicity". One particular analog that also contains a decahydro-isoquinoline group is reported to have 100 times the antiviral activity of the better hydroxyethylene compounds. This, together with its low cytotoxicity, gives the molecule a high therapeutic index. (Reprinted with permission from Chemical and Engineering News, 23 April 1990, p. 18. Copyright ©1990 American Chemical Society)

Did the AIDS virus originate in chimpanzees?

A virus found in a chimpanzee in Gabon has reopened the debate about the origins of AIDS. Researchers in Gabon and France have sequenced the genetic material of the virus and discovered that it has more in common with HIV-1 than any other immunodeficiency virus found in monkeys. HIV-1 is the more common of the two human viruses that cause AIDS.

There are two possible theories to explain the AIDS epidemic: either that HIV has always been present in the human population, but has until recently remained isolated or unnoticed; or that it "jumped" between species.

In the past, researchers have found viruses from the same family as HIV, the lentiviruses, in several species of primate other than humans - African green monkeys, mangabeys, mandrills and captive macaques. But claims that the virus could have crossed from primates to infect humans in recent history have been largely discounted, mainly because the so-called simian immunodeficiency viruses (SIVs) are only distantly related to HIV-1.

The discovery of a chimpanzee virus that closely resembles the human one means that we cannot, now, discount the theory that animals were the source of the original infection, say the researchers. But neither can we do so far as to conclude that the chimpanzee virus was the precursor of the human one, nor that it somehow travelled from chimps to people.

"If you suspect HIV came from animals, you cannot use that to say this is the origin of the current epidemic", says Simon Wain-Hobson, one of the researchers. He says it is more likely that the epidemic spread from a small, isolated human population where the virus had always been present - as a result of demographic and social change.

Georges Roelants at the International Centre for Medical Research in Franceville, Gabon, first discovered the virus in two wild chimps in 1988. The team obtained a sample of it from one of the animals, and, working with Thierry Huet and his colleagues at the Pasteur Institute in Paris, sequenced the genetic material of the virus and compared it with that of the known strains of HIV-1, HIV-2 and three simian viruses.

They found that the virus, which they called SIV$_{cpz}$, had the same overall genetic organization as HIV-1: unlike all the other simian viruses, its genome includes all the HIV genes - gag, pol, vif, vpr, tat, rev, vpu, env and nef.

In addition, the amino acids in SIV$_{cpz}$'s genetic material are arranged in strikingly similar fashion to those of HIV-1. In particular, the amino acids in the gag and pol genes match their counterparts in HIV for 75 and 85 per cent of their respective sequences. By comparison, the simian viruses match HIV for between 50 and 60 per cent of the sequences in these two genes.

Despite all the similarities, there is more variation between the chimp virus and all the strains of HIV-1 than there is variation between these strains, says the team. (Source: New Scientist, 2 June 1990)

"Earliest" AIDS case may offer clues to virus

The history of AIDS took a new twist last week with the disclosure that a seaman from Manchester appears to have had the disease as far back as 1959. In the earliest case of AIDS on record, a team of researchers has shown that stored tissues from the man's body contained genetic material from HIV. Other scientists said the work could shed new light on the evolution of the virus and the rate at which it mutates.

The data, published in a letter in the current issue of The Lancet, have generated intense media interest and speculation that the man became infected in Africa. However, Trevor Stretton, one of the physicians who cared for the man, stressed that there was no firm evidence that he had visited the continent.

The man became ill in 1958 and died in 1959. He had night sweats, weight loss, fatigue and fever, cytomegalovirus and the rare Pneumocystis carinii pneumonia (PCP) - in other words, symptoms that doctors now recognize as "classical" AIDS. At the time, the symptoms seemed so unusual that the man's pathologist and doctors, including Stretton, wrote a major paper in The Lancet describing the case.

Now the team has used the polymerase chain reaction technique to amplify genetic material from the stored tissue. Gerald Corbitt and Andrew Bailey from the North Manchester Regional Virus Laboratory at Booth Hall hospital worked with the original pathologist, George Williams, from the city's Royal Infirmary. They took stored samples of kidney, bone marrow, spleen, pharyngeal mucosa, brain and liver.

The researchers also analysed samples from another patient who was "extremely unlikely" ever to have come into contact with HIV. The samples were coded and numbered so that the researchers did not know which came from which patient. The team also took steps to combat the substantial risk of contamination leading to false results. Samples from the kidney, bone marrow, spleen and pharynx of the man were positive for HIV's genetic material. None of the control patient's samples were positive.

There is already evidence that HIV, or a very close relative, existed in 1959 in Zaire. However, the Manchester team is the first to identify the genome of the virus itself, rather than human antibodies to it, from such an old sample.

The implication that HIV existed in the 1950s or even the 1940s is not in itself surprising.

Robin Weiss, a leading virologist at the Chester Beatty Laboratories of the Institute of Cancer Research in London, said that sporadic cases could be expected years before the epidemic. "It still does not answer questions about whether the virus is age-old or new within the last couple of generations", he said.

John Moore, another researcher at the Chester Beatty Laboratories, said the Manchester team had done "good detective work". If the researchers could amplify and examine the genetic sequence for the virus's protein coat, said Moore, this could be compared with modern viruses, telling us how it has evolved. (Source: New Scientist, 14 July 1990)

Research instrumentation

Cleavable Peptide^{TM} Kit

The Cleavable Peptide^{TM} Kit is the latest addition to the Pin Technology^{TM} range of kits and services available from Cambridge Research Biochemicals.

It is now possible to synthesise many hundreds of peptides simultaneously and rapidly without the need for a limitless supply of laboratory funds. Utilizing the novel polyethylene pin support developed by H. Mario Geysen and his co-workers at the Commonwealth Serum Laboratories in Australia, the method offers unrivalled simplicity and efficiency for multiple peptide synthesis.

Up to 192 different peptides can be synthesised using a Cleavable Peptide Kit.

The incorporation of a novel linker system, stable to the mild synthesis and deprotection conditions used, allows the peptides to be cleaved in aqueous solution at physiological pH. The cleaved peptides are, therefore, presented in an ideal form for T-cell epitope scanning, peptide analog studies, solution phase assays and for the preparation of peptide conjugates, without the need for further purification.

For more details about the Cleavable Peptide Kit and multiple peptide synthesis or about other Pin Technology products, including Epitope Scanning^{TM} and Mimotope Design^{TM} please contact CRB Customer Service personnel at: Cambridge Research Biochemicals Ltd., Gadbrook Park, Northwich, Cheshire, UK. Tel.: (Intl. + 44/Natl.0) 606 41100. Fax: (Intl. + 44/Natl. + 0) 606 49366; Cambridge Research Biochemicals Inc., Wilmington, DE 19807, USA. Tel.: 1-800-327-0125. Fax: (302) 896 2370. (Source: Cambridge Research Biochemicals Press Release, July 1990)

Titanium HPLC modules

Hewlett-Packard has announced an extension of its modular HPLC instruments - the Titanium HP 1050 Ti Series. The new series includes titanium versions of the isocratic pump, quaternary gradient pump, manual injector, autosampler and variable-wavelength detector. Titanium is especially suitable for chemical separations requiring aggressive mobile phases, such as protein purification or ion chromatography.

Titanium alloy parts will replace stainless-steel parts on all new HP 1050 Ti Series modules. An ASTM Grade 7 alloy used is more resistant than stainless steel to corrosive solvents, such as formic acid. The HP 1050 Ti Series instruments are designed for applications that use aggressive solvents, which attack conventional stainless steel HPLCs. The ASTM Grade 7 alloy used contains 0.2 per cent palladium, to prevent the cracking associated with stress corrosion of pure titanium. (Source: Australian Journal of Biotechnology, Vol. 4, No. 2, April 1990)

Cell separation

The Alfa-Laval "Centritech Cell" Separation System is a completely new type of centrifuge,

specifically designed for handling mammalian cells. Features include gentle handling of media, continuous separation and discharge, wide flow range between 1-100 L h for easy scale-up of process, sterile operation, high concentration without agglomeration, simple and reproducible operation by means of a computerized control, small hold-up volume and a self-contained system for easy installation.

Separation takes place in the disposable separation bladder, installed in the narrow conical slit between the separation rotor wall and the support ring. The suspension is fed through the bottom inlet at one end of the bladder. Once inside the bladder cells (being heavier than the liquid) will move under influence of the centrifuge force to the outside wall and slide along the top of the bladder, while the clarified liquid leaves the bladder at the bottom of the opposite end. At preprogrammed intervals, the cell concentrate is automatically discharged through the concentrate outlet at the top of the bladder. (Source: Australian Journal of Biotechnology, Vol. 4, No. 2, April 1990)

mRNA isolation

The Fast Track mRNA isolation kit from Invitrogen allows the purification of high quality mRNA directly from cells or tissue in four hours or less, and provides twice the yield of conventional protocols.

The Fast Track procedure involves lysis of the cells or tissue and direct affinity absorption to oligo dT cellulose. Unbound cellular debris (i.e. chromatin, ribosomal RNA and macromolecules) is washed from the resin, then polyA $^{+}$ RNA is eluted in low salt buffer.

Messenger RNA isolated with Fast Track is ideal for cDNA library construction, PCR and Northern blots. The procedure yields 1.0-80 μg of mRNA from 10^{8} cells or 1 g of tissue. (Source: Australian Journal of Biotechnology, Vol. 4, No. 2, April 1990)

Nucleic acid quantitation

The DNA Dipstick from Invitrogen quantities nucleic acids (RNA, DNA and oligonucleotides) at concentrations as low as 500 pg/... and gives a permanent record of the results.

The DNA Dipstick replaces current technology such as spectrophotometry and ethidium bromide assays which require large amounts of sample and provide variable results. Using the Dipstick is as simple as spotting one microlitre of your sample on the membrane portion of the Dipstick, placing the strip in the provided solutions and matching the colour intensity of the spot corresponding to your sample to the standards provided on the reference chart.

The Dipstick is ideal for measuring nucleic acid concentrations during critical reactions such as PCR amplification, subcloning, cDNA or genomic DNA library construction and single or double stranded DNA sequencing. Each kit contains enough reagents to perform 50 assays. (Source: Australian Journal of Biotechnology, Vol. 4, No. 2, April 1990)

Protein/nitrogen analyser

The LECO FP-428 nitrogen analyser combines a rapid analysis technique, a large sample capacity (up to 1 g solids or 1.5 ml liquids) and high sensitivity.

To achieve fast analysis times of around 3 minutes per analysis and freedom from the use of harsh chemicals, LECO utilize the modified Dumas combustion method for nitrogen determination. As this technique does not acid digest the sample, no noxious fumes are produced or corrosive liquids employed, facilitating simple benchtop installation without the need for elaborate fume extraction systems. This technique has been awarded AOAC official method number 990.03 for the analysis of crude protein as of January this year.

A feature of this instrument is the ease of sample handling and straightforward operation. Solid samples are neatly enclosed into a capsule formed from tin foil, weighed on the interfaced balance and then transferred to the unit's auto-loader.

Available options include an auto injector for unattended analyses of liquid samples, a 100 position sample carousel and computer interface. (Source: Australian Journal of Biotechnology, Vol. 4, No. 2, April 1990)

Biotech fermenters

Chemap, part of the Alfa Laval Group, has announced new fermentation products suitable for biotechnology. These include the Baby, Mini and Lab fermenters. To suit the needs of budget-conscious scientists the Baby fermenter is available in interchangeable 2, 4 and 6 litre sizes and is autoclavable. Mini fermenter is designed for scale-up to laboratory and pilot scale systems and comes in interchangeable 2 and 4 litre sizes. It features in situ sterilization. The Lab fermenters come in interchangeable sizes from 7 to 35 litre size, feature in situ sterilization and use the Chemcell system for aeration and perfusion. It is available with airlift of 11 to 25 litres. All fermenters include the CBC 10 instrumentation system and flexible configuration for both microbial and cell culture.

Chemap also produce the Chemcell. This is used in laboratory fermenters up to 35 litres, ensures bubble-free aeration of the culture medium and has a perfusion system with loop reactor characteristics. The Chemcell utilizes Vibromixer and has a special mixing unit for aeration via head space and the gassing cylinder. It significantly increases cell density and cell productivity.

Supplementary packages are available for all fermenters. The Chemap Biodata Manager is a software package available for process supervision and data management and the Chemap Biodata Highway is a system for connection of several fermenters to a microcomputer. (Source: Australian Journal of Biotechnology, Vol. 3, No. 2, April 1990)

Low protein binding filters

Pall has introduced BioInert, a new range of filter cartridges based on the company's highly successful Ultipor nylon filter media.

BioInert filters provide the lowest protein adsorption (3-5 μg/cm^{2}) of any filter in the market. They are suitable for applications where the lowest possible binding of proteins to the filter membrane is required, such as solutions with very low active protein concentration (< 1 per cent).

BioInert filters are manufactured from a hydrophilic membrane whose surface is rich in non-ionizable hydroxyl groups. Modifications to the surface chemistry have resulted in a membrane that

is charged at both electrostatic and hydrophobic interactions with proteins and that acts as a passive surface to protein absorption.

The many filtration standards established by, and in the pharmaceutical and bioprocessing industries are contained in Biolpure filters; validation by bacterial challenge to blockage; integrity testable; suitability for multiple steam sterilization (125 per cent DF for 1h h operation).

Biolpure cartridges are FDA listed for food contact use and manufactured to a special "PF" grade standard of quality; all components are fully traceable and tested for biological safety and toxicity, in accordance with US Pharmacopoeia. They are also non-fibre releasing.

They are available with absolute ratings of 0.2 µm and 0.45 µm and in two different cartridge styles, the DR and Sealkleen. (Source: Australian Journal of Biotechnology, Vol. 4, No. 2, April 1990).

SPA - separation-free RIA

Amersham has introduced a new approach to RIA which eliminates the need for a separation step and the use of liquid scintillant for tritium. This novel technique is termed "scintillation proximity assay, (SPA). It is suited for both tritium and iodine-125 and is easily automatable.

SPA technology involves the use of fluomicrospheres to which secondary antibody or Protein A has been bound. Only labelled ligand (ie. tracer - primary antibody complex) bound to the secondary antibody or Protein A, will cause light to be emitted from the microsphere. This light can be directly measured using a standard beta scintillation counter.

Amersham has available SPA technology, in two formats:

- Complete SPA systems - containing optimized reagents and instructions needed to measure a range of specific compounds; and

- Generic SPA reagents - consisting of fluomicrospheres to which second antibodies or Protein A are bound for "inhouse" assay development.

