OCCASION

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

DISCLAIMER

FAIR USE POLICY

CONTACT

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

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

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

Genetic Engineering and Biotechnology Monitor

Issue No. [illegible] [illegible] 1990

Special in this issue: An article on safety, biotechnology and the problem of international trade-offs, prepared for the Monitor Dr. Morris Levin and Dr. R. Wachbroit of the Centre for Public Issues in Biotechnology, Maryland Biotechnology Institute, USA.

CONTENTS

CONTENTS (continued)

CONTENTS (continued)

A. POLICY, NEWS AND OTHER EVENTS

UNIDO news

New head for ICGEB's Trieste laboratory

Francisco Baralle has been named as the new Head of the Trieste component of the International Centre for Genetic Engineering and Biotechnology (ICGEB) by its 41-nation Preparatory Committee. His selection came during the Committee's fourteenth session, 31 January - 2 February 1990.

An Argentinian biochemist, Mr. Baralle is currently Scientific Director of the Istituto Sieroterapico Milanese S. Belfanti in Milan as well as Visiting Professor at the University of Brescia. Succeeding Arturo Falaschi, who was appointed ICGEB Director last year, he is expected to take up his duties this June.

The Committee approved a reorientation of the rolling five-year programme for July 1990 to June 1995. During 1994-1995 long-term post-doctoral training will be increased by 20 additional years for both the New Delhi and Trieste laboratories, making a total of 48 years each. Because of the scarcity of post-doctoral fellows in many ICGEB member countries, long-term pre-doctoral training will be introduced in 1991-1992, when permanent facilities are ready at both sites.

In 1990, 50 per cent more training courses will be offered at the Centre than last year. Likewise, long-term fellowships are expected to increase to 30 compared with the current 16 that have been awarded so far.

With the need to mobilize more funds to expand the current five-year programme as well as carry out the rolling plan, the Committee agreed that funding could be accepted from companies in the Centre's member States according to an adopted set of guidelines and in keeping with ICGEB statutes. It also welcomed UNIDO's proposal to create a multi-donor trust fund, which would pool voluntary contributions to help pay for the establishment and functioning of ICGEB.

The Centre should follow an active policy, the Committee recommended, of patenting its research results. Work should also be continued towards developing guidelines on ICGEB's patent policy.

As several member countries have yet to adopt formal safety guidelines for biotechnological research, manufacture and release of products into the environment, the Committee felt that the Centre should play an important role in creating awareness as well as in adoption of common guidelines among its member States.

Current members of ICGEB are Afghanistan, Algeria, Argentina, Bhutan, Bolivia, Brazil, Bulgaria, Chile, China, Colombia, Congo, Cuba, Ecuador, Egypt, Greece, Hungary, India, Indonesia, Iran, Iraq, Italy, Kuwait, Mauritania, Mauritius, Mexico, Morocco, Nigeria, Pakistan, Panama, Peru, Senegal, Spain, Sudan, Thailand, Trinidad and Tobago, Tunisia, Turkey, Venezuela, Viet Nam, Yugoslavia and Zaire.

The Committee's next session is scheduled for June 1990 in Vienna.

Meanwhile India has reaffirmed its support of ICGEB in an exchange of letters between Indian Permanent Representative Peter Sinai and UNIDO's Director General Domingo L. Siazon, Jr.

This extends the former agreement on basic terms and conditions governing the UNIDO ICGEB project from January 1990 to March 1991. During this period, the Five-Year Programme (1989-94) will be underway, with the New Delhi laboratory focusing on plant biology, immunology, molecular biology of hepatitis and malaria, design and synthesis of peptide antigens for disease resistance and synthesis of oligonucleotide probes used in DNA research.

The other laboratory, at Trieste, will carry out research on regulation of DNA replication in human cells, molecular biology of the cancer-causing Papilloma virus, protein structure and lignin biodegradation.

The programme's long-term training will familiarize developing-country scientists with genetic engineering and biotechnological techniques as well as allow them to undertake specialized research, integrating their training into on-going projects. Short-term training will consist of practical courses centred around specialized techniques or subject matter.

United Nations and other organizations' news

WHO predicts more AIDS in women

AIDS in the 1990s is increasingly likely to afflict women, with disastrous consequences for society as the disease is transmitted to a generation of babies, according to Jonathan Mann, director of the World Health Organization's global programme on AIDS.

On the eve of a major conference in Paris on the implications of AIDS for mothers and children, Dr. Mann said that in some regions the proportion of women with AIDS was likely to equal or be even greater than that of men.

Of the 600,000 victims of acquired immune deficiency syndrome reported to date, 150,000 have been women. Dr. Mann said that of the 500,000 additional cases expected to develop in 1990 and 1991, about 200,000 will be women, most of them of child-bearing age.

The ratio of male to female AIDS victims is not evenly distributed. In sub-Saharan Africa, where it is heterosexually transmitted, about half the victims are women.

In the United States, the ratio has been about five men to one woman, but newly reported cases include a higher proportion of women who have become infected through their own drug use or through sexual contact with male drug users.

In the English-speaking Caribbean, AIDS was mostly confined to homosexuals in the early 1980s but now affects about as many women as men - a trend that Dr. Mann said was increasingly likely to become apparent in the developed world.

The conference, organized by the World Health Organization and the French Government, brought together 40 health ministers and 600 specialists for four days of discussions about the problem. The

issue is still relatively unexplored compared, for example, with the study of AIDS and homosexuality in Western societies.

Dr. Mann said it was appropriate that the last major conference in the decade of AIDS should be dedicated to the situation of women and children.

The World Health Organization estimates that of the six million people reported to be infected with human immunodeficiency virus, or HIV, and who eventually are likely to contract AIDS, about one-third are women. From 20 to 40 per cent of their children will be born with HIV infection.

Not only will these children quickly develop the disease, Dr. Mann said, but the loss of their parents to the disease may mean there is no one left to care for them.

Already, about 1 per cent of the mothers giving birth in Paris hospitals have the HIV infection, Dr. Mann said. In New York City, about 3 per cent of mothers have the infection and this means that there will be 50,000 to 100,000 AIDS orphans in the city in a single generation, he said. In Kampala, Uganda, nearly a quarter of all mothers are infected and infant mortality rates have nearly doubled as a result of the disease.

Dr. Mann said AIDS was gaining momentum in areas that already were seriously affected and spreading to such new areas as Eastern Europe, West Africa and parts of Latin America and Asia. (Source: International Herald Tribune, 27 November, 1989)

Regulatory issues

UK genetic engineering rules in force from 1 November

New regulations which replace the UK's Health and Safety (Genetic Manipulation) Regulations 1978 came into force from 1 November 1989.

Researchers planning to release genetically engineered organisms into the environment will have to give the Health and Safety Executive (HSE) 30 days notice for genetic experiments - and 90 days notice of plans to make any environmental releases. The plans will need to be accompanied by a risk assessement, to be prepared according to a standardized format. Research projects will also have to be supervised by a genetic manipulation safety committee. (Source: Biotechnology Bulletin, Vol. 8, No. 9, October 1989)

COSHH regulations 1988

A new UK Code of Practice for the Control of Substances Hazardous to Health (COSHH) Regulations 1988 was introduced on 1 October, providing new legislation for employers under section 16 of the UK Health and Safety at Work Act 1974. This code of practice has particular relevance for employers - including biotechnology companies and large R & D facilities - whose workers are at potential risk of contracting hepatitis B and HIV through contact with blood and body fluids.

The COSHH Regulations provide practical guidance to employers regarding compliance with their duty to protect their employees who may be exposed to substances hazardous to health. Failure to comply with the code may be taken by a Court in criminal proceedings as proof that an employer has contravened the regulations.

According to the code, "A substance should be regarded as hazardous to health if it is hazardous in the form in which it occurs in the work activity, whether or not its mode of causing injury to health is known, and whether or not the active constituent has been identified".

Under the COSHH Regulations, blood and body fluids (e.g. saliva, urine or semen) could be substances hazardous to health if they contain transmissible viruses known to be injurious to health such as hepatitis B and HIV. SmithKline & French Laboratories sees the new regulations as something of a commercial opportunity. While it is not yet possible to vaccinate employees against HIV, the company feels that employers may now be more inclined to initiate hepatitis B vaccination programmes. Vaccination against hepatitis B has been available since the early 1980s, with genetically engineered vaccines introduced in the UK in 1987. (Source: Biotechnology Bulletin, Vol. 8, No. 9, October 1989)

Explicit environmental risk analysis procedure

An explicit, step-by-step environmental risk analysis procedure is needed for field tests of genetically modified organisms, according to the USA's National Research Council. Decisions by regulators should take account of the familiarity of the modified organism, the ability to control the organism and the potential environmental effects. US Drug Agency and the Environmental Protection Agency have so far approved field testing of about 80 modified organisms. They are considering changes in their regulatory approach. The new report, requested by the Biotechnology Science Co-ordinating Committee, points out that although much less is known about microbial ecology than about crop plants for instance, there is still enough knowledge on which to base a rational scientific assessment of the risks involved. Micro-organisms present an increased risk of further mutations or passing of altered genes to wild populations, but these risks can be evaluated. (Extracted from Chemical Marketing Reporter, 16 October 1989)

Field tests: A weightier message

Field tests of genetically modified organisms continue to stir up public apprehension and have prompted proposals for strict regulations. A new report by the US National Research Council suggests that these fears are largely unjustified.

On 20 September, the council released a report, "Field Testing Genetically Modified Organisms", 1/ that US officials hope will provide a basis for uniform regulations. It has two basic themes: (i) there is no conceptual difference between altering a plant or microbe by classical breeding techniques or by gene splicing; and (ii) regulators should evaluate field tests of genetically engineered organisms on the basis of the potential hazard of the product itself rather than the molecular techniques by which it was made.

The importance of the report is that it says field tests of genetically modified organisms can be evaluated for their risk on a scientific basis, a major point, at a time when groups in Europe are calling for a moratorium on field testing novel

1/ "Field Testing Genetically Modified Organisms: Framework for Decisions" (National Academy Press, Washington, D.C., 1989.)

organisms and US states are debating whether to pass their own regulations on field testing. The report provides a framework of scientific questions, in order of importance, that should help regulators assess the risk of proposed experiments. The report may also help federal agencies to establish categories of field tests that pose little risk, which would speed up the regulatory process. (Extracted from Science, Vol. 245, 22 September 1989, p. 1329, Marjorie Sun. Copyright AAAS 1989)

General

Human genome project: Five-year plan taking shape

A meeting of the National Institutes of Health's human genome committee in Bethesda, Md., marked the first public release of a draft document that will provide the blueprint for the first phase of the US effort to map and sequence human DNA.

The meeting, held in early December, also presented an opportunity for project organizers to respond to persistent complaints that the genome project and other directed initiatives, are to blame for the current funding squeeze at NIH.

The draft five-year plan provides a comprehensive overview of the project's goals and how it intends to achieve them. The plan is being prepared at Congressional request by NIH and the Department of Energy, the two agencies that have received earmarked funding for the initiative. After further revision and final approvals, the plan is to be submitted to Congress in early 1990.