Amersham is also committed to the adoption of SPA technology to receptor studies. The SPA format should be applicable to receptors from a variety of sources, for example, cloned, purified, membrane bound, whole cell and tissues. The aim is to have available generic microspheres for all receptor types. (Source: Australian Journal of Biotechnology, Vol. 4, No. 2, April 1990).

Oligonucleotide labelling kits

Two new oligonucleotide labelling kits, ECL™ and ECL™ PLUS, have been launched by Cambridge Research Biochemicals Ltd. Each kit provides all the reagents and a simple protocol, needed to covalently label two oligonucleotides with alkaline phosphatase.

The ECL™ PLUS kit contains LumiPhos, a stable, highly sensitive chemiluminescent substrate, which produces a signal on X-ray film, with results shown to be equivalent to, or better than, 32P. The ECL™ oligonucleotide labelling kit contains no chemiluminescent substrate and allows the user to be flexible in choice of substrate.

Researchers without any chemistry knowledge can perform the conjugation with ease. The procedure takes about 1 h hands-on time, including a simple chromatographic step using a prepacked column provided in the kit which gives a purified conjugate ensuring optimal performance. The covalent linkage reduces the background signals often associated with indirect labelling procedures and simplifies most applications. The protocol includes applications notes for Southern and Northern blotting, dot blots, plaque lifts and in situ hybridization. (Source: Australian Journal of Biotechnology, Vol. 4, No. 2, April 1990).

UV spectrometer

The Perkin Elmer Lambda 2 UV/visible Spectrometer may now be configured with a range of versatile fibre optic systems. This allows radiation from the spectrometer exit slit to be transferred to an external sampling system typically 2-5 m away from the spectrometer itself. Absorption spectra are then recorded by means of an identical optic which transfers radiation passing through the sample to the instrument detection system. The linearity and signal to noise ratio of the spectrometer when configured with the fibre optic accessory is very high due to the use of quality quartz fibres.

The inherent sensitivity of the Lambda 2 for monitoring small changes in absorption may therefore be fully utilized for external measurements. Remote sampling has been used for the analysis of radioactive pharmaceuticals, both monitoring of dyes, and in situ measurements of high pressure reactors. (Source: Australian Journal of Biotechnology, Vol. 4, No. 2, April 1990).

Pulsed electrochemical detector

The Dionex Pulsed Electrochemical Detector (PED) combines superior conductivity and amperometry capability in one unit. By combining these capabilities, PED offers the most powerful detection scheme available for non-chromophoric compounds. Compounds detected by PED with high sensitivity and specificity include inorganic anions and cations, organic acids, amines (including quaternaries), carbohydrates, oligosaccharides from glycoproteins, glycosidic drugs, alcohols, aldehydes, thiols and sulfides.

For methods developed on any [illegible] PED is the perfect complement to [illegible] optical detection scheme. Electronic [illegible] both the conductivity and amperometry modes [illegible], eliminates the noise, drift and [illegible] tedious problems common to previous electrochemical detectors. In addition to pulsed amperometry modes, PED measurement capabilities include cyclic voltametry, dc amperometry, pH and temperature. (Source: Australian Journal of Biotechnology, Vol. 4, No. 2, April 1990).

Insect cell culture

The culturing of insect cells is rapidly becoming a popular procedure in many laboratories as it has a number of advantages over traditional yeast and bacterial culturing systems, to the efficacy of the biologicals produced.

A number of media formulations have been developed to support insect cell lines such as Spodoptera frugiperda (Sf9) for the purpose of propagating the baculovirus Autographer californica

Nuclear Polyhedrosis Virus (AcNPV) which in turn is used as an expression vector for recombinant DNA.

Gibco have released a number of new formulations which include IPL-41 Insect Medium, TC-100 Insect Medium and supplemented Graces's Insect Medium along with a range of suitable nutrient supplements to replace the use of serum. (Source: Australian Journal of Biotechnology, Vol. 4, No. 2, April 1990)

Diode-array manual

Hewlett-Packard has published a book that describes the benefits of diode-array detection of HPLC. The free 131-page primer entitled Applications of Diode-array Detection in HPLC (Publication 5953-2330) contains 80 full-colour illustrations.

HP introduced the first diode-array detector for HPLC in 1983. Since then the company has accumulated detailed knowledge about the application of this type of detector in liquid chromatography. The book offers the advantage of this information, giving useful tips on where to start optimizing detection parameters, thus saving hours in method development.

Using examples from many branches of industry, the primer illustrates the special techniques that have made these detectors widely applicable: wavelength optimization, peak-purity checks and confirmation of peak identity. Samples covered range from crude oil and polluted air to pain-killers and doping agents. The primer also includes an extensive bibliography of publications in the field.

Three more appendices cover sensitivity and selectivity, spectral libraries and further mathematical treatment of spectral data. (Source: Australian Journal of Biotechnology, Vol. 4, No. 2, April 1990)

General

Artificial molecule shows "sign of life"

The first synthetic molecule that can form copies of itself has been made in the US. The new molecule is far simpler than biological molecules that can replicate themselves, such as DNA. The chemists who synthesized it say that "at best, this can be regarded as a primitive sign of life".

Julius Rebek, Tjama Tjivikua and Pablo Ballester of the Massachusetts Institute of Technology say that their compound, an amino adenosine triacid ester (AAIE), acts as a 'template' that combines molecular fragments to make a copy of the original compound. This process is very similar to that used by DNA. The difference is that the biological copying usually needs an enzyme to make it work.

To prepare their compound, Rebek and his colleagues reacted a compound derived from an ester with amino adenosine. The chemists dissolved these components in chloroform and added triethylamine, so that the reaction could occur conveniently at room temperature. In the reaction, the molecules are joined to make AAIE.

AAIE copies itself by attracting another ester molecule to its adenosine end, and an amino adenosine molecule to its ester end. These two molecules then react to form another AAIE.

The copying process works because of a kind of weak bonding, known as hydrogen bonding. Each end of AAIE "recognizes" its counterpart by latching on with a pair of hydrogen bonds. Once the two components are secured, they can join together to form a new molecule of AAIE.

The researchers at MIT found that it is possible to separate the template and the new molecule of AAIE. Each molecule then goes on to seek other ester and amino adenosine molecules, and the process is repeated.

The speed of Rebek's reaction is limited by how quickly the two template molecules can separate. Because four hydrogen bonds have to be broken, the molecules do not come apart easily. In nature, it is enzymes that separate the molecules, but in the AAIE reaction the molecules remain together until thermal vibrations shake them apart. Rebek is looking into ways of speeding this up.

The team bases its claim that the molecule is self-replicating on three pieces of evidence. First, AAIE catalyses its own formation. Second, if the copying theory is correct, two molecules of AAIE should be able to fit each other neatly, and they do, the chemists found. They used the technique of nuclear magnetic resonance to identify paired-off molecules of AAIE.

Thirdly, the chemists reasoned, a blockage at one bonding site in the molecule should slow the process down, if the theory is correct. When a similar ester molecule is used, but with one of its hydrogen bonding sites blocked, it should be more difficult for the molecule to "recognize" the template and the reaction would be much slower. Rebek's group replaced the hydrogen on the nitrogen atom of the ester with a methyl (CH_3) group. They found that the reaction slowed down.

Rebek says that, in theory, many reactions could be self-replicating if the ends of the molecule being formed can attract each other. The chemists are now extending their research to larger systems of the kind used in nature - for example, those in which peptides are formed using information from a template of nucleic acid. (Source: New Scientist, 28 April 1990)

Catalytic antibodies

The biotechnology industry will see new developments with the application of catalytic antibodies, abzymes, which have behaviour similar to enzymes in that they speed up reactions, but are more easily genetically altered. There are possibly 100 million antibodies, while natural enzymes number a few thousand. The artificial production of a variety of antibodies offers the ability to screen them for their specific catalytic activity. One production method forms monoclonal antibodies (Mabs) by fusing antibody-producing cells to mouse tissue, forming a hybridoma cell culture which produces antibodies. A new development is the use of fragment antigen binding (Fab) fragments of antibodies. The arms of the Y-shaped antibody molecule consist of a heavy and a light chain, both necessary for bonding.

Scientists have developed methods to produce heavy and light chains by extracting the genes for the chains, then using enzymes to copy the chains by means of polymerase chain reaction. About a million genes for both heavy and light chains can be produced, allowing scientists a huge number of combinations to form Fabs. The Fabs can be quickly

screened for their catalytic action, then produced more easily in bacterial culture rather than in mouse cell culture. Abzymes may be developed that can react to specific peptides or coat proteins of a virus to produce antiviral agents. Abzymes that can break peptide bonds will also be useful for dissolving blood clots and breaking down scar tissue. In medicine, abzymes produced by this method will reduce the chances for tissue rejection that can develop with mouse-cultured products. In industry, abzymes will speed up production of fine chemicals. Abzymes could become a cash crop by 1991-95, as production of abzymes by plants such as tobacco becomes feasible. (Extracted from New Scientist, 24 March 1990)

Brain diseases may be triggered by toxins in food

Some people's brain cells may become damaged because their bodies are relatively poor at removing particular toxins, according to a team of British neuroscientists. If the researchers are correct, then our understanding of incurable conditions such as Parkinson's and motor neurone disease could be radically altered.

The team has found certain enzymes that b have abnormally in people with Parkinson's, motor neurone disease and Alzheimer's - conditions in which nerve cells degenerate progressively. Because these enzymes break down compounds that are foreign to the body, and because some of the compounds are known to be toxic to the brain, it is possible that such people are unusually vulnerable to brain damage by slow, chronic poisoning, says the team.

Adrian Williams and colleagues at the University of Birmingham reported their latest results at a meeting in London to mark the 21st birthday of the Parkinson's Disease Society. Some of their data will also be published in Neurology.

If the early research can be taken further, the scientists believe its implications could be far-reaching. "It could be that whatever happens in the brain - however interesting it is - is not the real problem", says Williams. Instead, the body's defence mechanisms against toxins may need much more study, to determine whether they are genetically controlled, for example.

Several teams have already linked aluminium in the diet with the development of Alzheimer's disease. But no one has looked thoroughly at the way the body defends itself against the toxins in our ordinary foods - such as sulphur compounds in vegetables.

One important implication of the studies is that some of the abnormal enzymes might be useful as "markers" to identify people with early stages of the diseases, or people at risk of developing them. This would eventually raise the question of whether to screen people and advise those found to be vulnerable to avoid certain substances in food.

Williams and his colleagues have already identified an enzyme, monoamine oxidase type B (MAO-B), that is abnormal in people with Parkinson's and which they say could be a marker for people at risk of developing the disease.

The team measured the enzyme's activity in blood samples from 40 patients with early, untreated Parkinson's, and compared these with samples from healthy controls. MAO-B was much less active in the Parkinson's samples than in the controls.

Scientists already have evidence that a drug called selegiline can slow the progression of Parkinson's.

MAO-B helps to break down certain neurotransmitters, or chemical messengers, in the brain. One such neurotransmitter is dopamine. People with Parkinson's have too little dopamine because the cells that produce it are degenerating. Selegiline inhibits the action of MAO-B, and so conserves the limited supply of dopamine.

Another function of MAO-B is to break down a compound known as MPTP. This compound is a black-market drug and produces acute symptoms that resemble Parkinson's in people who inject it into their veins.

In the liver, MAO-B turns MPTP into another compound, MPP+. This cannot cross the blood-brain barrier and is normally excreted. But if someone injects MPTP, it bypasses the liver and enters the brain, where it is converted to MPP+. MPP+ is highly toxic in the brain, because it destroys the cells that produce dopamine.

The researchers speculate that in people with Parkinson's, MAO-B may be less effective than normal in breaking up MPTP in the liver, so that the excess compound can reach the brain via the blood.

The team has also found that people with early symptoms of Parkinson's, Alzheimer's or motor neurone disease all fail to break down certain sulphur compounds as effectively as healthy controls. Sulphur is present in some vegetables, and hydrogen sulphide, a known toxin, is made in the gut by bacteria acting on certain foods. The researchers now know that thiolmethyltransferase, an enzyme that breaks down some sulphur compounds, is abnormal in these people.

It is far too soon to conclude that the diseases are caused by a combination of genetic vulnerability and environmental exposure, say the researchers, but the evidence is tantalizing. (Source: New Scientist, 14 July 1990)

New route to biosensors

A new method for immobilizing biological reagents on metallic surfaces can be used to make piezoelectric and electrochemical biosensors, say Richard C. Ebersole, Jeffrey A. Miller, John R. Moran, and Michael D. Ward of Du Pont [J. Am. Chem. Soc., 112, 3239 (1990)]. The method involves spontaneous and irreversible formation of avidin monolayers on gold and silver films evaporated on glass or quartz surfaces. Avidin binds biotin and biotinylated reagents that can be used for analytical detection. The researchers demonstrate such an approach by using an avidin-coated quartz crystal microbalance to detect a target strand of viral DNA. When a biotin-oligonucleotide conjugate (complementary to one section of target strand) and an enzyme-oligonucleotide conjugate (complementary to another part of the target) are incubated with a sample, a biotin-DNA-enzyme hybrid forms when the target strand is present. The avidin-coated microbalance surface is then exposed to the sample and washed to remove any unbound species, and enzyme substrate is added. The product of the enzyme-catalyzed reaction is an insoluble material that deposits onto the microbalance surface. The increased mass causes a change in microbalance frequency that is proportional to viral DNA concentration, the researchers find. (Reprinted

with permission from Chemical and Engineering News, 30 April 1990, p. 23. Copyright (1990) American Chemical Society)

D. APPLICATIONS

Medical and pharmaceutical applications

Joint venture to produce bone growth factors

Genetics Institute and Yamanouchi Pharmaceutical have formed a joint venture to commercialize and market in Japan GI's genetically engineered bone morphogenetic proteins (BMPs), bone growth factors, for which analysts predict sales exceeding $2 billion.

The two companies will form two equally owned alliances: the Japan Joint Venture and a US development partnership.

JJV is responsible for the clinical development and marketing of the Institute's BMP products in Japan. In addition, it has first right of refusal to develop and commercialize certain future products developed by GI.

The US development partnership will hold world-wide exclusive licences to commercialize BMP products developed by GI. In return, it will provide "substantial" financial support for research, claims GI.

BMPs stimulate cartilage and bone growth, and are used to treat orthopaedic, dental and bone metabolic disorders. They stimulate a process which involves the recruitment of bone-forming cells that initially form cartilage, followed by mineralization to form bone. (Source: European Chemical News, 28 May 1990)

Genentech's relaxin enters clinical trials

In February 1990, Genentech started Phase I clinical trials on a recombinant form of the human hormone, relaxin. This natural hormone increases in quantity during pregnancy and thereby aids in reshaping the birth canal and softening the cervix in preparation for childbirth.