According to the plan, the project - expected to take about 15 years and $3 billion to complete - will analyse the structure of human DNA and determine the location of an estimated 50,000 to 100,000 human genes on 23 pairs of chromosomes. In addition, the genomes of a series of model organisms, such as Escherichia coli, will be studied to provide comparative information and to serve as test platforms for new technology being developed to facilitate the project.

The plan requests essentially the same funding recommended in previous genome meetings and reports. This is about $200 million a year, adjusted for inflation, for the 15-year term of the project, which is scheduled to begin 1 October 1990, the start of the federal fiscal year 1991. The plan also recommends that $121 million of these funds be made available for construction of new laboratory space over the next five years.

Both academic and industrial institutions are eligible for centre grants, for which applications are already being submitted. NIH plans to fund three centres in 1990 and a total of 10 to 20 over the next five years. DOE already has three centres in its national laboratories that focus on mapping of specific human chromosomes and is considering whether to open more.

The overall strategy for the project's first phase is to concentrate on genomic mapping and technology development and to leave most of the detailed sequencing for later, when automation will have improved and the costs of sequencing will be lower. Scientific goals for the first five years of the project are to assemble maps for all human chromosomes based on the concept of sequence-tagged sites developed recently by Maynard V. Olson of Washington University School of Medicine and others; to improve current sequencing methods and to develop new ones in order to lower sequencing costs to less than $1.00 a base pair, from about $5.00 now; and to develop software and data bases to support large-scale mapping and sequencing efforts. (Abstracted with permission from Chemical Engineering News, 11 December 1989, p. 4. S. Borman, Copyright (1989) American Chemical Society)

San Diego meeting gives lift to genome research

A number of potentially profound new findings in molecular genetics research were reported at a human genome conference in San Diego last October. The findings appear to vindicate the belief of most researchers involved in this field of "big science" that the genome should be studied in its entirety rather than piecemeal.

What was shown, too, is that development of methods for mapping and sequencing the genome faster and cheaper can at the same time yield important research results.

For example, in one of the more startling reports at the meeting, Michio Oishi, of the University of Tokyo, described a technique developed in his laboratory called differential genomic DNA cloning. The technique allows rough comparisons of uncharacterized DNA from two sources to detect differences.

Oishi compared DNA obtained from different organs of single rats. In such a study, geneticists would routinely predict that DNA from all organs except the immune system should be identical. Oishi's data suggest, however, that DNA from brain tissue might be organized somewhat differently than DNA obtained from the liver, heart, or kidney of a rat. If the alternative explanations are eventually ruled out, Oishi's discovery that neural DNA is somehow rearranged or amplified during development would change a fundamental concept in biology.

Two other papers gave evidence that immune system genetics, already brutally complex, may turn out to be even more complicated than had been thought. It has been known for some time that immunoglobulin and T-cell receptor diversity are generated by recombination of the genetic elements that encode these proteins.

Such recombination occurs among loci lying relatively close together on a chromosome. Tasuku Honjo, of Kyoto University, and Hans Zachau, of the Technical University of Munich, presented independent research that suggests that the genetic recombination that generates immunoglobulin diversity may also occur between different chromosomes. Until now, exchange of material between different chromosomes was thought to be universally deleterious to the organism. (Abstracted with permission from Chemical Engineering News, 9 October 1989, p. 5-6. R. Baum, Copyright (1989) American Chemical Society)

US Industrial Biotechnology Association

The US Industrial Biotechnology Association has publically supported the National Institute of Health initiative to completely map the human genome, providing funding is not withdrawn from other areas of biomedical research. It is expected to cost $3 billion to achieve the NIH objective and it is likely to take 15 years. However, the Vice President of Hoffmann La Roche expects that new therapeutic approaches to the treatment of genetically based components of disease could save $50 billion a year in the US alone. International

competition and possible collaboration are matters yet to be agreed.

The President of the IBA was also critical of the lack of a fully integrated and supported biotechnology policy in the USA. He has outlined the IBA policy in seven areas:

- The Capital Gains Tax rate needs to be lowered from the current 28 per cent to encourage investment in new stand-up companies;
- The R & D tax credit is too restrictive for fast-growing biotechnology companies as it limits the credits to an increase in R & D expenditure of 100 per cent over a base period;
- Intellectual property rights are being disregarded in other countries and GATT should tie this to trade so as to ensure universal protection for intellectual property;
- The Patent and Trademark office must take action to reduce the backlog of biotechnology patent applications being held up, currently about 15,000 and a delay of 26 months.
- There should not be a farmer's exemption to animal patents as this would discourage investments in an area that promises to significantly benefit US agriculture;
- Science education needs revitalising in schools, colleges and universities to stop the trend away from science and engineering careers;
- More Federal support is needed for basic research in universities and colleges to counter the decline over the last four years.

(Source: ABA Bulletin, Vol. 4, No. 6, December 1989)

Participants needed for ASTM Task Group on Quality Control of Culture Media

Participants are needed for a task group on quality control of culture media, sponsored by E48.01 on Materials for Biotechnology, a subcommittee of ASTM standards-writing Committee E-48 on Biotechnology.

Due to the need for standards development in the area of mycoplasma testing, this task group will standardize the methods of mycoplasma detection in cell cultures and serum. This activity will be of special interest to all laboratories and commercial firms using cell cultures as substrates in research and for production. Three standard practices have been drafted and are undergoing review:

1. Standard Practice for Direct Detection of Mycoplasma in Cell Culture by Agar Growth.
2. Standard Practice for Indirect Detection of Mycoplasma in Cell Culture by Bisbenzamide DNA Flurochrome Staining.
3. Standard Practice for Large Volume Testing of Serum for Mycoplasma Contamination.

All interested parties are welcome to participate. For more information contact the task group chairman, Dr. Antonio R. Moreira, Schering Corporation, 1011 Morris Avenue, Union, NJ 07083, 201/820-6470 or John Vowell, ASTM, 1916 Race Street, Philadelphia, PA 19103-1187, 215/299-5496.

Committee E 48 is one of 135 ASTM technical standards-writing committees. ASTM (American Society for Testing and Materials) is one of the largest voluntary standards development systems in the world. (Source: ASTM News Release, 1 December 1989)

"Alternative Nobel" rewards researchers

Twenty years of perseverance in the face of prejudice and indifference from the Western scientific establishment underpins the award to two Ethiopian scientists of this year's Right Livelihood Award.

Aklilu Lemma and Legesse Wolde-Yohannes won the "alternative Nobel prize" for discovering a natural molluscicide, and devising a community-based method of employing it against the snails that carry the schistosomiasis (bilharzia) parasite.

Schistosomiasis, a debilitating and eventually fatal disease, afflicts more than 200 million people in Africa, Asia and Latin America. It is carried by flat-worms into the liver and other organs.

In 1964, Lemma discovered that the berries of a native Ethiopian plant, the endod or soapberry plant (phytolacca dodecandra), contain a potent toxin that can, in minute quantities, kill the snails carrying the schistosomes. Two years later Lemma established the Institute of Pathobiology in Addis Ababa University to continue his work.

By 1968, the World Health Organization published the results of their first study on endod by Lemma and his colleagues. It showed that the molluscicide is present only in the fruit and not in other parts of the endod plant. There followed a small five-year trial of the toxin.

Then came the first stumbling block. The Ethiopian Government needed help from the WHO to begin larger trials. For that, the WHO needed further studies to confirm the safety of the molluscicide on human and animal life. Those additional studies needed money that the Ethiopians did not have. Although the WHO did have funds for such studies, it failed to support the research.

Worse still, says Lemma, the WHO discouraged alternative donors from becoming involved with endod research in Ethiopia. Commercial companies were not interested in underwriting further research.

Support from "friends" over the past five years has led to further work on toxicology of the molluscicide as well as on the breeding and production of improved endod varieties. (Source: New Scientist, 11 November 1989)

Biotechnology firms close to meeting expectations

Biotechnology firms are said to be close to meeting expectations for revolutionary products and profits. A list of new drugs is close to completing clinical study and is expected to be marketed soon. Most of the preparations are designed for somewhat specialized use. However, these new classes of drugs that are genetically engineered operate at a fundamental biological level. Therefore, several of

their possible applications may yet be discovered. Also, firms such as Amgen, Biogen, Centocor, Chiron, Cetus, Genentech, Immunex, Genetics Institute and Xoma, are in a healthy financial position to fortify and capitalize on their R & D. (Extracted from Barrons, 25 September 1989)

ATCC News

New freeze-dried medium for the axenic cultivation of giardia species

The ATCC has announced the availability of a new medium, Keister's Modified TYI-S-33 Medium, for the axenic cultivation of a group of Giardia protists. The medium comes packaged as a freeze-dried preparation, complete with serum, and ready for immediate use upon rehydration with water. Each lot of medium has been tested for sterility and its ability to promote growth equivalent to cultures grown in freshly prepared medium. A single package provides ingredients sufficient to prepare 4 tubes of medium containing 13 ml each. The main advantages of this medium over medium that is mixed in the lab include a longer shelf-life and more convenient preparation. Enquiries: ATCC/Marketing NR 45, 12301 Parklawn Drive, Rockville, MD, 20852, USA. (Source: ABA Bulletin, Vol. 4, No. 6, December 1989)

New bacterial strains available from the ATCC

ATCC has the following bacterial strains available for research and industry applications:

Legionella gormanii ATCC No. 43769 from pneumonia patient; Legionella quinlivanii ATCC No. 43830 from water; Neisseria gonorrhoeae ATCC No. 43785 - CDC QC organism from male urethra, susceptibility testing of enoxacin; Eubacterium timidum ATCC No. 33093 - type strain from subgingiva in periodontitis: Spiroplasma sp ATCC Nos. 43207 thru 43211 - possible biological control for insects; Corynebacterium sp ATCC No. 43752 - possible pollution control organism, dehalogenates haloalkanes; Rhizobium galegae ATCC No. 43677 - nitrogen fixer on Galega orientalis. (Source: ABA Bulletin, Vol. 4, No. 6, December 1989)

New feeder cells for promoting the growth of fastidious cell lines

ATCC has added the Swiss albino 3T3 mouse embryo cell line, ATCC No. CCL 92, to their feeder cell product line. The irradiated feeder cells, catalogue No. X-48, are used to support the growth of fastidious cell culture systems. The cells have been irradiated so that division has been halted but metabolism retained. The Swiss 3T3 feeder cells are supplied as frozen 1ml. aliquots in quantity sufficient to seed up to 150 cm2 of surface area. The ATCC also offers irradiated MRC-5, a human diploid lung fibroblast cell line (catalogue No. X-55) and STO, a mouse embryonic fibroblast cell line (catalogue No. X-56) for use as feeder cells. (Source: ABA Bulletin, Vol. 4, No. 6, December 1989)

First International Marine Biotechnology Conference, Tokyo, Japan, September 1989

The First International Marine Biotechnology Conference was hosted by the Japanese Society for Marine Biotechnology jointly with the Foundation for Advancement of International Science (FAIS), the International Scientific Committee for Biotechnology (COBIOTECH) and the International Council of Scientific Unions (ICSU) in Tokyo on 4-6 September 1989.

The meeting was attended by about 400 scientists and industrialists - th more than half the participants from outside of Japan. The intensive scientific programme was divided into six major topic areas: micro-organisms, microalgae, macroalgae, fish, shellfish and other animals, supporting technology and interfacial subjects.

The sessions on micro-organisms contained papers on the biotechnological potential of marine bacteria, especially those from hydrothermal vents and psychrophilic bacteria. A common theme in these sessions, as well as those on algae and other marine organisms, was the production of a very wide range of novel bioactive compounds in the marine environment and the existing and potential applications of these novel molecules in medicine and industry. In many ways it was gratifying (and a little sad) to see this intense activity in the area of marine pharmacology which really began on an industrial scale at the Roche Research Institute of Marine Pharmacology in Sydney in the 1970s. Areas of special interest were antineoplastic compounds, antibiotics and marine toxins.

The extensive microalgae sessions described various algae and algal mass culture systems which are being used, or are proposed to be used, for the production of fine chemicals such as carotenoids, fatty acids and hydrocarbons. The continued work on hydrogen production by algae was also well covered. Some interesting new areas presented included work on the genetic transformation of cyanobacteria and other algae, and the use of monoclonal antibodies to identify red tide organisms. There appears to be a bright future for monoclonals in environmental monitoring for toxic algae.

The macroalgae sessions were almost equally split between papers on tissue culture and protoplast culture of macroalgae, and studies on commercially useful compounds such as polysaccharides and flavourings from these algae.

The sessions on fish and other marine animals showed the rapid advances which are being made in the areas of gene transfer and the production of transgenic fish of a wide range of a wide range of species.

The potential of these techniques for aquaculture and for the production of specific molecules such as growth hormones should be very great. Other papers covered areas such as the use of monoclonal antibodies and DNA probes for the diagnosis of pathogens of molluscs, the use of by-products from the fishing industry to produce biochemicals such as cold-adapted enzymes and components for media for the culture of micro-organisms etc.

The more than 160 papers and posters presented at this meeting show that marine biotechnology is definitely here to stay and has extremely wide application to all areas of industry, including production of new antifouling methods, aquaculture, human and animal health, food processing and environmental management.

There was also a special evening session on the global effects of atmospheric CO_2 accumulation (the "greenhouse effect") and the role marine biotechnology can play in its management and amelioration.

The conference also illustrated that marine biotechnology is definitely a growth area (at least outside of Australia). In Japan the Marine

Biotechnology Institute Co. Ltd. has been established with a joint investment of 800 million Yen by 24 companies. Two new research facilities at Kamiashi and at Shimizu are being constructed and should be open in 1990 and the company has purchased an 87 m research vessel. The Institute presently has 29 researchers in a wide range of fields. Similarly, the University of California at Santa Barbara has constructed a new $US 8.5 million marine biotechnology laboratory. Other similar projects are underway elsewhere in the world. (Source: Australian Journal of Biotechnology, Vol. 3, No. 4, October 1989)

The traditional food grain of South America

A single, recurring image dominates the landscape of the high Andes of South America: thousands of small agricultural plots, bordered by stones, on steep hills.

Hillside farming is one way to protect crops, even if only for a few days, from the killer frosts that arrive first on the exposed plains. A consistent feature in this patchwork of plots is the traditional food grain, quinoa (Chenopodium quinoa).

Annual rainfall in this long strip of South America is low - 300 to 600 millimetres. By using time-proven crop combinations, usually including quinoa, farmers minimize losses caused not only by frost but also by lack of moisture.

The peasant farmers of the high Andes - an area stretching from Colombia and Ecuador, through Peru and Bolivia, to Chile and Argentina - have grown quinoa for centuries. In fact, it was a staple in the diet of the people of the Inca Empire. Today, quinoa is cultivated and harvested much like other cereal crops, but its very special properties are not forgotten by the descendants of the Incas.

Victor Mamani lives in the village of Jiscuani, near Lake Titicaca, some 3,800 metres above sea level. Like most farmers in the area, he grows enough quinoa to feed his family.

Recipe for longevity

"My children need quinoa because it contains calcium and will prevent cavities", he says. He knows it is also good for adults and points to the previous owner of his farm, who is 96 years old, as living proof. According to Mr. Mamani, a diet of quinoa, barley, and cheese should be given credit for the man's longevity.

Quinoa is rich in protein - 16 per cent compared with 10 to 12 per cent for other cereals. What is noteworthy about this protein, however, is not the quantity but the quality. It contains a balance of amino acids unmatched by wheat, maize, barley or potatoes. In fact, 37 per cent of quinoa's total protein is composed of essential amino acids in proportions similar to those found in milk. The grain contains more of the amino acids methionine, cystine, and lysine than most vegetable plant sources. These essential acids enable it to act as an effective food substitute for meat and oilseeds.

For this reason, quinoa is a major ingredient in the diets of some 10 million inhabitants of the high Andes. It can be boiled and eaten like rice, added to soups, popped like popcorn and brewed into a beer known as chicha blanca. Its green leaves can be used in salads or for animal feed, and the stalks are burned in cooking stoves, composted, or consumed by grazing animals.

Despite its nutritional value and versatility as a food, quinoa was for a long time considered a plant of limited agronomic and commercial potential, even within its own natural growing region. Although it has the biological potential to yield up to 4,000 kilogrammes per hectare, in practice cold weather and low rainfall combine to severely limit yields. Among the 120,000 farm families who grow the crop in Bolivia, for example, yields have sometimes been 400 kilogrammes or less per hectare.

Furthermore, research methods were not geared to a crop grown in association with maize, barley and faba beans, on tiny isolated farms of only one or two hectares. Only at high elevations is quinoa grown as a single crop, usually after potatoes.

Another drawback is the presence of a bitter compound called saponin in the hard seed coat of quinoa. To remove the compound, quinoa is washed in running water and then dried for a few hours or cooked immediately. Alternatively, the grain can be dehulled mechanically or by hand, but this does not remove all the saponin.

Finally, because quinoa has a low gluten content, a crucial substance in the production of wheat products, it cannot be used to manufacture bread, pasta and biscuits. Yet in Bolivia, in the early 1980s, the Government, faced with rising prices for imported wheat, rice and maize, attempted to introduce quinoa flour. It introduced a law requiring 5 per cent substitution of quinoa flour in the processing of foods. But insufficient production and inadequate processing facilities have made the law impractical.

Production on the rise

Over the past decade, though, quinoa production has experienced a resurgence, thanks in large measure to the Instituto Boliviano de Technologia Agropecuaria (IBTA). With the support of funding by the International Development Research Centre (IDRC) of Canada, IBTA has created, since 1979, a regional research base for genetic selection and refinement of cropping practices.

Together with quinoa researchers in Peru, Ecuador and Colombia, IBTA has established the Andean Crops Network, whose members meet yearly to exchange scientific information and the latest research results.

The key quinoa researcher in Bolivia is Humberto Gandarillas. Coaxed out of retirement to head IDRC's quinoa project, he was a logical choice because of his quinoa seed research in the 1960s which helped to broaden the genetic pool and spawn an ambitious breeding programme.

Under the first phase of the IDRC-supported work, Mr. Gandarillas and his fellow researchers succeeded in breeding improved varieties of quinoa. Under controlled conditions, some new strains are yielding as much as 5,000 kilogrammes per hectare.

In Bolivia, the area planted to quinoa has increased at an average annual rate of 34 per cent since 1979. IBTA estimates that 40 per cent of the total area is now sown with improved quinoa varieties, primarily Sajama, developed by

Mr. Gandarillas in the 1950s. Facilities such as the Patacamaya research station are distributing enough of the modern varieties, especially the called Chukapaka, throughout Bolivia to seed 3,000 hectares per year.

There have been some disappointments though. On-farm trials revealed that some new varieties, including Chukapaka, were not well adapted to certain regions. Although Chukapaka promised high yields and good tolerance to frost, it turned out to be a "late" type - that is, subject to early frosts and therefore not suited to some areas.

Some new varieties also proved to be susceptible to mildew and poor response to fertilizers was also observed because of poor environmental conditions. Nitrogen boosted yields only in those regions with irrigation or adequate rainfall, and neither potassium nor phosphate application was seen to benefit the plants.

Improving the yield of the quinoa crop itself, however, has not been the prime goal. The researchers are more interested in increasing quinoa's dependability and contribution to the overall farming system. That is, they hope to ensure that the farmer's limited resources are used to the best advantage and production risks are minimized.

A third phase of quinoa research by IBTA was approved by the IDRC's Board of Governors in 1985. The aims are to continue improving quinoa, distribute the superior varieties, and to study and improve farming practices. The researchers will also transfer their results to technical staff and farmers.

Socioeconomic and agronomic surveys are helping the researchers to uncover variations in quinoa farming. Topography differs from valley to valley and nuances in cropping systems have evolved within small areas. These differences affect a farming community's potential for successfully adopting new varieties.

Extension difficulties

Passing on research results via the extension system to those most in need has been a problem in Bolivia, as in many countries. Resources in Bolivia are barely adequate to keep researchers motivated and only a small proportion of the national budget is committed to agricultural extension. Working with subsistence farmers under the harsh conditions of high altitude areas is poorly paid and not very well rewarded by promotions within agricultural institutions.

However, the assistance of foreign donors has enabled researchers to promote extension in novel ways. Under the IDRC-supported quinoa project, for example, one- or two-day courses are offered to farmers four or five times a year. Each attracts from 25 to 40 participants. Topics include nutritional value, grain characteristics, pest and disease tolerance, growth habits, and optimum cropping practices.

The project has also produced a video that has proven to be more effective than Spanish publications for communicating information to local farmers who speak mainly Quechua and Aymara.

IDRC recently established pilot plants in the Andes to make quinoa processing more efficient. And, in addition to the Bolivian research programme, it has sponsored a three-phase programme in Ecuador and funded quinoa research in Colombia.

It will still be a few years before it is clear whether quinoa can be restored to the prominent position it enjoyed several hundred years ago. In the meantime, the Andean nations, with their economic difficulties and limited resources, will need continued support from donors for research to improve highland crops and farming systems. (Source: TWAS Newsletter No. 11, April-June 1989)

Ethical matters

At a four-day European meeting on Genetic Heritage and Human Rights held in Paris at the end of October, a series of workshops were devoted to discussions of research on the human genome and its implications, predictive medicine, in vitro fertilization and biotechnology, from both a scientific and an ethical perspective. Participants formulated recommendations dealing with, among other subjects, the freezing of embryos, the psychological dangers of screening for as-yet incurable monogenetic diseases or diseases that appear only later in life, genetic "finger-printing", the need to conserve genetic diversity through gene banks and the existing dangers of eugenic choices. A summary of each of the 13 workshops and their recommendations will be published at the end of the year, followed at a later date by more extensive proceedings. (Source: Nature Vol. 342, 9 November 1989)

B. COUNTRY NEWS

Australia

Education leaflets launched

The Australian Biotechnology Association is launching its first five leaflets in a new series designed for use in schools and by the public at large. The leaflets are designed to be factual and to contain examples of Australian biotechnology. It is expected that when completed the series will contain some twenty topics. The first five leaflets are titled:

What is biotechnology?
What is genetic engineering?
Biotechnology and plant agriculture.
Biotechnology and animal agriculture.
Biotechnology and medical diagnosis.