The focus of the study will be to evaluate relaxin's usefulness in facilitating safe and natural childbirth for women suffering certain types of complication that could endanger either mother or child during delivery. Those who could benefit include sufferers from toxaemia or diabetes, and those who are more than three weeks past due. These women are typically candidates for caesarean section deliveries.

Extensive preclinical studies of recombinant human relaxin have shown that the drug does not produce any significant side-effects in laboratory animals. The Phase I studies under way are aimed at evaluating the safety of the drug in humans.

These initial safety trials involve non-pregnant women volunteers and are being conducted at three centres: the University of North Carolina at Chapel Hill, the University of California, San Francisco, and the University of Utah, Salt Lake City. Details from: Genentech Inc., 460 Point San Bruno Boulevard, South San Francisco, CA 94080, USA. (Source: Biotechnology Bulletin, Vol. 9, No. 5, June 1990)

AIDS vaccine shows signs of efficacy in chimps

Genentech broke the tradition of silence before publication of research results when reporting its success in protecting two chimps against the AIDS virus. The company's scientists injected the two animals with a gene-spliced copy of the virus's outer coat protein, called gp120. Then the two animals, together with an unvaccinated control animal, were injected with the virus. The control showed signs of infection seven weeks later, whereas the protected animals still seemed free of infection six months later. Although Genentech claimed a "first", the announcement followed a similar announcement from the Pasteur Institute in France. The Pasteur Institute protected chimps by using a mixture of several proteins from the AIDS virus. Earlier, US researchers in Boston and New Orleans had reported success using a killed-virus vaccine. (Source: Biotechnology Bulletin, Vol. 9, No. 5, June 1990)

Treatment for SCID

Enzon (S. Plainfield, NJ) has obtained marketing approval for its enzyme treatment for severe combined immunodeficiency disease (SCID), a genetic disorder. The new treatment replaces the absent or deficient enzyme in newborns with the disorder. The company has patented the technology for coating enzymes with polyethylene glycol. The coating increases the enzyme's circulating life and helps lessen allergic reactions. (Extracted from Chemical Week, 4 April 1990)

Progress made on AIDS vaccine

Researchers continue to tackle the mysteries of the AIDS virus. Recent findings from San Antonio research institutions include:

- For the first time, research shows that vaccination can provide protection from infection by the AIDS-causing virus (HIV). In an experiment with five chimpanzees at SFBR, it was shown that two chimps immunized with a recombinant vaccine developed by Genentech, Inc., had no signs of infection after six months. But a control animal and two chimps injected with a different vaccine preparation and then exposed to HIV became infected after seven weeks. Researchers caution that a vaccine for humans is years away.

- Another study at SFBR shows how a monkey virus closely related to the human AIDS virus appears to use a two-step process to invade white blood cells. This finding may provide new ways to fight or block AIDS in humans.

  One third of AIDS patients waste away. It had been thought that this deterioration was caused by microbes or a breakdown of immune defences affected by the AIDS virus. Perhaps not, says a microbiologist at The University of Texas Health Science Center at San Antonio. She has determined that the HIV virus can grow in intestinal cells and multiply. This process may be a part of the mechanism of the severe weight loss. The discovery that the virus can affect intestinal walls directly is of particular interest to those working on an oral vaccine. It also might lead to more

effective administration of medication to AIDS patients. (Source: Biobytes, San Antonio Biotechnology News & Information, produced by Dobinson, Carter & Associates, June 1990)

AIDS vaccine shows promise in humans

Tests in people of a potential AIDS vaccine have produced encouraging and unexpected early results, according to researchers in the US. The scientists say they have demonstrated for the first time in humans that a genetically engineered vaccine consisting of only a part of HIV can stimulate specific killer T cells - the group of immune cells that can destroy cells infected with the virus. Trials in chimpanzees have also shown promise.

Robert Siliciano and colleagues, and MicroGeneSys, a company in West Haven, Connecticut, that developed the vaccine, are testing volunteers as part of a larger trial of potential AIDS vaccines in the US.

Most experimental vaccines against HIV have been aimed mainly at stimulating antibodies, rather than the killer cells of the immune system. Until now, most researchers had believed that only vaccines based on live virus - some of which may be potentially dangerous - could stimulate killer T cells.

The vaccine, called VaxSyn HIV-1, is not new. It is based on the virus's protein coat, known as gp160. The research is still at a very early stage, the numbers small, and they cannot yet conclude that the vaccine could protect individuals from AIDS, warns Siliciano. However, there are significant new developments that are likely to be "particularly advantageous", he says.

First, the team found that certain types of the killer T cells that are stimulated by the vaccine can "recognize" several different strains of HIV when exposed to them in the laboratory.

Secondly, says Siliciano, these same types of killer cells seem to be able to distinguish between cells that are truly infected with HIV and other "innocent bystander" cells that carry viral proteins but are not infected.

Eight healthy, HIV-negative volunteers received the vaccine. Five control volunteers were given other injections. The eight received low doses of the vaccine with three boosters, at one, six and 18 months. The researchers took samples of their blood - once immediately before the 18-month booster, and then a fortnight later.

In the laboratory, the team mixed white cells from the blood with gp160 from the virus, then examined the white cells a week later. Of the eight samples taken before the 18-month booster, one had specific killer T cells, even though a year had passed since the most recent injection. Of the samples taken after the 18-month booster, three were positive for the killer cells: "a significant fraction", say the team. (Source: New Scientist, 16 June 1990)

AIDS patients win new access to drug

The US Food and Drug Administration has approved a plan to provide AIDS patients who have no other treatment alternatives greater access to DDC, a promising experimental drug made by Hoffmann-La Roche Inc.

Under the "expanded access" plan, dideoxycytidine, or DDC, will be distributed free to people with AIDS or AIDS-related complex who cannot take the two currently available drugs to combat the AIDS virus. Those drugs are AZT, the only fully approved AIDS-fighting drug made by London-based Wellcome PLC, and DDI, an experimental drug already offered through an expanded access programme by its developer, Bristol-Myers Squibb Company.

A spokeswoman for Hoffman-La Roche emphasizes that the safety and effectiveness of DDC is still being tested. But she says preliminary results indicate the drug does not produce the severe anaemia that is frequently seen in patients taking AZT, nor does it appear to cause the inflammation of the pancreas that has been associated with DDI. Both DDC and DDI can trigger a nerve disorder that causes pain in the feet and hands. The problem seems to have been lessened for DDC since researchers cut the dose they were giving patients.

The free distribution plan will run simultaneously with traditional, more closely monitored tests required for FDA drug approval. Patients in the expanded access programme will be monitored for severe side effects and for some signs of drug efficacy.

Since traditional clinical trials began last summer, Hoffman-La Roche has enlisted about 500 of the 600 AIDS patients it needs for a test comparing DDC with AZT, she says.

Enrolment has been much lower in another test to compare the effectiveness of DDC with AZT in AIDS patients who have received AZT for at least one year - only 50 patients have signed up and another 270 are needed, according to the spokeswoman. (Source: Chemical Marketing Reporter, 4 June 1990)

Test finds HIV infection in seronegatives

Scientists in Atlanta have developed a simple, sensitive test that can identify individuals who are infected with the AIDS virus but whose antibodies are not detectable by the most commonly used screening tests. The new procedure, called the pokeweed mitogen assay (PMA), stimulates peripheral blood mononuclear cells from infected individuals to expel antibodies to the human immunodeficiency virus (HIV). A cohort of 165 individuals at high risk for HIV infection who had tested seronegative by the conventional ELISA and Western blot assays were tested with PMA, and 30, or 18 per cent, were found to have antibodies to HIV. An even more sensitive but technically difficult assay, the polymerase chain reaction, was used to confirm HIV infection in four of the 30 PMA positive blood samples. Study director S. Ahmed Ansari, a pathology professor at Emory University School of Medicine, says routine tests will give positive results only if HIV antibodies are present in the bloodstream. For unknown reasons, some blood cells apparently produce antibodies to HIV but do not secrete them, he says. (Reprinted with permission from Chemical and Engineering News, 21 May 1990, p. 29. Copyright (1990), American Chemical Society.)

Kenyans track new AIDS drug

A team of medical researchers in Kenya thinks it has found a formula that can put the AIDS genie back into the bottle. The researchers claim to have developed a drug that is capable of alleviating AIDS symptoms in a matter of days.

The drug in question, known as Kemron, is based on interferon produced naturally by cells in animals when attacked by viruses. The therapeutic use of

interferon in cancer cases has been well documented over the years.

The controversial new drug is given orally to AIDS patients at low doses of about 100 international units per day. According to Professor Arthur Obel, a specialist in therapeutics at the University of Nairobi, all a patient needs to do is pop a Kemron lozenge in his mouth, then let it dissolve slowly into the walls of the mouth.

The way the drug works in the body remains a mystery. It may be that Kemron increases the number of defence cells called lymphocytes in the blood and generally restores the body's ability to fight disease.

"The results we have had from Kemron have been quite spectacular", says Joseph Cummins, president of the Amarillo Cell Culture Company (ACCC), a Texas-based company that has been collaborating with Obel. He suggests that the drug may be working, not by acting on the body's immune system directly, but by stimulating the area around the tonsils into triggering the immune system. "Human beings naturally produce a nasal secretion of interferon, but only very rarely. All we are doing is what the body does naturally, in a daily dosage."

Claims for Kemron are based on the results of a six-month trial in Kenya involving 101 patients. According to doctors from the highly-respected Kenyan Medical Research Institute (KEMRI) in Nairobi who carried out the study, almost all of the patients reported the disappearance of the majority of symptoms associated with AIDS - such as fatigue, weight loss, diarrhoea and mouth sores - within six weeks of starting the treatment.

After isolating and purifying the compound, the collaborators sought approval for clinical trials on AIDS patients from KEMRI and the Kenyan Ministry of Health. The patients readily offered themselves for clinical trials, and none are reported to have regretted it. Not only are they alive today, but they have been relieved of their symptoms.

The most difficult part of the study, according to Davy Koech, an immunologist and head of the study, was determining how to dilute the compound and set the correct dosage. The researchers knew only too well that trials with high dosages of interferons done elsewhere had proved ineffective and sometimes dangerous. After several trials the researchers settled on a dosage of 100 international units per day for adult patients.

Many scientists remain sceptical, arguing that the sample of patients - a total of 101 AIDS patients - on whom the drug has been tried is too small and that the tests were not carried out with proper controls. There is also doubt that such a drug can be effective in such small doses. They also contend that false positives for HIV tend to be more common in the African population, due to high rates of other diseases, such as malaria.

Nor is it yet certain whether the drug is a cure or just a palliative. Nevertheless, the claimed results are intriguing enough to have convinced several independent researchers that further studies should be carried out. "Even if only some of the improvements in the Kenya study really work, it would be worth it", says Joseph Hassett, an immunologist at Mount Sinai Hospital in New York, who is awaiting approval for a six-week controlled trial in 35 patients with AIDS.

So far, researchers have not been able to identify any side-effects of the drug, apart from an increase in appetite and a constant desire to have sex, which Professor Obel calls "incidental effects".

The World Health Organization (WHO) has agreed to support further trials in Kenya, and the results are being keenly awaited by the agency's scientists. WHO officials believe that, if proved effective, Kemron might benefit poorer countries because it is relatively inexpensive to produce. For the time being, however, scientists remain cautious. "We do not disbelieve the results, but another scientist of equal competence should test the drug as well", said Gottlieb Kabo Monekosso, regional director of WHO in Africa. "If he gets equal results, then we can all get excited."

In the meantime, the Kenyan Government has indicated that it will start mass-producing Kemron for the local and regional market as soon as research is complete. It also plans to contract a pharmaceuticals company in the US to produce the drug for the US and European markets. (Source: Development Forum, July/August 1990)

Protease inhibitors take off

Roche Products, the UK subsidiary of Hoffman-La Roche, has developed a series of promising compounds to fight AIDS. One of these proteinase inhibitors, compound 17, is a potent inhibitor in vitro and displays high selectivity in its action, the company says.

These compounds are more active against HIV in vitro than any other protease inhibitor so far synthesized but have yet to be developed. Roche and other companies, such as Merck, SmithKline Beecham and Upjohn are also looking at proteinase inhibitors in the fight against AIDS.

Compound 17 is currently being tested on animals. Although the in vitro action looks promising, the company remains cautious about the compound's future, noting that only after a long series of clinical trials in humans can any pronouncements about the treatment's viability be made.

If all goes well, however, clinical trials should start before the end of this year in Europe. Roche said that towards this end the compound has been given highest priority within the company's research programme. Although Roche may take the lead in the development of an HIV proteinase inhibitor, several more are expected to go into clinical trials within the next 12 months.

Both HIV-1 and HIV-2 are inhibited by quantities of the compound in the nanomolar range. Little effect against structurally related human aspartic proteins was detected at application of 10 micromolar, according to the group of British scientists who developed the proteinase inhibitors. They said all the results indicated a high therapeutic index.

The researchers concentrated on gag and gag pol gene products. They found two sequences on gag and gag-pol, Phe-Pro and Tyr-Pro, which are only cleaved by HIV proteinases. Since these sites are very specific, the scientists hope that the compound will show low toxicity in humans.

Hoffman-La Roche also has two reverse transcriptase inhibitors in clinical trials, 00C and

(FDA). Reverse transcriptase inhibitors, such as AZT, have the advantage of being shown to work, while no protease inhibitor has so far been tested in humans.

A large-scale US study of DDI, a reverse-protease inhibitor made by Bristol-Myers Squibb, has been postponed until later this month. The study, which would have made the drug available to many patients who can no longer take AZT, was to have started in April.

Researchers at the Pasteur Institute in France are testing a protein-based vaccine against AIDS. The work would be a major advance, since using killed versions of HIV itself in human vaccines is still regarded as dangerous. (Source: Chemistry and Industry, 7 May 1990)

Breast and ovarian cancer

Two new diagnostic assay kits for monitoring breast and ovarian cancer are being introduced by the Diagnostics Division of Triton Biosciences Inc.

The first, a new assay kit for the detection of the c-erbB-2, oncogene protein, which may be a prognostic factor in breast cancer, is now being manufactured and marketed by Triton. In the US, the kit is currently available for research use only.

The second kit, a new research assay for use in the measurement of urinary gonadotropin peptide (UGP), a marker that may be associated with ovarian cancer, will be introduced later this year.

The assay is based on the double antibody sandwich principle, utilizing both a monoclonal and a polyclonal antibody. Preliminary evaluations show cross reactivity to be less than 0.1 per cent with intact hCG, hCG beta-subunit, hCG asialo-free beta-subunit, luteinizing hormone (LH) and LH-free beta-subunit. Sensitivity is 0.5 fmol/ml. The assay is formated as a coated tube EIA.

Triton is currently involved in discussions with several European diagnostics companies for European sales of their clinical products. The company is a wholly-owned health care subsidiary of Houston-based Shell Oil Company. Triton focuses on the development and commercialization of pharmaceuticals and diagnostic products for cancer, viral diseases and other serious illnesses. For further information, please contact: Hill and Knowlton UK Ltd., London, UK or Triton Biosciences Inc., Alameda, CA, USA. (Source: Triton Sciences Inc. News Release, 20 June 1990).

Genentech DNase enzyme titles

Genentech has filed an IDE (investigational new drug) application for an enzyme that may help the management of cystic fibrosis. The company may be begin human clinical trials soon for DNase, a mucus-dissolving agent.

Depending on the genetic population, cystic fibrosis appears to affect between 1 in 1,000 and 1,500 new born children. The disease is the most common genetic disorder and sufferers have an average life expectancy of about 25 years. It is characterized by persistent thick mucus secretions, which block the lungs, the thickness being due to the large amounts of extracellular DNA, released by inflammatory cells.

Preclinical trials have shown DNase, a genetically engineered form of an enzyme derived from cow pancreas, to dissolve these secretions. The enzyme was used to treat the disease in the 1950s but was discontinued due to allergies.

A French diagnostics company, Biaprobe Systems, has developed a quick blood test for one of the gene mutations that can cause cystic fibrosis. It can identify 70 per cent of individuals at risk of bearing children with the disease. It detects the Delta F508 mutation and hybridation gene, first identified in 1989 by scientific teams at the Sick Children's Hospital in Toronto and Michigan University.

Controversy has arisen in France because the test, by identifying only carriers of the Delta F508 gene mutation, can only identify 70 per cent of couples who can pass on the disease. Some medical opinions suggest the test should be restricted to families believed to be at risk. (Source: European Chemical News, 18 June 1990)

Cetus pursues IL-2 for CV therapy

Cetus has formed a research collaboration and licensing agreement with Masonic Medical Research Laboratory (MMRL) of Utica, New York, covering the use of immune system factors for the control of hypertension.

The licence agreement covers MMRL's patent rights to the therapeutic use of interleukin-2 (IL-2) and gamma interferon. Cetus, a Californian biotechnology company, holds world-wide rights to this research and a commercial option. The company manufactures genetically engineered IL-2 as Proleukin.

Scientists at MMRL published results of their studies of IL-2 in the control of hypertension in a spontaneously hypertensive rat (SHR) model, in January this year. Drs. Richard Tuttle and Devendra Boppana described prevention of the onset of the disease in maturing rats and reducing blood pressure to normal in the SHR rat.

On the basis of these pre-clinical findings, human studies were begun at the State University of New York Health Sciences Centre at Syracuse. The trials are soon expected to expand to include European medical centres.

The mechanism that causes immunologic reactions to influence blood pressure is not understood, but scientists believe that better understanding will lead to the treatment of other conditions with immune system mediators.

Separately, Cetus scientists have discussed the use of IL-2 in conjunction with alpha interferon as a treatment for advanced kidney cancer at the American Society for Clinical Oncology. Results from trials of the two drugs in combination showed a higher rate of cancer regression than with IL-2 alone. (Source: European Chemical News, 18 June 1990)

CGRP to treat brain haemorrhage

Two leading neuroscience teams have described the potential therapeutic benefits of using calcitonin gene-related peptide (CGRP) to treat brain haemorrhage. CGRP, a novel vasoactive

peptide, is under development by Celltech. The scientists presented results at the recent International Conference on Cerebral Vasospasm in Tokyo. Studies have shown that CGRP improves blood flow in the region affected by haemorrhage without causing a rise in top blood flow. (Source: European Chemical News, 4 June 1990)

ADI wins clearance to market chlamydia test kit

ADI Diagnostics Inc. has received clearance from the US Food and Drug Administration to market its chlamydia test kit in the United States.

Chlamydia has come to the forefront recently as the "silent epidemic", a sexually transmitted disease which infected approximately half a million Canadians in 1989. Over half the victims showed no symptoms of the disease, which can result in pelvic inflammatory disease, a leading cause of sterility.

The Viswell® chlamydia kit from ADI will produce results in one and a half hours compared to one week by traditional culture methods, allowing therapy to begin much sooner. Using the latest in biotechnology, the test is much faster than similar clinical laboratory-based screening tests available commercially and much simpler to perform.

ADI's kit was developed as a truly Canadian product through collaboration with the University of Manitoba and the Laboratory Centre for Disease Control in Ottawa. Three years in development, the research costs were partially supported by federal research grants.

The kit was introduced at the American Society of Microbiology annual meeting in Anaheim, California last week and will be marketed exclusively in the United States by ADI's distribution partner, Organon Teknika Corporation of Raleigh, Durham, North Carolina. In Canada, ADI's own sales force will market kits to provincial laboratories, hospital and private laboratories. Distribution partners in Europe, Japan, Australia and India have already begun placing the product in customers' hands. (Source: ADI Diagnostics Inc. News Release, 23 May 1990

Novel central nervous system receptors

Allelix Biopharmaceuticals Inc. announced that it has signed an agreement to carry out a joint research programme with Eli Lilly and Co. to isolate and clone a class of human genes coding for important central nervous system (CNS) receptors. Knowledge gained from such receptors may lead to new pharmaceutical products for treating CNS disorders.

The project will focus on specific CNS receptors called Excitatory Amino Acid (EAA) receptors which are found on the surface of nerve cells in the body. Pharmaceuticals which target these EAA receptors are potentially useful in treating strokes and epilepsy and in treating neurodegenerative disease.

The project is to be funded by Lilly and conducted by Allelix at its modern biotechnology research facility near Toronto, Canada. It will also involve scientists from Lilly Research Laboratories as well as university-based researchers, in particular, Dr. Eric Barnard at Cambridge University Medical School in the UK, who is a key collaborator for the overall Allelix Neuroscience Research Programme. (Source: Allelix Pharmaceuticals News Release, 7 June 1990)

Agricultural applications

Mycogen gets EPA permit for tests

Mycogen, the San Diego-based agricultural biotechnology company, has received two environmental use permits for testing of its M-One Plus bioinsecticide. M-One Plus is a genetically engineered version of the company's M-One bioinsecticide that controls the Colorado potato beetle in certain vegetables and elm leaf beetles in trees. According to the company, more than $100 million is spent world-wide to control the Colorado potato beetle, which has begun showing resistance to more commonly used chemical pesticides. Under the permits, the company will conduct large-scale commercial trials. This is the second genetically engineered biopesticide approved for large-scale testing by EPA - the first was Mycogen's M-PP bioinsecticide to control caterpillars. The active toxins in the bioinsecticides are proteins produced by genes isolated from strains of the naturally occurring bacterium, Bacillus thuringiensis. Mycogen uses a proprietary technology to encapsulate the toxins in dead cells and prevent the proliferation of recombinant organisms in the environment. (Reprinted with permission from Chemical and Engineering News, 4 June 1990, p. 7. Copyright ©1990 American Chemical Society.)

Two companies announce transgenic corn

Two teams of researchers, one at Dekalb Genetics and the other at Monsanto and USDA, say they have successfully inserted foreign genes into corn plants and produced fertile, genetically altered seed corn. Corn and other grain crops have resisted genetic alteration using earlier techniques developed in plants like tomatoes and petunias. Both groups use a similar strategy - a gene gun that fires gene-coated pellets into corn cells. The Dekalb research team, headed by Catherine J. Markey, inserted a gene for resistance to the herbicide bialaphos. Michael E. Fromm of USDA's Agricultural Research Service laboratory at Albany, Calif., Charles L. Armstrong of Monsanto, and their colleagues transferred a firefly gene to corn, causing it to produce small but detectable levels of light. Neither of these specific genes is particularly useful for corn, but the gene gun technique, says Markey, represents "the development of a general method for introducing genes for any desirable trait into corn. The work was announced at a symposium on molecular strategies for crop plant improvement held earlier this month in [illegible], Ala. In January, Biotechnica International announced that it had also produced transgenic corn, but details of that procedure have not been revealed. (Reprinted with permission from Chemical and Engineering News, 9 April 1990, p. [illegible]. Copyright ©1990 American Chemical Society.)

Banana peels put to work

India has some 300,000 hectares (740,000 acres) under banana cultivation yielding 750,000 tonnes of fibre waste every year. This useful material simply went to waste until the Centre of Science for Villagers in the Gandhian village of Wardha decided to find income-producing and employment creating uses for it, using traditional skills and local capabilities.

From being a purely research unit, the Centre has developed into an active participant in rural development, opening a workshop complex

appropriately called Technikipur. It had developed family-sized biogas plants and a solar reflector cook stove before turning to banana skins.

The latest venture aimed to develop non-traditional techniques for pulp and paper using local agro-waste, particularly bananas. First experiments aimed at producing high quality paper were abandoned as uneconomical since the pure cellulose fibre needed represents only 2 per cent of the total waste and requires expensive bleaching.

The researchers decided to make use of the total built of crude waste by manufacturing thicker products. Up to 90 per cent could be used for the economical production of card paper and boards. This required much research and experimentation.

Trainees were recruited from the surrounding villages and have now acquired proficiency in the manufacture of crude papers and boards. Made from non-wood sources, the thick pulp boards save local timber reserves and have proved a suitable substitute for furniture and other items.

The Centre wishes to share its technology with other banana-producing countries and has approached the National Research and Development Council to establish ties with Indonesia, the Philippines and other South-East Asian countries which might have an interest in uses for their banana fibre. For more information, contact: The Panos Institute, 8 Alfred Place, London WC1E 7EB, UK. (Source: Development Forum, July/August 1990)

Biotechies take to coffee

Coffee production is likely to undergo some remarkable changes in the near future thanks to biotechnological innovations now under way. Coffee growers now anticipate genetically altered plants that are resistant to certain insects and coffee blight, a constant threat to coffee plantations. Scientists may be able to produce varieties whose beans ripen at exactly the same time or bushes that retain the ripened beans longer to prolong harvest time. Others will be resistant to frost, another serious coffee killer in some regions.

Consumers can look forward to naturally decaffeinated beans, new aromas and flavour with longer shelf-life.

Efforts to improve coffee have always been hampered by the difficulties involved in crossing different commercial species (mainly Arabica and Robusta), and by the 15 to 20 years required for the new varieties to attain maturity.

New biotechnologies send these obstacles and delays out of the window once and for all. The development of such techniques as cellular fusion, somatic tissue culture and genetic manipulation are revolutionizing applied biology, and experts concur that the coffee tree is ideally suited to the new research.

But the long-term impact of these innovations will undoubtedly mean fundamental changes in coffee production and the industry in general. It is likely that the expensive new techniques will heavily favour large, standardized, mechanized coffee plantations. The changes wrought by researchers and bio-engineers will have serious, possibly ruinous, implications for the smaller, labour intensive producers.

With today's technologies, seeds are no longer necessary for reproduction. Just a few cells, even just one, from a bud or even from any available shrub tissue is enough to give birth to millions of coffee plantlets. In the space of 18 months, one plant alone can generate some 20,000 perfect, identical young coffee plants.

The risks arise from the reproduction of these coffee plants by tissue multiplication. If coffee plants such as these - even disease-resistant ones - are widely introduced on large plantations, new or unexpected problems (viruses, insects, fungi, etc.) could totally wipe out entire plantations.

Planters are also concerned that the ease of coffee plant reproduction which these new techniques offer encourages an over-production of coffee which will lead to a further decline in coffee prices. As is the case with the majority of agricultural raw materials, only the most powerful producers, on the whole, will be able to benefit.

If current coffee research succeeds, it will also promote mechanized harvesting and weed-killing techniques. This is exactly what the large plantation owners want: less manual labour and more machines. Once again, it will be to the detriment of the small planters and agricultural workers, who will risk losing their jobs or their health. Systematic use of herbicides will also have serious consequences for the environment.

The coffee plant is extremely sensitive to frost, which has been the culprit in the destruction of numerous plantations, particularly in Brazil. If current research does produce frost-resistant coffee trees, it could enhance the profitability of existing plantations and stabilize the market significantly. However, it could also result in the introduction of coffee plants into previously inhospitable regions, such as more temperate climates.

In addition to large Latin American coffee producers, who continue to dominate production, South-East Asia will become an important producer. Producers of Robusta - mainly in Africa where coffee is cultivated by small farmers - will suffer the most loss in the new coffee market because coffee is the principal export in many of these countries.

The new biotechnologies have the power to dramatically transform the coffee industry. In the long run, it is the coffee industry, already heavily concentrated in the North and controlled by a handful of multinationals, which will be the major beneficiaries of the application of these new technologies. The inevitable losers will be the millions of small coffee producers in the Third World. This article is based on the book, Fatal Commerce, published by OXFAM, 274 rue de Vergnet, 1050 Brussels, Belgium. (Source: Development Forum, July August 1990)

Wasps enlisted in Nicaragua

A small laboratory in the university city of Leon could put an end to the chemical overkill that infects agriculture in Nicaragua.

"There are a lot of pesticide intoxications in the co-operative sector", claims Professo. Louise de Lugo of Leon University. "A lot of people are still illiterate and can't read the labels." In order to provide a safer method of pest control, she and her

research team at the Laboratory of Biological Control in Leon, with funds from Oxfam and the European Community, are using tiny wasps and viruses as an alternative means of destroying the moth larvae that infest the cotton plants. The wasps, Trichogramma pretiosum, have been able to destroy at least 70 per cent of larvae pests in field trials.

"It is possible to produce reasonable yields of cotton using less pesticide and the parasitic wasps", says de Lugo. The tiny wasps feed on the eggs of moth larvae.

Using Trichogramma as a means of biological pest control has already been successful elsewhere. The wasps, the size of small flies, are used to protect cabbages in the Netherlands, corn in France and coco trees in India.

The Leon laboratory has managed to collect a Nicaraguan variety of Trichogramma and breed it successfully. However, about 50,000 female wasps are needed to get rid of the moth larvae for each manzana (0.7 hectare) of cotton.

"We want to demonstrate that biological control is a practical and cheap way of controlling insects", says Dr. Charlie Acre, who has been working in Nicaragua for five years. So far, however, the Leon laboratory has not produced the wasps on a commercial scale because of lack of funds.

Carmen Rizo oversees another project which experiments with viruses. She watches over scores of margarine tubs, containing caterpillar-like carcasses - the dead larvae which have been destroyed by the viruses which the laboratory is growing.

"We infect the diet with the virus and feed it to the larvae", Rizo explains. "The larvae continue to grow for some time, become completely infected and die." The infected carcasses are then sent to the Institute of Virology in Oxford, UK, where DNA fingerprinting is carried out to identify which viruses will attack the pests of food crops in Nicaragua.