The new leaflets will form part of a kit being prepared by the ABA. (Source: Australian Journal of Biotechnology, Vol. 3, No. 4, October 1989)

ICI/UNSW ephedrine agreement

A contract has been signed between ICI Australia, Unisearch Ltd. and Associate Professor Peter Rogers from the Department of Biotechnology for a project designed to improve the bioconversion of benzaldehyde to various pharmaceutical products. Recently ICI announced that it would build a plant at Newcastle to produce cough mixture ingredients based on three salts of ephedrine. The world market is supplied currently from China using various plant sources and from the Federal Republic of Germany using a synthetic process. The plant will produce up to 300 tons per year of ephedrine salts based on a yeast bioconversion process and will use a substrate from the Australian sugar refining industry. Overseas markets are estimated to be growing at between 5 and 8 per cent a year and

export earnings of about $45 million per year are projected. Production is expected to commence in the latter half of 1989.

The group under the direction of Professor Rogers will work on strain enhancement and improved fermentation technology. The research team at UNSW has had considerable experience with high productivity fermentation processes and in association with Unisearch Ltd. currently holds three world-wide patents in the field. (Source: Australian Journal of Biotechnology, Vol. 3, No. 4, October 1989)

Plant cell culture at CSIRO plant industry, Canberra

An integral part of the CSIRO Division of Plant Industry (Chief: W.J. Peacock) in Canberra is the plant cell culture laboratory headed by Dr. P.J. Larkin and Dr. R.I.S. Brettell. The research work carried out is based around the applications of cell culture for the improvement of crop and pasture species. An important strength of the laboratory is a close association, both physical and academic, with other units both within and outside the Division which provides opportunities for collaborative research of mutual benefit. It allows access to a wide range of additional expertise in areas such as molecular genetics, virology, nematology, analytical techniques in biochemistry and field trials.

The crops under study fall into two main groups, namely, large grain cereals and legumes (both forage and grain). Cell culture techniques are being explored and expanded in their uses for increasing the genetic understanding and improvement of these crops, and also to investigate problems of cell biology and the genetic and environmental processes operating in vitro.

Plant transformation

Much effort is being directed towards the delivery of specific DNA gene constructs into cells from which transformed plants can be obtained. These techniques will allow the introduction, into many crop species, of agronomically useful genes that were not previously available. Genes of interest include those for protein quality and insect and herbicide resistance. The method commonly used for dicotyledonous plants employs engineered vectors of the naturally infective bacterium Agrobacterium tumefaciens which integrates the required genes into the host plant.

Joint projects are being carried out to transform subterranean clover, lucerne, lupin and peas using this technology. Also protoplast culture systems which can be used for transformation experiments have been developed for lucerne and subterranean clover. Other work in this division includes the transformation of such species as Flaveria, cotton and tobacco. Cereals, however, and other monocotyledonous plant species are not normally infected by Agrobacterium and require other techniques, such as delivery of the DNA into protoplasts by electrical pulses, manipulation of conditions allowing bacterial infection or the physical penetration of cells by DNA bearing projectiles or needles.

Cereal transformation

For the transformation of cereal species the main line of endeavour utilizes protoplasts (cells from which the wall has been removed) into which DNA is electroporated. The protoplasts can be cultured and under appropriate conditions transformed plants regenerated. Embryogenic cell cultures have been established for rice and wheat is the most suitable material from which to isolate and culture stable protoplasts. Plant regeneration has been achieved from rice protoplasts and the techniques necessary for stable transformation of non regenerable rice and wheat cell lines have been developed.

A variety of gene constructs are being electroporated into several species of monocotyledonous protoplasts to identify the genetic signals necessary for the optimal expression of introduced genes. The potential of non-protoplast based alternative transformation techniques is also being investigated. These include shooting DNA coated micro-projectiles into certain tissues such as anther-derived embryoids.

Culture-derived genetic modifications

(Collaboration with Molecular Genetics Group, Division of Plant Industry.)

Maize acts as a convenient tool for observing jumping genes (transposable elements), as their activity or lack of it can be reflected in the colouring pattern of the kernels. Lines with inactivated transposable elements when passed through a period of culture and regenerated may show reactivation of these elements. Preliminary results suggest that this phenomenon is related to the degree of methylation of the elements.

Other genetic changes, including alterations in gene sequences, have been identified in maize plants regenerated from tissue culture. For example mutants in the alcohol dehydrogenase gene have been identified and shown to result from single base changes.

Wheat chromosome manipulation

In addition to the introduction of alien DNA by direct gene transfer, two current projects on wheat involve a combination of tissue culture and classical breeding techniques to introgress parts alien chromosomes into a useful wheat background. The results of these projects indicate that a tissue culture phase can be used to induce the somatic transfer of useful genes from one species to another.

Cereal cyst nematode resistance in wheat

(Collaboration with the Victorian Crops Research Institute, Horsham)

Cereal cyst nematode (CCN) is a major pest of crops of the southern wheatbelt in South Australia and Victoria. A gene which confers near immunity to CCN is located on rye chromosome 6R. Cell culture is being used to induce a transfer of this single, dominant gene into wheat.

Cultures were initiated from immature embryos of wheat containing a single, whole addition of chromosome 6R. The regenerated plants were then screened for possible introgression events. Initial selection is based upon differential transmission of resistance to CCN attack to progeny of regenerants.

Chromosome breakage is indicated by segregation from resistance and/or loss of up to five isozyme markers also located on the long arm of 6R. The most advanced material has exhibited high levels of transmission of resistance over a number of generations, chromosome breakages and loss of the

chromatin. Confirmation of an introgression event will be made using in situ hybridization of the chromosomes with a rye-specific DNA probe.

Barley yellow dwarf virus (BYDV) resistance

(Collaboration with the Chinese Academy of Agricultural Sciences)

Resistance to this economically important virus has been found in Thinopyrum intermedium located on a group 7 chromosome. Chromosome addition lines for this chromosome have been produced in the wheat variety Vilmorin 27. Such monosomic addition lines have been cultured in vitro to induce alien gene introgression as in the CCN resistance work. An alternative approach taken is to use a mutation of the homologous pairing inhibitor locus (phlb) to allow recombination at meiosis. Subsequent generations of regenerated lines have been selected for BYDV resistance, but also against markers for other genes in the Thinopyrum chromosome. Cytological analysis of selected plants has revealed the normal number of twenty-one wheat chromosome pairs.

Barley yellow dwarf virus infections of cereal protoplasts

(Collaboration with the Virology Group, Division of Plant Industry)

The virus is phloem-confined and transmitted only by aphids so an in vitro infection system is desirable for testing "synthetic-resistance" genes. Such genes coding for virus coat proteins or able to interfere directly with virus replication mechanisms are likely to be expressed at the level of the single cell. Using electroporation or polyethylene glycol treatment, wheat suspension of cereal leaf protoplasts can be infected with BYDV. Infection is confirmed by immunolabelling of cells, ELISA of extracts and Northern blots for newly synthesized viral genome. This is the basis of a test for the effectiveness of the "synthetic-resistance" genes under development by the Division's Virology Group.

Bloat-safe and nutritionally improved forage legumes

Bloat is a serious condition caused in ruminants by the formation of stable protein foams in the rumen. Condensed tannins when present in the leaves of forage legumes protect from bloat in ruminants and also decrease the digestion and waste of protein during passage through the rumen. This increases the efficiency of protein utilization in the animal and leads to faster lean weight gain in young animals.

In vitro work with tannins from different sources has identified the preferred tannin types. The bio-synthetic pathway is being confirmed using HPLC for intermediate identification. The enzymes missing from lucerne and subterranean clover are being identified with a view to cloning and engineering this capacity into lucerne using molecular biology. Trials are also in progress to fuse protoplasts of tannin-containing legumes with those of lucerne. This should allow selection of cells and subsequently plants which have acquired the capacity to produce leaf tannins but retain the superior agronomic qualities of lucerne. (Source: Australian Journal of Biotechnology, Vol. 3, No. 4, October 1989)

New gene cloning technique

Researchers at the Peter MacCallum Cancer Institute, Melbourne, have discovered how to clone genes which earlier were difficult or impossible to clone in large numbers. The discovery will have economic and medical research benefits.

In medical research, it will help genetic engineers seeking causes and cures for cancers and other diseases by cutting down the time taken to multiply a gene from a single original.

The economic benefit is that by speeding the process of cloning plant genes, economically important plant strains, such as improved grain will be quicker to mass produce.

There has been a problem in working on one gene out of many thousands in each cell because some genes cloned very inefficiently by the conventional method of reproducing them in certain strains of E. coli bacteria. The genes would clone in some strains of E. coli but not in others.

Strains of E. coli were tested. A vital test system was cloning plant DNA because it has many methyl groups on it.

Researchers were able to demonstrate that genes with lots of methyl groups on them were recovered at very low efficiency with conventional strains of cloning bacteria. But these genes could be cloned readily by using a mutant strain of E. coli that lacked an enzyme encoded by a gene called RGL.

The RGL protein in normal bacteria interacts with methyl groups on DNA, acting to break down heavily methylated DNA and resulting in genes cloning inefficiently or not at all.

Experiments proved that because it lacked the offending enzyme, the RGL-minus strain of E. coli permitted DNA to clone correctly. (Source: Australian High Commission, New Delhi, Newsletter No. 4 (1&2) (1989) 6)

Austria

First five Doppler laboratories launched

Austrian industry took a step towards improving its access to basic research in September 1989 when it launched the first five of an estimated 20 "Christian Doppler Laboratories" in fields of potential commercial interest, ranging from biotechnology to expert systems. The project is sponsored by the Austrian nationalized industry Österreichische Industrieholding AG (ÖIAG), subsidiaries of which produce steel, aluminium and chemicals as well as electronic and mechanical components. The rest of the laboratories will be chosen by 1991.

The laboratories, to be located at universities or existing research institutions, are named after the Austrian physicist and mathematician Christian Andreas Doppler (1803-1853), eponymous discoverer of the effect by which relative motion between a source of sound waves and a listener alters the perceived pitch of sound. ÖIAG will give each institution up to three million Austrian schillings ($225,000) in one to five-year grants, hoping to attract good young researchers to work with the senior scientists around whom each Doppler Laboratory will be organized. (Source: Nature, Vol. 341, 12 October 1989)

Belgium

SKB to expand vaccines plant

Belgium's SmithKline Biologicals, a subsidiary of SmithKline Beecham, is extensively expanding its vaccine manufacturing facilities in Rixensart, south of Brussels.

The expansion plans are twofold. They include new manufacturing, warehousing and distribution facilities to meet a growing demand for Engerix-B, the company's genetically engineered vaccine for hepatitis B. The second part of the investment will be for the production of viral vaccines derived from mammalian cells.

Meanwhile, the EC Commission has opened a procedure against the finance proposal, saying that it is "outside the usual rules for State aid" and "threatens to distort competition". Under the EC framework, State aid can usually only be made available for full-scale manufacturing facilities in designated development areas. (Source: European Chemical News, 30 October 1989)

European Community

New rules for field releases

New rules will prevent any EC member nation from banning genetically engineered products accepted in other EC countries. The 12 environment ministers approved a directive that will regulate field release of engineered organisms. Approval of such releases must be granted by an appropriate national authority, who must notify the EC and other member nations. They can comment on the experiments. Each nation can decide if it will require public hearings. A commercial product licence granted in one country might be reviewed if many nations object to it. Otherwise, a product approved in one country must be approved in all 12 nations. (Extracted from New Scientist, 30 September 1989)

EC announces bovine hormone moratorium

In September 1989 European Agriculture Commissioner Ray McSharry made the long-expected announcement of a 15-month moratorium on the use of the genetically engineered hormone bovine somatotropin (BST). The moratorium is to allow for further study of the product.

The moratorium (which the EC prefers to call a "period of evaluation") must still be approved by the Council of Ministers, which will meet soon to discuss the matter. The European Parliament has also been asked to comment. The Commission will issue a report based on the studies by October 1990. A decision on licensing is expected to follow.

US and EC officials are struggling to avoid a trade war over BST, which is expected to set a precedent for the licensing of other biotechnology products in Europe. (Extracted from Nature, Vol. 341, 28 September 1989)

European Commission tables new proposals on genome research

Officials in Brussels have approved new plans for a controversial research programme in human genetics aimed, in particular, at providing support for research in the 12 member States of the European Economic Community on sequencing the human genome.

Earlier this year, the European Commission withdrew its first version of the programme, which followed objections from the European Parliament about the lack of adequate consideration of the social and ethical implications of the research to be carried out. It was the first time that the Commission had withdrawn a research programme in the face of parliamentary disapproval.

The critics cited in particular the title of "predictive medicine", which was initially given to the programme, as illustrating their fears that the results of the research could be used to discriminate against individuals shown to be genetically susceptible to certain diseases.

The Commission's new version, which will now be submitted once again to the Parliament, has systematically deleted any reference to the use of the research to develop "advanced genetic technologies", medical risk forecasting, or the transfer of genetic techniques to medicine. While the ultimate goal is still said to be the "prevention and treatment of human diseases", the words "predictive medicine" appear only once, as an area in which "unacceptable developments" must be "precluded". This includes the heritable modification of human genes, and the use of genetic analysis for monitoring individuals.

The revised plan, which was written by the commissioner for research, Filippo Maria Pandolfi, must be approved by the Community's research ministers. Provided they and the Parliament accept it, scientists will be able to submit research proposals early in 1990.

The new programme would then begin a year later than originally planned, and would run until 1991, taking two years instead of three. The budget remains 15 million ECU. This is not an increase in funding, because much the same work that was originally planned for the three-year programme is expected to be done in the two years.

The planned scientific content of the programme is unchanged. The funding will pay for increased communication and co-ordination among European scientists, with the aim of improving the mapping of genetic traits by studying families, the setting up of "clone libraries" of human DNA, the development of techniques and training.

The new proposal says that the Community must develop integrated data bases of genetic information in Europe. European scientists are concerned that such data bases are now controlled mostly by the US. The new proposal deletes a plan to make genetic material and DNA probes available free of charge to scientists. (Extracted from New Scientist, 25 November 1989)

Federal Republic of Germany

Court halts genetic engineering plant

A decision by a court in the Federal Republic of Germany has prevented Hoechst from producing genetically engineered human insulin at a new plant in Frankfurt. The ruling places a question over the whole future of genetic engineering in that country.

In ordering Hoechst to stop work on the plant, the State's superior administrative court may have set a precedent for other State authorities obliged to rule on other genetic production plants planned in the country.

As the Hesse judges see it, State authorities are in no position to authorize production plants using r-DNA technologies until statutory law has been passed, setting down framework conditions for laboratories and industrial facilities to work with. The legislation is currently being debated by Parliament, but passage is not expected before 1991.

In the meantime, the Government has set up an interministerial committee to study the effects of the court ruling and the possibilities for having genetic projects approved in the interim period.

State authorities in Hesse say they see no legal basis for authorizing Hoechst subsidiary Behringewerke's plans for a plant at Marburg to produce erythropo[illegible]EPO) from genetically manipulated mouse cells.

Drugmaker Grünenthal faces less environmentalist opposition to its plans to produce pro-Urokinase fron E. coli bacteria in North Rhine-Westphalia. However, authorities there may also feel their hands are tied. In Rhineland-Palatinate, municipal authorities in Ludwigshafen are studying plans to build a 5,000 tpa test facility for its tumour necrosis factor (TNF) drug. More than 600 objections to this project were filed and the company was forced to redraft its application redefining the scope and providing more details on safety precautions. Baden Württemberg, where several drugs are being produced using r-DNA technologies, is the only state to have approved such projects.

Meanwhile, US group Eli Lilly plans to build a $115 million plant for genetically engineered human insulin at Fergersheim, near Strasbourg; start up is envisaged for 1993. (Source: Manufacturing Chemist, December 1989)

Strict laws slow research

Strict laws concerning biotechnology may force companies to conduct biotechnology research elsewhere. BASF, for example, recently decided to build a genetic engineering laboratory in Boston, MA, rather than in the Federal Republic of Germany, due to the existence of about 12 laws or regulations that make it difficult to conduct biotechnology research in the Federal Republic of Germany. One regulation requires companies to seek public approval for their plans, making it impossible for a company to plan expeditiously. Environmentalist opposition has made it extremely difficult for companies to get approval for the production of products such as human insulin, saruplase or tumour necrosis factor. The only plant in the Federal Republic of Germany that makes a recombinant substance is Dr. Karl Thomae's recombinant tissue plasminogen activator plant at Biberach.

National opposition to new technologies also has affected the nuclear industry, and may also soon force an end to research on human embryos. (Extracted from New Scientist, 26 August 1989)

France

Squibb builds new laboratory

The Squibb Corporation, the US pharmaceutical company, is to spend more than FF 280 million on a basic research initiative in molecular biology at the Université Louis Pasteur in Strasbourg, on the Franco-German border. The deal includes construction of a laboratory and support for about 50 scientists for the next seven years. In return, the company will have the right to claim up to half of the projects carried out within the laboratory as theirs, with the option of an exclusive world licence should patentable results emerge.

Under the agreement, researchers will remain free to choose their research themes, without interference from Squibb. The arrangement also does not preclude other companies from taking out licences on results in which Squibb has no interest. Publication of important results will not be affected by the deal, with a maximum delay of around 45 days in the case of a patent application. Where a licence is taken out, Squibb will pay royalities to CNRS and INSERM.

In recent years, there have been several other examples of pharmaceutical giants, such as Hoechst and Bristol-Myers (now merged with Squibb), investing in basic research. Last July construction began on a neuroscience research laboratory at the University of Oxford under a similar 12-year arrangement with Squibb. (Extracted from Nature, Vol. 341, 5 October 1989)

R-P forms cancer drug joint venture with Chugai

Rhône-Poulenc Santé and Japan's Chugai Pharmaceutical have reached an agreement in principle to form a 45:55 joint venture for the development in Europe of Chugai's granulocyte colony stimulating factor (G-CSF).

G-CSF has wide potential in treating cancer and AIDS. It is in clinical trials in Japan and Europe, and the two firms believe it warrants accelerated examination by registration authorities. (Source: European Chemical News, 20 November 1989)

India

Sequencing bargain in India?

Genome mapping is not a high priority at the Indian Department of Biotechnology (DBT), whose annual budget is $30 million, but Pushpa Bhargava, director of the Centre for Cellular and Molecular Biology in Hyderabad and a member of DBT's scientific advisory committee, claims that India has "all the capabilities" to do the work, and at a fraction of what the United States plans to spend.

Because most of the money spent on the project would go towards salaries, India could map the entire human genome for less than $200 million spread over 15 years, according to Bhargava. He also argues that India could put itself in a good bargaining position with other countries who want the results. But a more compelling reason, Bhargava suggests, is that India might not benefit from human genome work going on elsewhere.

Bhargava's proposal has few supporters, however, and many disagree with his cost estimate. According to S. Ramachandran, secretary to DBT, the project would require not just manpower, of which India has a plentiful supply, but also equipment, reagents and enzymes, which would have to be imported. G. Padmanbhan of the Indian Institute of Science, one of six laboratories in the country with the facilities to sequence DNA, said he "would rather sequence the DNA of a pathogenic organism that causes disease in Indians than that of a human being". (Source: Nature, Vol. 341, 21 September 1989)

AIDS legislation

Legislation introduced in the Indian Parliament makes AIDS a notifiable disease, and requires regional health authorities to co ordinate counselling as well as treatment for people infected

by the AIDS virus. But the proposed law also imposes criminal penalties on any HIV-infected person who knowingly donates blood, semen or organs, and gives the Government power to quarantine those with AIDS.

Whether these more stringent actions will be put into practice remains in doubt for reasons of both cost and logistics. Each Indian state will be required to designate a health authority to which general practitioners must report cases not only of AIDS but also of drug addiction. The authority is expected to provide health education, counselling, medical treatment and follow-up for notified HIV-positive cases; drug addicts will also be tested for HIV infection. Also introduced will be mandatory HIV-testing for blood donors.

The state authorities are also empowered to remove any infected person to a hospital or to some other place to prevent that person from becoming a risk to society. The bill provides $10 million for creation of counselling, hospital and rehabilitation facilities.

Even before the law comes into force, there are doubts about how effectively it can be implemented. If followed strictly, the new law would require the 1,450 people, mostly prostitutes, known to have AIDS to be rounded up and sent to places of special care or to counselling centres. But no such centres exist.

It is feared that compulsory notification will also drive people away from medical practitioners, who are themselves averse to breaking doctor-patient confidentiality. And no private hospital in India is prepared to handle a patient infected by HIV. (Source: Nature, Vol 341, 21 September 1989)

Collaboration on biopesticides for India and Thailand

Ecogen Inc. and the Gujarat State Fertilizers Company Ltd. have agreed to collaborate on the development of bioinsecticides and biofungicides for use in India. They will jointly develop biological insecticides based on Bacillus thuringiensis, a bacterium with insecticidal activity.