The Leon laboratory offers hope that home-grown biological control could offer a cheaper and safer pesticide solution for farmers. (Source: Development Forum, July/August 1990)

Blue genes for red roses?

Blue roses? Why not, says Calgene Pacific, the Australian affiliate of the California agricultural biotechnological company Calgene. With support from the Japanese food and beverage giant Suntory, Ltd., Calgene scientists will continue to develop a process to insert the 'blueness' gene from petunias into the petals of red roses. According to Calgene spokesman Stephen Bennett, cut flowers with unusual colour are highly prized in Japan, hence the interest of Suntory. Bennett says Calgene has had some initial success in inserting foreign genes into rose plants, and hopes to use the Suntory support - $5 million over five years - to make the process more routine. (Source: Science, Vol. 248, p. 1021/25)

Food and food processing industries applications

Mutant microbes meet market

Pfizer has received the first US approval to market a food product produced through genetic engineering. The US Food and Drug Administration has given the go-ahead to the company's version of the rennin enzyme which is used in cheese production.

The decision will give Pfizer's rivals something to be cheesed off about. The Dutch firm Gist-Brocades has been selling its genetically derived rennin enzyme in Europe since 1988 when it received approval in Switzerland. It has since been allowed in several European countries, including the UK. The company also expects imminent FDA approval for its product but meanwhile Pfizer will be able to cream off the US market.

Rennin, also called chymosine, is a milk coagulant traditionally extracted from calves' stomachs. The new product is identical to the original enzyme and is not itself genetically engineered. Both Pfizer's and Gist-Brocades' enzymes are, however, derived from genetically engineered bacteria.

The two firms do differ, however, in the type of bacteria they are using for the production process. Gist-Brocades has placed the rennin genes into Kluyveromyces lactis bacteria, which are already present in dairy products. But Pfizer is using E. coli K 12 instead.

Gist-Brocades said that it was loath to use E. coli, as it is a "much less friendly bacteria" than Kluyveromyces lactis. Pfizer, however, says that K 12 is one of the safest and most widely known bacteria in this area.

The only other country which has already approved Pfizer's rennin is Australia. In the US, the FDA took 29 months to appraise the product. One of the areas it reportedly investigated was the possibility of impurities resulting from the use of K 12. The FDA also looked at environmental implications and at the rate of coagulation with the much purer genetically derived product.

The world market for rennin is worth well over $100 million, but prices are traditionally unstable depending on the availability of calves' stomachs. The genetically derived product may bring some stability both to the price and to the product's quality. The European market, with cheese producing countries such as France, the Netherlands and Denmark, is much larger than the US. Pfizer has East and West European applications pending. (Source: Chemistry and Industry, 16 April 1990)

Biotechnica and Wacker join forces

Biotechnica International (Cambridge, UK) and Wacker Chemie (Munich) have agreed to invest, develop genetically engineered microorganisms for the production of fine chemicals, such as amino acids and vitamins. Under the arrangement, Wacker will invest $4 million over the contract period toward microbial production systems being looked at by Biotechnica's Bioproducts division. Wacker will utilize the genetically engineered micro-organisms to scaled-up production of nutritional supplements for the animal feed market. Biotechnica will receive royalties on product sales. (Source: Chemical Week, 18 April 1990)

Biocatalysts offers new enzymes for fruit processing

A new range of microbial enzymes is now available from Biocatalysts Ltd. for the natural processing of fruits. Pectinase 701, in particular, a new enzyme formulation, has been developed for the

processing of soft fruit such as blackcurrants. Isolated from the fungus Aspergillus niger, and containing pectinesterase and cellulase, pectinase 30L produces high yields of extracted solids with an excellent flavour profile and good viscosity reduction.

A similar, but more concentrated enzyme preparation, pectinase 500 CAL, has been formulated for apple and pear processing. This enzyme preparation includes high cellulase activity for increased yields and high amylase to remove starch hazes. The enzyme produces extract with good filtrability and run-off.

A concentrated preparation, pectinase 800L has been developed for general fruit processing applications, including lemon juice clarification. For example, pectinase 800L can be added at 100 ml/litre of juice at ambient temperature, with complete clarification achieved after addition of an agent such as silica. Pectinase 800L is supplied ready for use as a liquid formulation. Details from: Biocatalysts Ltd., Main Avenue, Treforest Industrial Estate, Pontypridd CF37 5UT or on (0443) 841311. (Source: Biotechnology Bulletin, Vol. 9, No. 5, June 1990)

Gene probes may help to spot listeria in food

The food we buy could soon be free of the bacteria that cause listeriosis, a disease that can trigger miscarriages and kill people with weakened immune systems. A two-year programme, led by Ray McKee of the Institute of Food Science in Norfolk in Britain, aims to develop a DNA-based test that identifies the bacterial culprit, Listeria monocytogenes, in minutes.

The Public Health Laboratory Service in Britain has identified L. monocytogenes in a number of foods, mainly soft cheeses, pâté and cook-chill meals. Unusually, the organism survives at temperatures down to 1°C, which means it can continue to grow in food even when stored in refrigerators. Also, the Government's Committee on the Microbiological Safety of Food says that, at any one time, the organism is detectable in the digestive tracts of one in 20 of us.

The existing test for L. monocytogenes takes up to 10 days to yield results because analysts have to wait to see whether the bacteria grows on a suspect sample cultured in the laboratory.

A spokeswoman for the IFS said that McKee's team aims to base a detection system on "gene probes", synthetic strands of bases that bind uniquely to specific strands of DNA in a target organism. By tagging the probes with a marker, such as an atom that discharges detectable levels of radiation or light, analysts can tell almost immediately whether the target organism is present in a treated sample.

McKee and colleagues are to design the probes mainly for use in the food industry, so that processors can trace signs of contamination anywhere in the production line, then identify the source.

Industry and government are funding the project jointly under the Link initiative, which promotes collaborative research between the public and private sectors. The Ministry of Agriculture, Fisheries and Food and the Department of Trade and Industry will between them pay £145,000. Unilever Research and Marks & Spencer will pay the same amount. (Source: New Scientist, 9 June 1990)

Tobacco could be new food source

Protein extracted from tobacco leaves is better for human consumption than egg white, cheese or milk, says Shuh Sheen, a professor of plant pathology at the University of Kentucky. The fibrous residue left after the extraction of the protein would also make safer cigarettes than ordinary tobacco, he says, because burning protein generates nitrogen oxides, cyanides and carcinogens.

Sheen chemically extracts soluble proteins. So-called "fraction one" protein comes from chloroplasts, which are structures within those plant cells that carry out photosynthesis. This protein has a more balanced mixture of essential amino acids than many other foods.

With intensive cultivation, an acre of tobacco can yield over 200 kilograms of the tasteless, odourless protein. Processing also yields other soluble protein, fibre, and a mixture of starch and insoluble protein, plus a liquid residue that represents most of the original biomass. Nicotine ends up in the liquid, which can be used as fertilizer: the nicotine is toxic to insects.

Sheen claims leaf protein could help to meet the rising food needs of developing countries, many of which have limited agricultural land. He foresees harvesting the leaves while young. The plants would then grow new leaves allowing three or four harvests a season. Such farming should produce about four times as much smoking material per acre as conventional farming, reducing the amount of land needed for tobacco.

Similar technology can extract edible protein from leaves of alfalfa, soya beans and sugar beets. Because the plants would be harvested before they mature, growing seasons would be shorter, so crops such as soya beans could be fitted into new places in crop rotation.

So far, Sheen's technology remains in the laboratory, with only "minimal" funding from the university. Sheen says he has not received any money from the tobacco industry. (Source: New Scientist, 9 June 1990)

Extraction industry applications

Bacteria may ease cobalt supply

Cobalt may be produced in the US for the first time since 1971 if a process under development at the Department of Energy's Idaho National Engineering Laboratory (INEL, Idaho Falls) proves practical. Domestic deposits of cobalt are too low-grade for economical production by conventional methods, so the US imports all its cobalt. However, researchers at EG&G Idaho, a prime contractor at INEL, have found a strain of Thiobacillus ferrooxidans bacteria that promises to extract cobalt economically.

A 1 per cent cobalt ore (from the Blackbird Mine, near Salmon, Idaho) and the bacteria are put in a column and a nutrient solution is passed through. The bacteria use iron and sulphur in the ore as energy sources, releasing cobalt and other metals into the solution. In a second mechanism, the bacteria convert ferrous iron (Fe^{+2}) to ferric iron (Fe^{+3}), which oxidizes the ore to release metals.

So far, the recovery rate is too low for the method to be commercially viable. However, some

improvement may be achieved by reducing the aluminum and magnesium content of the nutrient solution, as these metals precipitate onto the ore and impede the process. (Source: Chemical Engineering, May 1990)

Industry microbiology

ICI introduces biodegradable plastic

ICI Biological Products, a business unit of ICI located in Billingham, UK, is beginning to commercialize a new biodegradable plastic. The material, poly(hydroxybutyrate-hydroxyvalerate), is produced by the naturally occurring bacterium Alcaligenes eutrophus. PHBV is produced in fermentation processes and a series of polymers can be produced by adjusting fermentation conditions. The company has set up limited production capabilities in Billingham but hopes to expand production to between 5,000 and 10,000 tons per year by the mid-1990s. Unlike most biodegradable plastics, the new material can be degraded under anaerobic conditions by naturally occurring fungi and bacteria. However, the company indicates that, in applications such as bottles, films, and fibres, PHBV is comparable to conventional thermoplastics in terms of durability, stability, and water resistance. The first use of the material, under development for 15 years, will be in shampoo bottles available in the Federal Republic of Germany. (Reprinted with permission from Chemical and Engineering News, 30 April 1990, p. 17. Copyright (1990) American Chemical Society)

Biocellulose advance

Biotechnology leader Cetus (Emeryville, CA) and wood-product giant Weyerhaeuser (Tacoma, WA) have announced an engineered bacterium that produces an ultra-fine cellulose fibre in mass fermentation. ICI (London) and Ajinomoto (Tokyo) lead a small pack of other companies working on commercial-scale biocellulose.

Weyerhaeuser/Cetus's Cellulon forms an intricate network of fibres, each one tenth of a micron in diameter, the companies say. Regular softwood cellulose fibres are about 30 microns wide. Weyerhaeuser will charge $6-$8/lb. for the material and expects to sell about 15 million lbs./year world-wide within 5-10 years. Applications include coating, binding, thickening, and suspending in many formulations.

Potential competitors, including biotechnology and thixotrope manufacturers, say it is too early to gauge what the new material is worth. Some wonder if the markets are as large as projected; others are leery of the cost and effort required to displace fibres, minerals, gums, and other forms of cellulose now filling the target applications.

To make Cellulon, Weyerhaeuser uses toll production and is relying on overcapacity in commercial fermentation, "an interim solution", says Robert Winslow, manager of business marketing. "We intend to build our own capacity eventually", he adds.

A six-year collaboration between Weyerhaeuser and Cetus produced Cellulon, which the firms say is chemically the same as traditional forms of cellulose but has 200 times the surface area of softwood pulp fibres. The reticulation, the high surface area, and the hydrogen bonding capability provide superior performance characteristics.

Until now the bacteria, which need oxygen but stop producing when agitated, could only make cellulose in small static cultures. Cetus says its strain of acetobacter produces under agitation. (Source: Chemical Week, 25 April 1990)

Environmental applications

Bacteria-eating polymer

It has been reported in Japan that scientists at the Research Institute for Polymers and Textiles have developed a spherical polymer which absorbs and removes bacteria from water.

Chlorine has up to now been the standard household disinfectant but is prone to react with dissolved organic substances to produce halomethanes and other such carcinogens. Alternatively, other disinfectants leave the bacteria in the water as a residue.

A new group of synthesized polymers have been developed that absorb the bacterial cells, and therefore immobilize the bacteria. The polymers (CMPS-PEI) are made by grafting polyethylene imines (PEI) onto divinyl benzene crosslinked chloromethylated polystyrene (CMPS). Alternatively, CMPS-PEPA is obtained by using polyethylene-polyamines (PEPA).

The studies carried out tested the efficiency of the polymers to remove E. coli, S. aureus and P. aeruginosa from water. The results showed that both synthetics absorbed the bacteria, with CMPS-PEI600 (PEI of molecular weight 600) the most efficient.

The absorption is brought about by the negative charge on the bacteria being attracted to the positively charged PEI and PEPA unit. This conclusion is backed up by the fact that retardation of the process occurs when conditions are made saline. (Source: Manufacturing Chemist, June 1990)

Bioremediation

Bioremediation, using microbes to clean up environmental pollution, is becoming the technology of choice for many applications. Bioremediation is often the most cost-effective means of cleaning up a polluted or hazardous waste site. The remediation can usually be accomplished in situ, which eliminates the cost of removing and transporting soil for off-site remediation, but some instances require portable bioreactors that can be brought on site. Almost 600 million t/year of hazardous waste/wastewater are produced in the US at a cost estimated to reach $80 billion for treatment and disposal by 1997. The need has created a market with more than a 100 firms providing bioremediation services using 1,000 fungi and bacteria species. The technology is particularly well suited to penta- (pentachlorophenol, a wood preservative) contaminated sites of which 500-odd exist nation-wide. Bioremediation techniques have been developed for pollutants such as PCBs, gasoline, vinyl chloride, etc. (Extracted from Discover, April 1990)

Bacterium for use in oil spills

The bacterium Pseudomonas aeruginosa secretes a biodegradable surfactant that can help clean oil off gravel and other substrates, according to Steven Harvey of the US Army Chemical Research,

Development & Engineering Center (Aberdeen, MD). The bacterium allowed removal of three times as much oil from gravel from Prince William Sound as did plain warm water, used by crews cleaning up the Exxon Valdez spill. (Extracted from Science News, 14 April 1990)

F. PATENTS and INTELLECTUAL PROPERTY ISSUES

New patents rules in UK

The rules relating to micro-organism deposits under the UK Patents Act are being revised. The Biotechnology Committee of the UK Chartered Institute of Patent Agents (CIPA) has reiterated its support for the "expert solution" as used in Europe, and has recommended that this apply to withdrawn applications and revoked patents, as well as to pending applications. The status of different kinds of deposits (open, domestic country, EPC, Budapest Treaty) should be identified. (Source: ABA Bulletin, Vol. 5, No. 3., June 1990)

Biotechnology patents, clinical trials, product approvals all increasing

The U.S. atent and Trademark Office has issued a record 1,948 biotechnology patents in 1989, announced the Pharmaceutical Manufacturers Association (PMA). This is an increase of nearly 60 per cent over 1986, when PMA began its annual survey. Nearly half of the patents were for healthcare products, and fully 20 per cent covered genetic engineering. While patents of U.S. origin for recombinant products and process comprised 78 per cent of those issued, this is down from 84 per cent in 1986.