The company has also signed a letter of intent with Asian Pacific Syndicate Company Ltd., based in Bangkok, Thailand, to form a biopesticide joint venture. The new company, to be called Biopesticide (Thailand) Company Ltd., will be located in Bangkok and licensed exclusively to develop, manufacture and market Ecogen's biopesticides in Thailand, Malaysia, Indonesia, Burma and Laos. Details from Ecogen Inc., 2005 Cabot Blvd. West Langhorne, PA 19047-1810, USA or on +1(215) 757-1590 (Source: Biotechnology Bulletin, Vol. 8, No. 10, November 1989)

Cost-effective media formulated for in vitro mass propagation of economically important plants

The research team of the Biotechnology Unit of IIT-Kharagpur, India has developed low cost media composing of natural ingredients, replacing conventional plant tissue culture media like Murashige-Skoog (MS), B5 etc. The ingredients used are as follows:

1. Agar agar has been replaced by a gelatinous extract of a herb.
2. Growth factors from leaf extract of a particular wild plant (under identification).
3. Minerals have been replaced by mixture of rock soils from different regions of India.

By varying the proportion of each ingredient, the formulation can be used as a root-initiation medium, shoot initiation medium or for callus culture. Successful trials have been given for many plants under investigation. It is estimated that the cost of this medium is about one fifth to that of MS.

A bioreactor and a support matrix have also been developed by the research team for large-scale continuous mass propagation. Investigations are on for the large-scale propagation using the newly developed bioreactor and the liquid medium.

The research team comprises Professor B.C. Bhattacharyya, Mr. S. Dey, Mr. P.S. Bhattacharyya and Dr. (Mrs.) N. Das. (Source: News release, December 1989)

Japan

Marine organism bioaccumulation study

Researchers at the Government Industrial Research Institute (Chugoku) are studying marine organism bioaccumulation mechanisms. The work builds on a discovery made during an outbreak of red tide in the Seto Inland Sea. Investigators discovered that diatomic algae (green and Gacillariophyceae) accumulated large amounts of phosphorus. Subsequent research revealed that Dunaliella, a form of green algae, absorbs useful elements such as gallium in its cell walls and deploys different absorption mechanisms for different elements. Dunaliella, a 5-micron single cell organism, is capable of storing phosphorus in concentrations in the 10^4 ppm range and arsenic in 10^3 ppm range within its internal structure. The algae can be used as means of removing valuable elements from sea water in useful concentrations. Research is going on to improve recovery rates. (Extracted from New Technology Japan, October 1989)

Japan expands genetic R and D

Twenty firms owned by Japan's Mitsui Group have created a new independent research institute by merging portions of their plant genetic engineering operations.

The new enterprise - Mitsui Plant Biotechnology Research Institute - is seeking to develop speciality chemicals and new strains of crops that are larger and more resistant to flood, drought, disease and insects. Like many other Japanese industries, the group will not see foreign joint venture partners, but plans to recruit plant pathologists and other scientists from all over the world to complement its own research staff. (Source: Manufacturing Chemist, December 1989)

The Netherlands

The threefold approach of the Dutch Directorate General for International Co-operation: Special programme on biotechnology

Biotechnology can have a positive as well as a negative impact on development. To advance positive and curb negative aspects, the Directorate General for International Co-operation (DGIS) of the Ministry of Foreign Affairs of the Netherlands has launched a special programme. Its objectives are threefold:

1. To broaden the discussion and the decision-making process in order to integrate

development concerns into the criteria for selecting biotechnology research topics,

2. To increase financial and technological co-operation with developing countries to improve the r own research capability, and

3. To enhance international co-ordination and co-operation in a field in which special programmes have started mu hrooming.

Biotechnology has a dualistic character. On the one hand it offers developing countries new possibilities for solving a number of important constraints. Biotechnology is in many ways an appropriate technology for developing countries. Although modern biotechnological research generally requires highly trained specialist researchers, the application of biotechnology is often uncomplicated, does not usually require much energy, is not highly capital-intensive, and (provided that it is used correctly) is also environmentally sound. In the field of production technology, it is possible to differentiate in terms of scale factors, thus permitting small-scale decentralized application. Furthermore, a number of conditions are present in developing countries which are favourable for biotechnology, e.g. a large turnover of biomass, and the possession of a wide variety of bioresources. Biotechnology has great potential for solving several critical problems in developing countries and could prove to be valuable in the effort of developing countries to become more economically self-reliant.

On the other hand, biotechnology may also lead to social, economic and environmental problems. Merely to state that biotechnology is appropriate, would be to neglect the fact that biotechnology may also be highly inappropriate and have considerable negative effects on developing countries and certain groups within these countries. Three trends can be distinguished which will predominantly have negative consequences for developing countries:

- Substitution of raw materials;
- Industrialization of agriculture, and
- Privatization of knowledge and technology.

These trends are a serious threat to export markets of developing countries and to small-scale food production, and will further widen the research and development gap between the third world and industrialized countries.

Whether a new technology will have a mainly positive or negative impact on society depends on the direction of the research and the socio-economic context in which the technology is introduced.

The direction of the research is largely determined by the current and future balance of power with regard to biotechnology. Current biotechnology developments are almost exclusively guided by economic considerations and biotechnology research is moving from the public to the private sector. Modern biotechnology is almost completely in the hands of the private sector and this has strong implications as regards the type of technology that will ultimately emerge and as regards the products developed. Biotechnology is, therefore, primarily used in fields where it can relatively easily lead to commercially attractive applications for which large and rich markets exist.

The current direction of biotechnology research excludes several potential applications which have important social advantages or are beneficial to the environment. If research priorities are not redefined and if developing countries are not enabled to influence the development of techniques to meet their own needs, biotechnology will not bring the heralded benefits to the third world. There is a high risk that developing countries become even more dependent on the industrialized countries.

To ensure that some of the expected benefits of biotechnology actually accrue, developing countries should be supported in building up local research capacity, and development-related research in industrialized countries should be stimulated. Especially biotechnology applications that are of a potential benefit to developing countries and that are not addressed by private enterprise should be stimulated within the context of development co-operation.

On the other hand, we h ve to study how possible negative consequences of biotechnological developments for developing countries could be limited - if not prevented. There is an urgent need for early warning systems. However, apart from early warning systems, we also need early listening systems. This means institutions in developing and developed countries apt and willing to anticipate changes stimulated by new technologies and act accordingly.

Special programme on biotechnology

Within DGIS, it was concluded that the aforementioned objectives could be addressed best by the establishment of a special programme "Biotechnology and Development Co-operation". This programme, which is to run for an initial period of five years, will consist of three elements:

1. Broadening of the discussion and decision-making process

Biotechnological research in the industrialized world has a market-oriented character geared to the interests of the private sector. Basically there is nothing against such an orientation. However, to permit a broader assessment of interests and prevent biotechnological developments in the Netherlands contributing to the widening of the gap between rich and poor countries, DGIS will try to include possible effects on the developing countries in the debate and decision-making process on biotechnology in the Netherlands. Biotechnology commissions should be expanded with development expertise and several checkpoints for appraisal should be incorporated in biotechnology programmes, initiated and subsidized by the Government; e.g. possible effects on the third world, and preference for projects with a spin-off to developing countries.

2. Financial and technical co-operation

Within this framework the following activities will be undertaken:

- Building up biotechnological research capability in developing countries through the transfer of technology (training, workshops etc.) and the supply of material (equipment, chemicals);

- Biotechnological research projects by and for developing countries will be initiated;

- Technology assessment studies will be carried out to appraise the social and ecological suitability of biotechnological techniques;

- Risk analyses with regard to the environmental release of genetically engineered organisms will be undertaken - within each project as well as general studies;

- Socio-economic studies of national and international relations (especially North-South and South-South relations);

- Evaluation of rules and regulations concerning the introduction of genetically engineered organisms, and a discussion of plant breeders' rights and patent protection in relation to developing countries;

- Conservation and free exchange of genetic resources by stimulating the establishment of good and freely accessible gene banks in developing countries and the upgrading of existing ones.

3. International co-ordination and co-operation

An internationally co-ordinated approach together with other bilateral donor agencies, the CGIAR, United Nations agencies and the World Bank is crucial. Especially now, since biotechnology is a relatively "new" area, still in development, and many agencies are working on a policy.

Furthermore, the international organizations are the fora that have to come forward with international policy with regard to biotechnology in general, and on issues like intellectual property rights and the environmental release of genetically engineered organisms.

During the phase of further operationalization of the programme, several activities have already been initiated, including, among others, the "Monitor Biotechnology and Development" and

- An international inventory of biotechnology policies and activities of several donor organizations and countries, United Nations agencies, development banks, and the CGIAR;

- The financing of several workshops and conferences, such as a conference on biotechnology and development, organized by the Society for International Development, a conference on priorities in future Dutch development research, and an FAO/CTA symposium on "Plant Biotechnologies for Developing Countries" (June 1989);

- An inventory of biotechnology applications for the improvement of cassava production, processing and preparation. DGIS plans to organize a workshop in early 1990 in which an attempt will be made to arrive at a co-ordinated effort in this field with several other donor agencies in a limited number of developing countries.

(Source: Monitor Biotechnology and Development No. 1, September 1989)

Tomato collaboration

Dutch plant biotechnology concern Mogen is to collaborate with the Agricultural Genetics Co. of Cambridge, UK, to promote insect resistance in tomato plants. Under the collaboration, Mogen's ability to introduce genes into plants will be combined with AGC's proprietary CpTI insect resistance gene. The companies intend to set up an international club of tomato breeding companies to commercialize the results. (Source: European Chemical News, 20 November 1989)

Spain

Kabi to take over pharmaceutical company in Spain

The Procordia-owned Swedish company, Kabi, has signed a purchase agreement with the Spanish pharmaceutical group, Fides, in Barcelona. Kabi will thereby strengthen its position on the expansive Spanish pharmaceutical market and gain access to products for the general practitioners sector. The Kabi Group in Spain will also become one of the larges enterprises in the Spanish pharmaceutical industry with projected sales of SKr 500 million and about 500 employees. The finalizing of the agreement is subject to the approval by the Spanish authorities.

Fides is a major domestic pharmaceutical company in Spain. It manufactures and sells products in the antibiotic, anti-inflammatory, and cardiovascular sectors. Fides has been engaged for quite some time in significant biological research on growth factors in the liver and on monoclonal antibodies for diagnostic purposes as well as other uses. (Source: Company News Release, 9 November 1989)

Sweden

Volvo divests Pharmacia stake

Volvo and State holding company Procordia have agreed to merge their pharmaceuticals and food activities in a move which will create a major international player in these sectors. The transaction involves Volvo exchanging its major interest in Pharmacia and its food division Provendor for a 40.7 per cent share of Procordia's stock. The combined company "will form a very strong Swedish pharmaceutical company, with major international competitiveness and greater potential to handle the ever-increasing research and development costs, which currently amount to slightly more than Skr. 1.8 billion", say Volvo and Procordia. It will be among the 20 largest pharmaceutical companies in Europe. (Extracted from European Chemical News, 18-25 December 1989)

United Kingdom

BioIndustry Association established to promote commercial biotechnology in the UK

The BioIndustry Association (BIA), formerly the Association for the Advancement of British Biotechnology, is the trade association for specialized biotechnology industry in the UK.