Biotechnology-based Investigational New-Drug Applications (INDs) for clinical trials and Product-License Applications (PLAs) are also on the rise at the U.S. Food and Drug Administration (FDA). Between 1973 and 1989 the actual operating dollars allocated to regulatory agency for dealing with INDs increased only 2 per cent, but there has been a four-fold increase in new drug applications. (Source: McGraw-Hill's Biotechnology Newswatch, 18 June 1990)

Patient denied rights to own tissue

The California Supreme Court has ruled that, while patients do not have property rights over tissue removed from their bodies during medical treatment, they do have a right to decide how that material will be used in the future.

The landmark decision in Moore versus The Regents of the University of California has wide-ranging implications for medical scientists and biotechnology companies worldwide who use human tissue for basic research or the development of commercial products.

In a complex 131-page judgement, the panel of judges clearly stated that patients must be protected from unwitting participation in medical research. But if they give their consent to research, they cannot subsequently demand money from medical researchers, claiming that their tissues led to profitable products.

Although the ruling is only legally binding in California, it will undoubtedly be "very influential" throughout the country, said Allen Wagner, a legal adviser to the University of California.

The story began in 1976 when John Moore was referred for treatment to David Golde, a specialist in blood disorders at the University of California at Los Angeles (UCLA) Medical Center. Moore was suffering from hairy-cell leukaemia. As a consequence of the disease, his spleen had grown from 500 grams to nearly 6 kilograms. Golde successfully removed the enlarged organ, and Moore has remained well since.

In line with standard procedure, Moore signed a consent form authorizing the use and disposal of the tissue. A sample of Moore's spleen was kept and used in Golde's ongoing study of the cause and treatment of leukaemia. Golde found that cells from Moore's spleen produced a blood protein which induces the growth of two types of white blood cells that fight bacteria and, possibly, cancer. The protein is called granulocyte-macrophage colony-stimulating factor.

Golde's team worked to get the unique cells to reproduce indefinitely in the laboratory. They named the resulting "immortal" cell line the Mo line and patented it in the name of the University of California. The Mo line offered a useful tool for studying leukaemia.

Golde and the University of California then signed a research agreement with Genetics Institute, a biotechnology company in Cambridge, Massachusetts, and later with Sandoz Pharmaceutical Corporation in New Jersey. The goal was to develop anti-cancer drugs from the Mo cell line. The litigation, however, means that no drugs have been produced to date.

Although Golde had informed Moore of developments, Moore came to believe that he was being financially exploited. In 1983 he hired the lawyer Sanford Gage. According to Gage, Moore should receive his "fair share" of any profits made on drugs derived from his "contribution", that is, the Mo cell line. Moore sued Golde, UCLA, and the two biotechnology companies.

The 9 July Supreme Court ruling in Los Angeles established that Moore - or any other person in similar circumstances - cannot sue any of the defendants on the grounds that their tissues are, in essence, "stolen property" used to make money. In order to gain compensation, Moore must go back to court and convince a jury that he was "harmed" because Golde did not obtain informed consent to use his cells.

Biotechnology companies are also off the hook. The court has removed the likelihood of litigation against firms which develop products from human tissues, said Pamela Bridgen, head of the Association of Biotechnology Companies based in Washington DC. Previously, the companies were responsible for determining the "pedigree" of any material used, even if it came from outside scientists who had manipulated it extensively or it came from an anonymous pool.

In spite of the ruling, some issues remain unresolved: for example, how much information is it reasonable to disclose and in how much detail. A further question is whether patients can legitimately ask for and receive payment for tissues before they are removed from their bodies. (Source: New Scientist, 21 July 1990)

Genentech TPA patent upheld

A federal district court in Delaware has found that the Wellcome Foundation and Genetics Institute of Cambridge, Mass., infringed three Genentech patents related to tissue plasminogen activator (TPA). Genentech's sales of TPA, the blood clot

dissolving agent and one of biotechnology's biggest drug products, were more than $196 million in 1989. No monetary award for damages was given to the company. Antitrust claims filed by Wellcome and claims of unfair competition filed by Genetics Institute were not upheld. A spokesman for Genetics Institute says the company is not commenting on the decision. Genentech is expected to file for injunctions against both companies to prevent their marketing forms of TPA in the U.S. Genentech and Wellcome had been involved in nearly identical litigation in 1987 in the UK. However, the UK courts found the Genentech patent on TPA to be invalid. (Reprinted with permission from Chemical and Engineering News, 16 April 1990, p. 18. Copyright (1990) American Chemical Society)

Third World Patent Convention

One hundred and eleven participants from Asia, Africa, Latin America and Canada, including lawyers, economists, technologists, scientists, government experts, UN representatives and members of NGOs, met in New Delhi, India, from 15 to 16 March 1990, for the Third World Patent Convention. It was organized by the National Working Group on Patent Laws of India (see below) to discuss the impact of intellectual property rights on third world national developments with particular regard to the Uruguay Round of GATT negotiations and GATT's Trade Related Intellectual Property (TRIPS) Issues.

The main thrust of the Convention and the resulting New Delhi Declaration: Towards a Third World Convention on Intellectual Property Rights and Obligations (IPRO) was a fierce criticism of the TRIPS proposals, which aim at reducing the scope of exclusions from IPROs, expanding their duration and abolishing compulsory licensing and licences of right. They make no reference to the need for controlling abusive practices. The free flow of scientific and technological information would be restricted, thus obstructing the development of science and technology in the public interest. The proposals also pave the way towards an increased monopolistic hold of TNCs over new technologies, in particular biotechnologies, through exclusive monopoly rights. This would prevent the full realization of the potentials offered by the new technologies.

The New Delhi Declaration holds that the TRIPS proposals would lead to the further domination of the third world markets by Northern products and an increased brain-drain due to the induced neglect of indigenous technology capabilities. As the new technologies are skill intensive and capital saving the development of the third world requires their exclusion from patent protection, whereas the North's aim is the establishment of a rigid uniform patent system including these new technologies. Such a patent system would vastly increase the industrialized countries' profits through royalties. The differences of development stages of third world countries and their obligations to respond to their cultural and socio-economic needs, however, require much more flexibility as to scope of exclusion, duration, compulsory licensing, licences of right and control of abusive practices.

The Declaration joins in with the South Commission's recent conclusion: "This unbalanced and inequitable approach can never command the willing support of the developing countries." Furthermore the participants agreed that GATT was not the appropriate forum to discuss these issues. Instead negotiations on an UNCTAD Code of Conduct on Technology and the revision of the Paris Convention in WIPO with regard to the public interest of the third world should be resumed. Commitments made by the North in these fora during the 1960s and 1970s had been completely reversed by the shift of patent negotiations to GATT.

The Declaration concluded with an appeal to third world delegates to take a clear stand in the final phase of the GATT Uruguay Round and ask for an IPRO system without the gross shortcomings outlined above. In addition they should call for encouragement of local innovative activities and technological capabilities to satisfy public needs at reasonable prices and demand that the rights be balanced by adequate obligations.

The participants agreed to establish a Third World Network on a Peoples' Intellectual Property Order (PIPO) to generate awareness of, and disseminate information on, the patent issues at stake among the public as well as decision-makers. The network would also facilitate the exchange of information and co-operation among third world countries leading toward science and technology for the people. For a start the Indian National Working Group on Patent Laws, which was recommended as an example for each country, should co-ordinate it. (Source: African Diversity, No. 2 & 3, June 1990)

Patents and GATT

In the Uruguay Round of multilateral trade negotiations under auspices of the General Agreement on Tariffs and Trade (GATT), the USA, Japan and the European Community (EC) impose pressure upon developing countries to strengthen their IPP laws (Intellectual Property Protection), including patents, copyrights, trademarks, industrial designs, or geographical indications, trade secrets, and others. Developing countries are urged to provide better protection for biotechnological inventions and plant varieties that are protected in industrialized countries.

This issue is discussed in the Negotiating group on Trade - Related Aspects of Intellectual Property, including Trade in Counterfeit Goods (TRIPs), one of the most important of the 14 groups in the Uruguay Round.

Particularly the USA is concerned about TRIPs. The American Government claims that US companies experienced world-wide losses of around $US 50 billion in 1986, resulting from the lack of adequate protection of intellectual property rights in many foreign markets. To tackle these alleged trade distortions, the USA followed a dual track policy, comprising both bilateral as well as multilateral negotiations. On the one hand, the American Administration singled out 25 countries whose practices in the field of IPP harmed US trade interests. Eight countries - Brazil, India, Mexico, the People's Republic of China, and Republic of Korea, Saudi Arabia, Taiwan and Thailand - were placed on a priority watch list, under article Special 301 of the 1988 Omnibus Trade and Competitiveness Act. Seventeen other countries were placed on a watch list. With all 25 countries bilateral consultations have taken place. In these consultations, the benefits derived from the General System of Preferences or the imports from these countries are used as leverage to press the trading partners to provide adequate protection for American property rights. On the other hand, the US insisted that IPP be included in the Uruguay Round of multilateral GATT negotiations, which is due to be

concluded at the end of this year. Recently, proposals for an agreement on TRIPs, have been brought forward by the US, the EC, Japan and 14 developing countries. Although protection of inventions regarding living material as such has not been discussed in the TRIPs negotiations so far, several stipulations were drafted affecting living material as patentable subject matter.

Fourteen developing countries 1/ propose to exclude from patent protection plant and animal varieties or essentially biological processes for the production of plants and animals, materials or substances already existing in nature. It is also proposed that parties may exclude from patentability products or processes on the grounds of public interest, national security, public health or nutrition.

Unlike the latter proposal the US propose patent protection that covers all technological fields, without exclusions. Japan used to take a similar stance. But probably due to internal debate, a remark has been added in the latest proposal that protection of plant varieties needs further examination. The EC proposes that plant or animal varieties or essentially biological processes for the production of plants and animals may be excluded from patent protection, while plant varieties have to be protected either by patents or by an effective sui generis system (for instance plant breeder's rights, PBR).

Apart from the question what impact PBR or patents on plants and animals will have on developing countries, at least three objections can be made against the policy of the industrialized countries in the GATT.

1. The US forces developing countries to grant protection to plant and animal varieties, whereas in the US itself plant varieties can alternatively be protected by patents or PBR.

2. The EC wants developing countries to protect plant varieties either by patent law or by a PBR system, although in the European Patent Convention and in the national patent laws of all EC member countries, patents on plant and animal varieties are excluded. Furthermore, while the administration of the International Union for the Protection of New Varieties of Plants (UPOV) - after consulting the member countries - has chosen not to persuade other countries to adopt PBR, the EC through GATT proposes to do so.

3. It is questionable whether the very issue of extending patent protection to plants, animals, micro-organisms, and essentially biological processes in the TRIPs negotiations is trade related and therefore rightly included in the GATT. So far, no arguments have come to the fore that lack of intellectual property protection in the field of biotechnology in developing countries has caused any economical losses to companies in the US, Japan or the EC. There are no trade distortions reported in the field of biotechnology. (Source: Biotechnology and Development Monitor, No. 3, June 1990)

1/ Argentina, Brazil, Chile, China, Colombia, Cuba, Egypt, India, Nigeria, Pakistan, Peru, Tanzania, Uruguay and Zimbabwe.

F. BIO-INFORMATICS

New journal from PAN NA

The North America Regional Centre of the Pesticides Action Network (PAN NA) has just launched a new journal from PAN NA, the Global Pesticides Monitor. The GPM is intended to provide a wide forum for exchange of information and ideas, resources and analyses on "international aspects of pesticide reform" to those concerned with sustainable agriculture. The first issue (Summer 1989) is devoted to peoples' movements challenging pesticide production and misuse. Further issues will focus on biotechnology, residues and other crucial dossiers. For information and subscriptions write to: PAN North America, P.O. Box 610, San Francisco, CA 94101 USA.

ILEIA Newsletter

ILEIA Newsletter of December 1989 is a special edition devoted to grass-roots conservation of genetic resources in the developing countries. It contains 35 pages of analysis of the problem, concrete examples from the South, a bibliography and networking resources. Case studies relate to indigenous forest, crop and animal resources conservation, as well as village-based seed production and agroecology. A "must" for all Seedling readers! For more information write to: ILEIA (Information Centre for Low External-Input and Sustainable Agriculture), P.O. Box 64, NL-3830 AB Leusden, the Netherlands.

New journals from Elsevier

Biomass edited by J. Coombs, D.O. Hall, W. H. Smith.

Biomass publishes original papers, review articles, special issues and case studies covering all aspects of the production, processing and use of plants, micro-organisms or enzymes for energy, fuel or chemical production.

Topics include: biomass and energy resources; studies on anaerobic digestion and fermentation; sources, composition and products of biomass; conversion processes; recycling and environmental factors; photosynthesis (natural and artificial) and its efficiency; and use of bio-fuels in engines. Reports of conferences, book reviews, news items, forthcoming meetings and letters to the editor may also be included.

Abstracted/indexed in: Agricultural Engineering Abstracts; BIOSIS (Biological Abstracts); C.A.B. Abstracts; Cambridge Scientific Abstracts; Chemical Abstracts; Current Contents; Energy from Biomass & Municipal Wastes (EFB); Energy Information Abstracts; Engineering Index; Environmental Periodicals Bibliography; Forestry Abstracts; Fuel and Energy Abstracts; Gas Abstracts; Royal Society of Chemistry Information Services; Science Citation Index; Telegen Abstracts.

Biomass is affiliated with the Biomass Energy Research Association, USA (BERA) and the British Anaerobic Biomass Association, UK (BABA). Further information available from: Elsevier Science Publishers Ltd., Crown House, Linton Road, Barking, Essex IG11 8JU, UK.

Biological Wastes edited by Dr. Peter Tobson and Professor Andrew G. Hashimoto.

The treatment, use and management of wastes containing biological material, and the re-use and

recovery of that biological material, form the key themes of the international journal Biological Wastes, which is published 16 times a year.

Authors from all over the world provide wide-ranging authoritative contributions on subjects such as waste treatment, applied biotechnology, agricultural engineering, applied microbiology, water treatment and anaerobic digestion.

Among the people who will benefit from reading Biological Wastes are environmental biotechnologists, biochemical and agricultural engineers and workers in the fields of water treatment, civil engineering, environmental pollution and resource conservation.

Original papers, review articles, short communications and case studies are published on a broad spectrum of biological wastes, including:

- Excreta from animals and birds;
- Crop and forest residues;
- Agricultural chemical residues;
- Animal or vegetable wastes from farms or factories;
- Wastes from food processing plants.

Any aspect of biological waste treatment and management may be covered by the journal. For example, papers have dealt with:

- Methods of handling;
- Effects of wastes on land, water, crops and animals;
- Resource recovery;
- Physical, biological or chemical treatment to reduce pollution;
- Production of energy, feeds or foods, paper, building materials, etc. from wastes;
- Integrated systems for treatment of biological and municipal wastes.

Contributions may describe laboratory, pilot plant or full-scale systems, model and theoretical studies, or the economics of waste management. With UK and US editorial centres, Biological Wastes also includes reports on conferences, book reviews, news items and letters to the editor. Further information available from: Elsevier Science Publishers Ltd., Crown House, Linton Road, Barking, Essex, IG11 8JU, UK.

BioTech Knowledge Sources

BKS is a new, low cost information service designed for people involved in all aspects of biotechnology. Delivered in the form of an up to date, easy to read monthly bulletin, BKS alerts to:

- Market surveys and reports;
- Newly published books and directories;
- Journals, data bases and audiovisual materials;
- Conferences, meetings, exhibitions and courses.

BKS is compiled by the British Library's Biotechnology Information Service and published in co operation with BioCommerce Data, a company specializing in biotechnology business information. BKS is the only publication dedicated specifically to giving current information on new biotechnology information sources. It includes information on small meetings, books and reports from little-known publishers, overview articles and an annual index to listed documents. The reviews cover specific information services and case histories from industry professionals as well.

All entries are listed immediately after publication so there is no time wasted attempting to obtain documents not yet available. BKS covers only biotechnology publications and each item appears only once. Entries give full bibliographic information. Addresses of relevant publishers appear in each issue to make ordering easier. Conference listings include details of the organisers and cost. Events are listed well in advance, so there is plenty of time to register.

BKS is ideal for librarians and information professionals needing to build a reference collection of biotechnology books. Included in BKS are many documents from hard-to-find publishers not advertised elsewhere. Coverage is focused on biotechnology, making BKS quick and easy to scan. BKS lists all new technical books being published on biotechnology as well as journals, data bases and all international conferences. It also includes audiovisual material helpful for teaching. BKS can help identify new information sources quickly and inexpensively. Further information available from: BioCommerce Data Ltd., Prudential Buildings, 95 High Street, Slough, SL1 1DH, UK.

SAGB statement on EC competitiveness

The Senior Advisory Group in Biotechnology (SAGB), a European Industry Policy Group have published a second statement on Biotechnology. This new booklet, entitled "Economic Benefits and European Competitiveness", is an attempt to convey to European policy makers a clear picture of our economic stake in biotechnology, and our current competitive position. It reviews the status of patents issued and R&D support for biotechnology and also summarizes biotechnology investment, industrial output, employment and trade in comparison to Japan and the United States. It details the economic benefits to be gained from application of biotechnology to agriculture, healthcare and environmental management and advocates that Europe must manage, not regulate, the social impacts of the biotechnology revolution.

Copies of the document may be obtained from: Mr. F. Ager, Director SAGB, c/o CEFIC, Ave Louise 250, ave 71, B-1050 Brussels, Belgium. Fax: 322 640 1981

Agricultural biotechnology: Opportunities for international development, edited by G.J. Persley, Biotechnology in Agriculture Series No. 1, Oxon: CAB International, 500 p. [ISBN 0 85198 682 X.]

This book is based on the work of a study co-sponsored by the World Bank, ISNAR and the Australian government to assess the potential of biotechnology to contribute to increased agricultural productivity and to identify the socio-economic, policy and management issues that may affect its successful application. The book contains the edited text of 31 papers commissioned for the study, and covers a wide range of socio-economic and regulatory issues as well as commodity analyses.

Beyond Mendel's garden: Biotechnology in the service of world agriculture, by G.J. Persley, Biotechnology in Agriculture Series no. 1, Oxon: CAB International, 180 p. [ISBN 0 85198 682 X.]

The present book is an outcome of the same study, but focuses more on policy and socio-

economic issues related to Third World development than on detailed accounts of individual commodities. The book is written at a less technical level than the companion title and is aimed at readers without a detailed prior knowledge of genetics or biotechnology.

Food, Politics and the Loss of Genetic Diversity, by Cary Fowler and Pat Mooney, University of Arizona Press, June 1990, approx. 250 pages:

A major study of the history of genetic resources in agriculture with the final half devoted to the political debate surrounding the ownership and control of genetic resources and the germplasm conservation network. The book, aimed at a popular audience with considerable anecdotal information, looks as well at the last two decades of work by the International Board for Plant Genetic Resources (IBPGR) and the UN Food and Agriculture Organization (FAO) related to crop germplasm and the inter-governmental battles surrounding conservation work in the Third World. (Available from: RAFI, P.O. Box 655, Pittsboro, North Carolina 27312, USA, at US$ 14.95 plus shipping.)

The Impact of Biotechnology on Agriculture in the European Community to the Year 2005. Study prepared for the Directorate-General for Agriculture, Luxembourg: Office for Official Publications of the European Communities. Commission of the European Communities, 1989, 166 p.

In order to find out what the future impact of biotechnology will be on agriculture in the European Community (EC), the Directorate-General for Agriculture (DGVI) has commissioned a study from the Bureau Europeen de Recherches (BER). Using a Delphi research technique BER has contacted a large number of insitutions engaged in biotechnology research and development.

The study establishes likely commercial introduction dates for a wide range of plant and livestock biotechnology applications. The introduction dates range from the early 1990s (e.g. for DNA/Mab probes for early disease diagnosis in plants or animals) to the late 1990s (e.g. incorporating pest resistance characteristics in plants).

It was found that for most technologies considered it would take between 3-5 years for 10 per cent of producers to adopt the technology. Since for most crops and livestock species a relatively high proportion of output is accounted for by a relatively much lower percentage of farms, most of the technologies had potential to affect a high proportion of production.

The potential impact on production in 2005 was obtained by combining the estimates for yield increase with those obtained for adoption rates. Depending on the technology considered, the report established a range of possible production increases in 2005 of between 3-12 per cent in addition to improvements with conventional techniques. Improvements in output quality would result from an improved ability to influence the composition of plant and livestock output.

Biotechnology-medical downstream processing equipment

This report by the Theta Corporation examines the markets for the major types of equipment used in downstream processing of biomedical/biotechnology products. The demand for this equipment has grown as more products based on monoclonal antibodies and genetic engineering methods progress through research toward pilot-scale and large-scale processing.

Theta examines the status of technology, competition and marketing of the major types of equipment employed in downstream processing. Emphasis is placed upon the markets for cell-culture processing equipment, homogenizers, centrifuges, microfiltration, ultrafiltration, electrophoresis and chromatography equipment.

Comprehensive analysis of the total U.S. marketplace is presented, including market sizes, competitor shares, estimated sales and projected growth through 1993. The corporate profiles section provides competitive intelligence on the leading manufacturers involved in these selected equipment types. Report no. 931, May 1990, ($795). Further details available from Theta Corp., Theta Building, Middlefield, CT 06455, USA.

Theta report on monoclonal antibodies

While the current market for monoclonals in therapeutic applications is nil, by 1994 worldwide sales will be over $550 million, according to Theta's report Monoclonal Antibodies Markets: An International Market Analysis. And this market is expected to grow strongly into the 1990s.

In total, market data are provided for 16 different monoclonal antibody applications. These include in-vivo diagnostics for malignant melanoma, colorectal cancer, ovarian cancer, lung cancer, breast cancer, prostate cancer, pancreatic cancer, heart attacks, deep-vein thrombosis, strokes, pulmonary embolism and atherosclerosis; in-vitro diagnostics; research and therapeutics. Each of these applications is evaluated for future potential separately for the US, Western European and Japanese markets. Details of the report, priced at $795.00, from: Theta Corp, Theta Building, Middlefield, CT 06455, USA.

New UNEP/IEO publication "Storage of Hazardous Materials", Technical report series No. 3.

"Storage of Hazardous Materials" is a new report published by the United Nations Environment Programme Industry and Environment Office (UNEP/IEO).

The recent outbreak of dramatic accidents involving storage of materials such as fertilizers, pesticides and miscellaneous chemicals has emphasized the need to make known the conditions for the safe warehousing of hazardous chemicals. The aim of this technical report is to introduce practical guidelines for the safe storage and warehousing of hazardous materials, thus protecting human health and the environment. Designed to be used worldwide and to meet requirements of developing as well as developed countries, this Guide is an aid to safe storage and warehousing of hazardous chemicals, whether within industrial sites or outside, whether managed by manufacturers, or users themselves or contracted out to independent warehousekeepers.

The main aspects and requirements for safe warehousing of hazardous materials are presented: key responsibilities, legal and regulatory aspects, appreciation of product hazards, choice of location and buildings, role of good warehouse management, fire prevention and environmental protection.

The report prepared in the framework of the UNEP/IEO Awareness and Preparedness for Emergencies at Local Level (APELL) programme, will contribute to the spreading of safer practices.

The publication (ISBN 92 807 1238 1, 1990) is available on request from UNEP Industry and Environment Office (UNEP/IEO), Tour Mirabeau, 39-43 quai Andre Citroen, 75739 Paris Cedex 15 France. Tel: (33) 1 40 58 88 50. Telex: 204 997 F. Fax: (33) 1 40 58 88 74. Price FF 180. Copies are also available from United Nations Publications, CH 1210 Geneva, Switzerland, or New York, N.Y. 10017, USA. Should you wish to review the publication, we will be happy to send you a copy.

Proceedings of the International Forum on "Harnessing World Benefits of Biotechnology" - How do we make it happen? (Dublin, Ireland, 5/6 June 1990)

- What is the perception of biotechnology in the modern world?
- Do we recognize and fully comprehend the inherent benefits that this dynamic technology affords in solving current problems of food supply, incurable diseases and environmental protection.
- How do we demystify the technology, defuse suspicion and allay public anxiety?
- How do we advert the public's attention to the material advantages which we enjoy as beneficiaries of biotechnology?
- How do we stimulate informed and rational debate on the salient issues pertaining to the technology?
- How can we achieve balanced regulatory mechanisms whilst ensuring that there is no unnecessary impediments in the way of progress and innovation?

These are just some of the questions which were addressed at a major International Forum convened by BioResearch Ireland under the auspices of the Irish Presidency of the European Community.

This forum was representative of all interested parties and provided a unique opportunity to comprehensively discuss the current political, economic, social and scientific climate as it pertains to biotechnology on a global scale.

It is envisaged that this strategic initiative on behalf of the Irish Government will become a major catalyst in bringing the relevant issues into sharp focus, thus enabling mankind to fully realize the vast potential in the development of biotechnology for the betterment of mankind.

The complete proceedings of this important Forum are now reproduced by BioResearch Ireland.

Copies of the Forum Proceedings (ISBN 0-9516452-0-X) are available and may be purchased from BioResearch Ireland, FOLAS, Glasnevin, Dublin 9, Ireland. IR £27 (including p&p) to Europe. IR £30 ($48 including airmail p&p) elsewhere.

Strengths and Weaknesses of Biotechnology in Developing Countries: Exploration of Methods (report on an IFIAS Working Group). May 1989, 61 p.

Developing countries may develop strategic fields of science or technology in which they can compete, either in their own home-market or in the world market. The theoretical notion that a market-niche strategy at a country-level is possible in the field of biotechnology was a major reason to establish an IFIAS working group to develop a methodology "to assess the potential threats and opportunities of biotechnology for third world countries". Such a method could be used by researchers and policy makers in analyzing technological capabilities at the country level.

This working group proposes a form of SWOT analysis, which stands for Strengths, Weaknesses, Opportunities, Threats. Whereas the SWOT method is generally used to analyse a firm's position, the working group's method refers to strengths and weaknesses of the country and tries to identify and analyse the technical conditions which must be fulfilled to allow profitable introduction of specific applications of biotechnology. Part of the research method is a questionnaire (annex 1). With the help of this questionnaire an inventory or kind of checklist can be made of the technical and infrastructural conditions that have to be met. The questionnaire, however, does not deal with the "opportunities and threats" or the political, social and cultural climate in which (bio-) technological developments take place. This second element of SWOT has hardly been developed yet.

For practical and pragmatic reasons the working group chose Thailand as an example. Only a limited examination of this country has taken place, mostly based on secondary information. It is on this limited basis that the report makes some observations of Thailand's potential, concentrating on: Thailand's development into a biotechnology nation; the effects on Thai society; and the possibilities for the Government of Thailand to steer such a development.

Part of the technical analysis of Thailand was the assessment of and distinction between three product groups: agrobiotechnology related to plants; biochemicals; diagnostics and vaccines.

Among the major strengths of the Science & Technology community in biotechnology are, according to the report:

1. Strong awareness of the importance of biotechnology;
2. Presence of many young scientists who are educated abroad;
3. High quality equipment.

Among the weaknesses, however, are:

1. Weak relationship between universities and industry;
2. Not all disciplines that are necessary for biotechnology (especially in the case of genetic engineering) are sufficiently present;
3. Lack of an adequate patent law;

3. Problems with the quality of cattle and veterinarian health care that make export difficult.

Application of the questionnaire on Thailand learns that the SWOT-method can provide a relative quick and cheap overview of a country's biotechnological position and possibilities. The working group recognizes, however, that a list of technical requirements is only useful when complemented by an analysis of the national and even international social context. Further details available from IFIAS - Project Development Office, Witmakersstraat 10, 6211 JB Maastricht, the Netherlands. Tel.: (31) 43-250465.

"Inside the Biorevolution": A new IOCU GRAIN publication

GRAIN and IOCU (International Organization of Consumers Unions) have just published Inside the Biorevolution: A Citizens Action Resource Guide on Biotechnology and Third World Agriculture. This guide was prepared by GRAIN staffers Henk Hobbelink and Renee Vellve, in collaboration with Dr. Martin Abraham of IOCU's Regional Office for Asia and the Pacific, with the hope of fostering a better understanding of the biorevolution among interested NGOs and providing them with resources to further their activities. Inside the Biorevolution is divided into three parts. After a thorough introduction, the first part is an annotated bibliography of key documents that report on or analyse different aspects of the biotechnology: the technology, the industry, regulatory issues, patenting life, third world impact and appropriation. Part Two provides a presentation and listing of various networks, organizations and agencies that are involved in some way with biotechnology in the North/South framework, either from the critical side (NGOs) or the technology transfer side (intergovernmental bodies). The third section lists periodicals that provide regular, up-to-date information on the development of biotechnology.