BIA focuses specifically on promoting the commercial interests of companies actively involved in biotechnology in the UK, whilst retaining strong links with service and academic sectors through associate membership. The Association currently has over 150 members including both emerging biotechnology companies and small to medium enterprises, as well as the biotechnology divisions of large organizations from all sectors of the industry.

The BioIndustry Association provides a range of benefits and services to members including:

- A contact network which allows biotechnologists and service organizations to meet to exchange ideas, develop ventures and solve problems.

- Export opportunities including trade missions, seminars, exhibitions and contacts with international trade organizations.

- A specialist information service, including regular news bulletins, annual handbook, house publications, commissioned market research, focused meetings and access to expert advice on specific issues.

- Representation of members' interests to public policy makers in the UK, Europe and internationally.

- Participation on standing committees on:

  Manpower, education and training
  Regulatory affairs and patents
  Public relations
  Finance for biotechnology
  Bioprocess equipment development.

For further information including details of membership, contact: Dr. Shirley Lanning, Executive Director, BioIndustry Association, 1 Queen Anne's Gate, London SW1H 9BT, UK. Telephone: (01) 222-2809, Fax: (0235) 511034. (Source: News Release, 4 December 1989)

United States of America

New advisory board approved

Approval has been given to the establishment of a new government advisory body on biotechnology, to be called the National Biotechnology Policy Board (NBPB). It will concentrate on technology transfer from university and federal research laboratories and the competitiveness of the US biotechnology industry.

Congress directed the National Institutes of Health (NIH) to establish the board in 1988 and wanted to see its first report in January 1990, but members of the board have not yet been selected from a list of about 80 candidates. Responsibility for establishing it lies with the NIH Office of Recombinant DNA Activities.

The board will consist of representatives from all the federal agencies that support or regulate biotechnology research, four university researchers, four representatives of the biotechnology industry, two members from state biotechnology development programmes, one member of a charitable institute and a bioethicist.

The Congressional Bioethics Board (CEB) was charged with reviewing reports from the NBPB, but is unlikely now to do so: after a short and controversial life, the CEB was dissolved on 1 October 1989.

Some of the NBPB's responsibilities, such as its mandate to "enhance basic and applied research", might overlap with those of the existing Biotechnology Science Co-ordinating Committee (BSCC), yet another advisory body in this field which has likewise not been without its share of controversy. The President's Office of Science and Technology Policy set up the BSCC in 1985 to co-ordinate the regulation of biotechnology across all the federal agencies. In 1988 it became bogged down in a dispute between the Environmental Protection Agency (EPA) and the Food and Drug Administration over whether the EPA should regulate non-coding as well as coding genetic sequences. An EPA rule on the regulation of genetically manipulated micro-organisms was delayed. (Extracted from Nature, Vol. 341, 26 October 1989)

Protein engineering research facility opens

A new research facility, the Center for Advanced Research in Biotechnology (CARB) has been established in Rockville, Md. CARB is an unusual co-operative venture of the National Institute of Standards & Technology, the University of Maryland, and Montgomery County, Maryland. Established in 1984, the center conducts research on protein structure, function, and engineering, and on rational drug design.

Activities include training of graduate and postdoctoral students, co-operative projects with visiting scientists, and R&D collaborations with industry. Collaborations are currently in place with Otsuka Pharmaceuticals, Japan, and Triton Biosciences, Alameda, California.

CARB's mission centres on protein engineering, the rational modification of the structure of a protein to improve its properties. To advance the field, CARB has set up programmes in biochemistry, X-ray crystallography, nuclear magnetic resonance spectrometry, and computational chemistry and modeling.

CARB scientists, working primarily in temporary facilities at NIST up to now, already have chalked up a number of accomplishments, including the determination of structures for β-lactamase (an enzyme responsible for bacterial antibiotic resistance) and chymosin (the principal enzyme used in the manufacture of cheese). In addition, center personnel have compiled a new biomacromolecule crystallization data base.

Administratively, CARB is part of Maryland Biotechnology Institute, which operates like a separate campus of the University of Maryland, although it is geographically dispersed. In addition to CARB, the institute is overseeing development of centres on marine, agricultural, and medical biotechnology, and on public issues in biotechnology. (Abstracted with permission from Chemical Engineering News, 4 December 1989, p. 5, S. Borman. Copyright (1989) American Chemical Society)

Chiron licenses viral diagnostics

California-based Chiron Corp. is to collaborate with Japan's Daiichi Pure Chemicals to develop a range of viral infection diagnostics for markets in Japan and Taiwan.

The agreement covers development of diagnostics for the hepatitis A, B and C viruses and human immunodeficiency virus (HIV). Commercialization of products is expected to lead to the formation of a joint venture between the two companies in Japan.

The agreement may be extended to other Asian countries, but Chiron retains technology rights for the rest of the world. In the US, Chiron has a separate partnership agreement with Ortho Diagnostic Systems to commercialize a series of immunodiagnostic products for hepatitis and AIDS. (Source: European Chemical News, 20 November 1989)

C. RESEARCH

Research on human genes

Key neurotransmitter receptor identified

The race to clone a glutamate receptor has ended in a sort of three-way tie, with three independent groups describing their results. The brain contains several types of glutamate receptors, which are proteins that play a crucial role in transmitting chemical signals between nerve cells. Michael Hollmann and colleagues at the Salk Institute for Biological Studies in La Jolla, California, report cloning a glutamate receptor from the rat brain. Keiji Wada of the National Institutes of Health and colleagues there and at the Salk Institute have cloned a frog version of a protein that binds the glutamate analog kainate, while researchers at Weizmann Institute of Science in Rehovot, Israel, working with Michael McKeown of the Salk Institute, have accomplished the same task in the chicken. The genes identified in the frog and chicken, however, are distinctly different from those identified in the rat, and they may be involved in other important processes in the brain. The discoveries may eventually lead to improved treatment for strokes and head injuries and to a new understanding of learning and memory. (Reprinted with permission from Chemical Engineering News, 11 December 1989, p. 16. Copyright (1989) American Chemical Society)

The structure of the "Second Genetic Code"

Biochemist Thomas A. Steitz and his colleagues at Yale University have for the first time shown how two of the cell's key molecules interact - an achievement that other researchers are hailing as a "landmark".

The two molecules in question - one a transfer RNA (tRNA) and the other an enzyme called tRNA synthetase - are critical components of the machinery that the cell uses to synthesize proteins. And by showing in detail how these molecules interact, the Yale group has greatly clarified a mystery that has puzzled researchers for some 30 years, ever since that machinery was first discovered.

In broad outline, of course, protein synthesis is well understood. First, the genetic information encoded in a stretch of DNA is copied into messenger RNA: a kind of molecular data tape that will direct how amino acids are incorporated into the new protein. Then, a swarm of tRNA molecules brings in the amino acids, lining them up along the messenger RNA so that they can be joined in a specified order.

However, to accomplish that task each tRNA needs its synthetase, which is the enzyme that links it to the correct amino acid. And therein lies the mystery: how do a tRNA and its synthetases recognize each other? There are 20 different synthetases in a living cell, one for each of the 20 amino acids needed to make proteins. There are likewise some 45 to 50 different tRNAs, each corresponding to one or more of the three-nucleotide codewords used by DNA and RNA to specify the amino acid sequences of proteins. And worst of all, every one of those tRNAs looks virtually alike: a sequence of about 75 to 90 nucleotide bases coiled like a tangled garden hose into a crude "L".

So how does a synthetase specializing in the amino acid glutamine make sure that it is not attaching that molecule to the tRNA for, say, methionine? How does the cell keep from getting its proteins hopelessly scrambled and thus making life impossible?

The Yale group's structure promises to provide some answers. "If there is a dictionary for the genetic code," Abelson says, "it resides here", in this tRNA-synthetase recognition process.

The synthetase that Steitz and his colleagues have imaged - both it and the tRNA are specific to the amino acid glutamine in the bacterium Escherichia coli - is actually among the simpler ones, consisting of just a single protein. And yet its interactions with the tRNA are startlingly complex, with multiple points of contact all along the inner side of the "L".

It is going to take a long time to sort out which of these interactions are crucial for recognition and which are not, says Steitz. Nonetheless, the images are already yielding some intriguing insights. (Extracted from Science, Vol. 246, p. 1122, 1 December 1989, M. Mitchell Waldrop, p. 1122. Copyright AAAS 1989)

Promising new route to produce antibodies

A technique for generating large numbers of monoclonal antibody fragments that has the potential to supersede current hybridoma technology has been developed by scientists at the Research Institute of Scripps Clinic and at Pennsylvania State University. Simplifying production and characterization of monoclonal antibodies, one of the essential tools of molecular biology, could have a major impact on biotechnology.

The technique permits the rapid production and characterization of what are known as Fab fragments of mouse antibodies. A Fab molecule consists of the variable regions of both the heavy (VH) and the light (VL) chains of an antibody. It has been known for many years that a Fab possesses essentially the same binding affinity as the antibody from which it is derived.

The new technique bears some similarity to research by scientists at the UK Medical Research Council's Laboratory of Molecular Biology. That method, however, generates a family of protein molecules consisting only of VH fragments.

R. Lerner, Director of the Scripps Institute, and S.J. Benkovic of Pennsylvania State University have been at the forefront of efforts to develop what are known as catalytic antibodies. The present research on Fab fragments was stimulated by a desire to develop a technique for assaying larger numbers of antibodies than was possible with traditional hybridoma production of monoclonal antibodies.

Lerner points out that reconstructing complete antibody molecules from the DNA encoding Fabs should be feasible, providing a route to monoclonal antibody production not involving hybridomas. (Abstracted with permission from Chemical Engineering News, 11 December 1989, pp. 5-6, R. Baum. Copyright (1989) American Chemical Society)

AAT gene may be inserted into T-lymphocytes

The gene for alpha-1 antitrypsin (AAT) could be inserted into human T-lymphocytes for reinjection into patients, according to R.G. Crystal of the United States National Heart, Lung and Blood Institute. AAT is needed to degrade neutrophil elastase. In people who lack a functioning gene for AAT, the neutrophil elastase can cause emphysema by the age of 40, with a mortality rate of 84 per cent by the age of 60. Current treatment requires weekly injections of AAT.