The guide is predominatly intended for third world NGOs and policy-makers who would like to have better access to information on the impact of biotechnology on third world agriculture and get involved with citizens' action groups working to counter the negative implications of the biorevolution. Copies of "Inside the Biorevolution" can be ordered from IOCU, P.O. Box 1045, 10830 Penang, Malaysia. Payment should be made by International money order or banker's draft made out to IOCU for the following amounts: US$ 10 (sea-mail delivery (6-8 weeks) world wide or US$ 15 for Asia Pacific), US$ 17 for Europe and US$ 18 for the Americas, Caribbean and Africa airmail delivery (2 weeks).

Biotechnology's Bitter Harvest: Herbicide-tolerant Crops and the Threat to Sustainable Agriculture

Biotechnology's Bitter Harvest is a new publication put out by the Working Group on Biotechnology (WGB), an American coalition of 12 NGOs. The report was prepared by WGB members Rebecca Goldburg (Environmental Defense Fund), Jane Rissler (National Wildlife Federation), Hope Shand (Rural Advancement Fund International) and Chuck Hassebrook (Center for Rural Affairs). It provides an in-depth survey of current U.S. corporate and public research on herbicide-resistant crops and trees, one of main focuses of agricultural biotechnology today. The authors analyse the dangers of such research - which will increase chemical pesticide use in farming - for the environment, agricultural sustainability and human health. They argue that public funds and research priorities should be devoted instead to sustainable agriculture and call upon citizens' groups to campaign against the pursuit of herbicide tolerance before it is too late. Copies of "Biotechnology's Bitter Harvest" can be requested from: Hope Shand, RAFI, P.O. Box 655, Pittsboro, NC 27312, USA.

US bioremediation set to grow

The US market for bioremediation - the use of microbes to dispose of waste - will increase to some $500 million by the year 2000, according to a recently published study. The study, Bioremdiation of hazardous and industrial wastes, estimates that this market is currently worth $100 million, including assessment services, treatments and inocular/nutrient sales.

Published by the US chemical consulting group, Falmouth Associates, of Portland, Maine, the report states that the costs of treating waste by bioremediation are on average $50-80/ton, compared with $250-650/ton for incineration and $200/ton or more for landfill disposal. This technique is said to be suitable for a wide range of chemical, petroleum and metal wastes.

In the US, some 250 ton/year of hazardous wastes are produced by 14,000 industrial plants. Around 80 per cent of this is disposed of in landfills. These figures do not include an estimated 20,000 sites which have been contaminated over the past 50 years and abandoned, nor groundwater problems, the report notes.

Bioremediation is reported to have been used successfully in clearing up part of the oil slick left by the Norwegian supertanker, Mega Borg, which exploded in the Gulf of Mexico in mid-June. Around 45 kg. of bacteria were spread over a 0.4 ha area of the oil slick.

Report on biotechnology and development and transfer of technology mechanisms

The Brussels-based organization Collectif d'Echanges pour la Technologie Appropriee has just published the report of a workshop organized by COTA in September 1988 on Biotechnologie et Developpement: Quels Tranferts? (in French only). Scientific and industrial experts participated in this workshop to discuss both technical aspects of biotechnology for developing countries and technology transfer mechanisms, with case studies from Latin America and Africa. Ethical matters regarding property rights and applications of biotechnology were also raised and presented in this 130-page report. Available from COTA, 18 rue de la Sablonniere, B-1000 Brussels, Belgium, for 350 BFR (Europe) or 430 BFR (outside Europe). Payment must be made by International money order only.

Seeds and genetic resources in Kenya

KENGO (Kenya Energy and Environment Organisations) has produced a series of documents on indigenous genetic resources in Kenya, stemming from their ongoing monitoring of the international seeds issue and conservation activities with local NGOs in th fields of agroforestry and indigenous trees. Seeds and Genetic Resources in Kenya (1989, 56 p.) gives an overview of the seeds issue and the situation in Kenya, while a collection of easy-to-follow technical support documents provide information on seed collecting, storage and handling

for several local crop types. The 1988 report National Expedition on Genetic Resources and Habitats provides a report on genetic resources conservation and utilisation in Kenya, drawing from a national expedition carried out in the western part of Kenya. KENGO also publishes a quarterly journal, Resources, to promote the sustainable use of natural resources in Kenya. For information and how to order write KENGO, P.O. Box 48197, Nairobi, Kenya.

Inventory of native plant seeds of New Zealand

The New Zealand Coalition for Trade and Development, the Seeds Action Network contact point in New Zealand, has produced a major inventory of the vegetable and native plant seeds of New Zealand. A Growing Matter is prefaced by Erna Bennet and provides an analysis of the "seeds issue" in an international and national perspective before presenting a survey of native New Zealand plants. The report closes with recommendations to national authorities and the NZCTD submission against the 1985 Plant Variety Rights Bill. Available from NZCTD, P.O. 11 345, Wellington, New Zealand.

A Survey of US-Based Efforts to Research and Conserve Biological Diversity in Developing Countries

The World Resources Insitute's Center for International Development and Environment has recently released A Survey of U.S.-Based Efforts to Research and Conserve Biological Diversity in Developing Countries. The survey results, dated October 1989, are drawn from an analysis of 873 projects in 86 developing countries. WRI's conclusion is that, given the magnitude of the problem of the erosion and loss of biodiversity in the South, US conservation funding for the Third World is extremely low: $37.5 million in 1987. Over half of the money went to Latin America and the Caribbean, while 16 per cent went to Asia, 12 per cent to Africa, and 11 per cent to global activities. Projects in Costa Rica, Panama and Mexico alone received 30 per cent of all such funding in 1987. Copies of the report can be requested from WRI, 1709 New York Avenue, N.W., Washington D.C. 20006, U.S.A.

Keeping Options Alive: The Scientific Basis for Conserving Biodiversity

Walter Reid and Kenton Miller of the World Resources Institute (WRI) have recently published a WRI report called Keeping Options Alive: The Scientific Basis for Conserving Biodiversity. The report gives a clear and thorough overview of bio and genetic diversity, what it means, where it is, how it is threatened and why, illustrated by much data. The authors identify research gaps and outline the framework of a biodiversity conservation strategy in anticipation of the impacts of global warming. "Keeping Options Alive: The Scientific Basis for Conserving Biodiversity", Reid and Miller, WRI, October 1989, 128 p. Available for US$ 10 (air post) from: World Resources Institute, 1709 New York Avenue N.W., Washington, DC 20006, USA.

Agricultural biotechnology: Introduction to field testing

Field testing manual - Agricultural biotechnology: Introduction to Field Testing is a manual for use by principal investigators, institutional officials, and insitutional biosafety committee members. It describes the principles and procedures for conducting safe experiments outside the laboratory using genetically modified organisms. Further information can be obtained from the Mississippi Agricultural and Forestry Experiment Station (MAFES). The price is $10.00 plus $2.50 shipping and handling ($6.00 for overseas shipment by airmail). Make remittances payable to "MAFES" and send order to: Agricultural Biotechnology, Attn: Dr. H.G. Purchase, PO Drawer V, Mississippi State, Mississippi, 39762. Foreign purchasers should pay by international money order in US funds or by cheque drawn on a US bank.

Public perceptions of biotechnology

1990 is likely to be the year when the public starts to ask itself questions about the value of high technology, about the risks and the impacts on the environment of new technologies. The issue of the release of genetically engineered organisms into the environment will no doubt be undergoing public scrutiny during the next twelve months and it is important for all biotechnologists, as well as the public, to be fully informed.

One aid in this process is a new book recently released by the Office of Technology Assessment in the USA. The office is the analytical arm of the US Congress and helps legislators to anticipate and plan for the positive and negative impacts of technological changes. The book is entitled New Developments in Biotechnology: Public Perceptions of Biotechnology. It is available from NTIS, 5285 Port Royal Road, Springfield, VA 22162 USA.

It behoves us all to develop soundly based views on the impact of the technologies we develop.

ABA pamphlets

The ABA has launched the first in its Biotechnology Education Pamphlet series. The ABA Council recognizes, as have many overseas organizations, the general trend away from science and engineering based education.

To help reverse this trend and to assist in the education of both the general public and schoolchildren, the ABA Council decided to produce a series of informative pamphlets on various aspects of Biotechnology. To date, six have been released:

1. What is Biotechnology?
2. What is Genetic Engineering?
3. Biotechnology in Plant Agriculture: More for Less.
4. Biotechnology in Animal Agriculture.
5. Biotechnology and Diagnosis.
6. Glossary of Terms in Biotechnology.

The standard of these pamphlets is excellent and is a credit to all those involved in their production. The Journal commends them to those working in biotechnology and recommends that they be used to foster a better understanding of biotechnology in the community at large. (Source: Australian Journal of Biotechnology, Vol. 3, No. 1, January, 1990)

NETT

The New European Information Network for Environmental Technology Transfer (NETT) has been formally established to help the exchange of know-how between companies and organizations in the rapidly developing field of clean and low waste technologies. The Association will provide a

framework for the provision of better information, advice and the exchange of knowledge. For more information contact: NETT Secretariat, Square de Meeus 25, B-1040 Brussels. Fax: 511 2522.

Malaria sequence data base

This data base is funded by a grant from WHO and is maintained at the Walter and Eliza Hall Institute of Medical Research.

It is intended as a comprehensive listing of all known malaria nucleotide and protein sequences and in its final form it will feature complete annotation of entries and listings of availability of nucleotide probes. It is part of an ongoing project to disseminate information on availability of reagents of use in malaria research.

The data base is distributed on computer discs and is updated two to three times per year. It is currently available free of charge.

The discs contain listings of malaria sequence in EMBL format, suitable for searching by programs that can access the EMBL data base, or by word processors.

Additionally, the sequences are listed in a text file suitable for importation into PC sequence analysis programes. Versions are available for IBM-PC computers and compatibles (all MS-DOS machines) in 3-1/2 inch or 5-1/4 inch formats, or for Apple Macintosh computers.

The data base can be installed on a minicomputer such as the DEC-VAX by transferrring the files from a PC using an appropriate terminal emulation program. To obtain the data base, Fax or write to: Dr. Ross Coppel, The Walter and Eliza Hall Institute of Medical Research, P.O. Royal Melbourne Hospital Victoria 3050, Australia. Tele: 61-3-345-2555 Fax: 61-3-347-0852. Please indicate which data base version you require. (Source: TDR News, No. 31, March 1990)

EuroBioMed

BioResearch Ireland, with associates in Denmark, the Netherlands and the Federal Republic of Germany have established a new biotechnology and medical technology information network, to be called EuroBioMed. The network will provide a means by which researchers, manufacturers, distributers and others involved in biotechnology and medical technology can develop contacts in other countries for co-operation. For further information write to: BioResearch Ireland, FOLAS, Glasnevin, Dublin 9. Fax: 370176.

G. MEETINGS

1990

November 1990

1-7 November Martuljek, (Ljubljana) Yugoslavia	European Federation of Biotechnology, Working Party - Symposium on Physiological Aspects of Product Formation by Filamentous Fungi. Further details from Dr. M. Legisa, "Boris Kidric" Institute of Chemistry, Hajdrihova 19, 61115 Ljubljana, Yugoslavia
15-16 November Boston, USA	New Horizons in Immunology. Further details from Ms. Diana Berger, Nature Publishing Company, 65 Bleecker Street, New York, NY 10012-2467, USA
15-16 November Montreal, Quebec, Canada	Biotechnology and the Environment: Managing the Risks. Further details from Ms. Denyse Pronovost, CREST, Universite du Quebec a Montreal, P.O. Box 888, Station "A", Montreal, Quebec, Canada H3C 3P8

December 1990

3-5 December Baltimore, USA	Analytical Molecular Seminar. Further details from Mrs. Janet Cunningham, Barr Enterprises, P.O. Box 279, Walkersville, Maryland 21793, USA
5-6 December London, UK	Enzymatic Catalysis: Structure, Molecular Interactions and Mechanism. Further details from The Scientific Meetings Secretary, The Royal Society, 6 Carlton House Terrace, London SW1Y 5AG, UK
10-13 December New Delhi, India	Biotek India '90. Further details from CONVEX - A Division of Applied Technology Services PVT Ltd., 14F Basant Lok, Vasant Vihar, New Delhi 110057 India
12-14 December Melbourne, Australia	Australian Society for Immunology Annual Meeting to be held in conjunction with meeting of Australian Societies for Experimental Biology. Further details from Dr. Jennifer Rolland, Clinical Immunology Laboratory, Department of Pathology and Immunology, Monash Medical School, Commercial Road, Prahran, Victoria 3181, Australia
12-15 December London, UK	Liposomes in Drug Delivery: 21 Years On. Further details from Conference Secretariat, Centre for Drug Delivery Research, School of Pharmacy, London University, 29-39 Brunswick Square, London WC1N 1AX, UK

1991

8-9 January La Jolla, California, USA	Amylin Symposium. Further details from Ms. Lisa Dimler, Amylin Corporation, 9373 Towne Centre Drive, Suite 250, San Diego, California 92121, USA
13-17 January Clearwater Beach, Florida USA	IUB Conference on Nucleic Acid Therapeutics. Further details from Dr. Eric Wickstrom, Department of Chemistry, University of South Florida, Tampa, Florida 33620 USA
27 January - 1 February Miami Beach, Florida, USA	Advances in Gene Technology: The Molecular Biology of Human Genetic Disease. Further details from the Miami Bio/Technology Winter Symposia, P.O. Box 016129, Miami, Florida 33101-6129, USA
9-12 April Paris, France	Bio-Expo 91. Further details from Bioexpo/SEPEI, 8, rue de la Michodiere, 7500, Paris, France
10-13 April Boston, USA	International Symposium on Pharmaceutical and Biomedical Analysis. Further details from Ms. Shirley Schlessinger, 400 E. Randolph Street, Suite 1015, Chicago IL 60601, USA

7-12 June Montgomery, Alabama, USA	International Conference on Sweet Potato Technology for the 21st Century. Further details from Dr. Conrad K. Bonsi, Programme Chairman, George Washington Carver Agricultural Experiment Station, Tuskegee University, Tuskegee, Alabama 36088, USA
9-15 June Frankfurt-am-Main, FRG	ACHEMA 91. Further details from The Secretariat, DECHEMA, P.O. Box 970146, D-6000 Frankfurt-am-Main, 97, FRG
August Jerusalem, Israel	Fifteenth International Congress of Biochemistry. Further details from Dr. N. de Groot, Department of Biological Chemistry, Hebrew University, Jerusalem 91904, Israel
24-27 September Leeds, UK	Biotech UK - First Conference on UK Biotechnology. Further details from Biotech UK, c/o Society for Chemical Industries, 14 Belgrave Square, London WC1X 8PS, UK
1992	
30 March - 2 April Cambridge, UK	Food Engineering in a Computer Climate. Further details from the Conference Department, Institute of Chemical Engineers, 165-171 Railway Terrace, Rugby CV21 3HQ, UK

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