Another possibility is to infect lung epithelial cells with a virus carrying the AAT

gene. If the virus can survive long enough, the infected cells could be directed to make AAT where it is needed. (Extracted from Science News, 7 October 1989)

Polypeptide made by genes on separate chromosomes

A polypeptide may be made by genes on separate chromosomes, according to researchers at the Beckman Research Institute of the City of Hope (Duarte, CA) and at the University of California (San Francisco). The polypeptide studied is part of glucose-6-phosphate dehydrogenase (G6PD). A gene on the X chromosome contains the information to make the minor polypeptide component of the enzyme, and part of the information needed for the major polypeptide. The rest of the major polypeptide is coded for by a gene on chromosome 6. How this is co-ordinated is not known. (Extracted from New Scientist, 30 September 1989)

Second protein may block metastasis

A protein inhibitor that may block the spread of cancer cells has been identified and purified by William G. Stetler-Stevenson, Henry C. Krutzch and Lance A. Liotta at the US National Cancer Institute. The newly purified protein inhibits collagenase IV, an enzyme secreted by cancer cells that degrades collagen in connective tissues, allowing cancerous cells to penetrate into connective tissue and spread to other parts of the body in a process known as metastasis. A similar protein, isolated in 1979 and called tissue inhibitor of metalloproteinase (TIMP), inhibits the activity of a different collagenase. Thus, the researchers suggest the name TIMP-2 for their new inhibitor. (Abstracted with permission from Chemical Engineering News, 23 October 1989, p. 17. Copyright (1989) American Chemical Society)

Discovery of new protein for treatment of neurological diseases

Scientists at Synergen have purified and used recombinant DNA technology to produce a new protein, called CNTF, that may be useful in treating serious diseases of the nervous system. The discovery group included Drs. Frank Collins, Drzislav Mismer and Leu Fen Lin, whose work has focused on identifying neurotrophic proteins involved in the survival, function and regeneration of cells of the nervous system.

CNTF is a potential therapeutic agent for nervous system dysfunctions called peripheral neuropathies. As many as half of all diabetic patients are believed to suffer from peripheral neuropathies, which can be severely incapacitating and sometimes life-threatening. Other targets of Synergen's neuroscience programme include Alzheimer's disease and Parkinson's disease. CNTF is produced in neural tissues and is released in response to injury.

The protein sustains cells in the nervous system that convey sensation and that control the function of muscles and organs. Synergen believes that its CNTF may be an effective treatment to prevent damage to these cells resulting from conditions such as diabetes and kidney dysfunction and from the toxic effects of chemotherapeutic agents used to treat cancer and AIDS. Nerve damage caused by these conditions is currently untreatable. Details from: Synergen Inc, 1885 33rd Street, Boulder, Colorado 80301, USA.

New gene discovered

A new gene that may play a major role in the body's development of immune defences has been discovered by researchers at MIT's Whitehead Institute for Biomedical Research. The human body produces a huge number of antibody types by shuffling and combining parts of various genes. The new gene is believed to make an important contribution to that recombination process by providing a blueprint for part or all of the enzyme responsible for reshuffling the gene parts. It is also possible that it functions as a regulator that switches on other genes. It has been named RAG-1 (recombination activating gene) by the researchers. According to them, it is somehow involved with the bone marrow cells that produce T cells and B cells, both of which are essential to the body's immune defences. Recently, a research team at Japan's Kyoto University said that they had also discovered a gene that plays a role in the bone marrow genetic recombination process. According to F.W. Alt of Columbia University's College of Physicians & Surgeons, who analysed the research of the Japanese team and that of the Whitehead Institute, the Kyoto University team's gene is different from the Whitehead gene but may be somehow related. (Extracted from New York Times, 22 December 1989)

Regulatory proteins may act on several genes

Special proteins that act as switches to control the expression of genes appear to act on more than one gene, according to recent evidence from a group of researchers headed by Keiko Ozato at the US National Institute of Child Health & Human Development. Along with collaborator Ettore Appella of the US National Cancer Institute, the researchers have isolated the gene for a protein that helps control expression of an important gene in the immune system called the major histocompatibility complex (MHC) class I gene. Examination of the amino acid structure of the regulatory protein shows similarities to other, seemingly unrelated, regulatory proteins, so the researchers checked to see if their protein would bind to the regulatory portion of other genes. They find strong binding to the regulatory portion of a quite different class of genes, those that respond to estrogen. Such multiple-functioning regulatory proteins make sense from the point of view of cell economy. Ozato suggests that competition between regulatory proteins also may explain why hormone-responsive tumours, such as those in the breast, lose their responsiveness to hormone signals as the tumour progresses. (Reprinted with permission from Chemical Engineering News, 6 November 1989, p. 24. Copyright (1989) American Chemical Society)

Hybrid molecule cleaves duplex DNA

Chemists at the University of California, Berkeley, have created a hybrid molecule consisting of a short oligonucleotide linked to a nuclease that sequence-specifically cleaves doubled-stranded DNA. Berkeley associate professor of chemistry Peter G. Schultz and colleagues demonstrated that a 17- or 19-nucleotide oligomer fused to staphylococcal nuclease will bind uniquely to the complementary sequence in partially denatured, supercoiled, plasmid DNA and subsequently hydrolize both strands of the nucleic acid. The design of molecules that sequence specifically cleave double stranded DNA at sequences 15 to 20 nucleotides in length is likely to be important in carrying out the sorts of manipulations required in mapping and sequencing genomic DNA. A promising

strategy that has been pursued by California Institute of Technology chemist Peter B. Dervan i-volves triple helix formation. Schultz's hybrid molecules avoid certain limitations associated with triple helix recognition. However, Schultz notes, at present the hybrid oligonucleotide nuclease is limited by its ability to cleave only supercoiled DNA. (Reprinted with permission from Chemical Engineering News, 6 November 1989, p. 24. Copyright (1989) American Chemical Society)

Genetic link for manic depression still sought

The linkage between manic-depressive illness and a gene located near the end of chromosome 11 is no longer persuasive, say the researchers who first reported the connection two years ago. The original claim that inheritance of this particular portion of a chromosome predisposed people to develop manic-depressive illness was based on a 10-year study of the occurrence of the disease within an extended family of Old Order Amish in eastern Pennsylvania led by Janice A. Egeland of the University of Miami. The researchers calculated the likelihood of the disease and the portion of chromosome occurring together by chance in their study group to be about one in 10,000. Now Egeland and 11 co-authors report two additional members of the family have developed the disease without having the gene and that the study has been extended to 16 other family members who, collectively, do not fit the predicted pattern. The findings do not mean that the disease does not have a genetic component, only that this study has not found it. (Reprinted with permission from Chemical Engineering News, 20 November 1989, p. 14. Copyright (1989) American Chemical Society)

Gene transfer test: so far so good

When US National Institutes of Health physicians began the first human gene transfer trials this spring, they hoped to show that anticancer white blood cells destroy tumours by selectively seeking out malignant tissue. Preliminary results from the first of five patients indicate that the experiment is working the way they predicted it would.

The gene transfer experiment was reviewed and re-reviewed a total of 15 times before receiving final approval by the director of the National Institutes of Health at the beginning of this year. In addition, it was subject to one lawsuit that sought to block the test on the grounds it had not received sufficient prior review. That suit failed in court and the experiment, which has been heralded as the first authorized test of human gene transfer, began on 22 May.

The experiment, conducted by Steven A. Rosenberg of the National Cancer Institute, involved therapy with tumour-infiltrating lymphocytes, or TIL cells, which has produced significant remission in a few patients with advanced melanoma that is generally resistant to existing forms of treatment. In an attempt to explain why TIL therapy works when it does, as well as why it fails more often than not, TIL cells were transduced in culture with a bacterial "marker" gene that would enable researchers to see where the antitumour lymphocytes go in the body. Rosenberg is one of a three-man team that includes R. Michael Blaese of NCI and W. French Anderson of the heart institute.

The patients' own lymphocytes were extracted from bits of solid tumour, labelled with the bacterial gene for resistance to the antibiotic neomycin (NeoR), grown to massive quantities, and then reintroduced into the patients' bloodstreams.

Speaking at a meeting of the National Cancer Advisory Board on 18 September, Rosenberg reported data from one patient whose tumours shrunk significantly after TIL therapy. Rosenberg's presentation to the board was scheduled at the request of industrialist Armand Hammer, the presidentially appointed chairman of the White House cancer panel that oversees the federal war on cancer. The NCI news office then called a press conference.

The patient, a 26-year-old woman with black, ulcerous masses of melanoma at as many as 30 sites on her body, is experiencing the kind of dramatic tumour regression that encourages Rosenberg to persist in experimenting with "adoptive immunotherapy" which produces some benefit in about 50 per cent of patients.

Rosenberg also reported safety data from all five patients who have received gene-labelled TIL cells so far. None has suffered any toxicity from the inert marker gene that was transferred along with the lymphocytes.

Blood samples and tumour biopsies were taken from each of the patients before the gene-labelled TIL cells were infused, and again on days 3, 5, 14 and 19 after therapy. All samples were blind. So it was only when the code for one patient was broken that Rosenberg and his colleagues got the news they were hoping for.

The TIL not only travel to tumours but also survive - even after three weeks, gene-labelled TIL could be found circulating in the bloodstream. Clearly, it is too early to say how long the TIL cells will persist but it is known that some lymphocytes live for years.

From the beginning, the plan was to study gene-labelled TIL cells in five patients and assess the results before proceeding to infuse an additional five allowed under the gene transfer protocol.

If data continue to suggest a connection between TIL cells homing in on tumours and tumours shrinkage, the researchers will begin searching for information about which cells in the TIL constellation are doing the job.

Beyond that, the hope is to use TIL cells as a vehicle for getting additional anticancer agents into tumours in an attempt at actual gene therapy. The NeoR gene is a marker, pure and simple, offering no therapeutic advantage. The next step will be to ask approval of a protocol to insert a gene for an active antitumour agent into the TIL population - perhaps a year from now. A likely candidate is the gene for human tumour necrosis factor (TNF) which has already been successfully transferred to human lymphocytes in vitro. (Source: Science, Vol. 245, 22 September 1989, p. 1325, B.J. Culliton. Copyright AAAS)

Cystic fibrosis gene identified

One of the most significant discoveries in the history of human genetics. That is how Dr. Ron Worton, geneticist-in-chief of The Hospital for Sick Children's Research Institute described the identification of the gene responsible for cystic fibrosis.

Scientists from Toronto's Hospital for Sick Children and the University of Michigan have pinpointed the molecular defect which causes cystic fibrosis.

The research which led to the dramatic discovery was spearheaded by geneticist Dr. Lap-Chee Tsui in collaboration with research fellows Drs. Johanna Rommens and Bat-Sheva Kerem, and Dr. Jack Riordan, director of the Hospital's Cystic Fibrosis Research Development Programme. Both Drs. Tsui and Riordan are faculty members of the University of Toronto.

The Hospital researchers worked in collaboration with a research team led by geneticist Dr. Francis Collins, an investigator in the Howard Hughes Medical Institute at the University of Michigan.

Cystic fibrosis (CF) is the most common of all genetic diseases; one in every 2,000 children is born with it. One in every 20 people carries the defective gene; if two carriers have a baby, they run a 25 per cent risk that the child will have CF. Although tests can confirm shortly after birth, carriers cannot be identified.

The discovery of the gene means that soon it will be possible to identify carriers - and ultimately provide counselling to couples at risk. Before large-scale testing is possible, scientists must first identify the other defects which cause the disease in the remaining percentage of patients. Dr. Tsui expects most of the remaining defects to be identified within the next year.

Discovery of the gene has also led to a new understanding of the disease which may give clues to possible new treatments. At present, treatment of CF is based on managing the symptoms; now that the defect has been identified, it will be possible to begin research into drug therapy to see if the problem can be corrected with medication at the cell level.

Research into cystic fibrosis has accelerated in the last few years as scientists began to get closer to the gene. One of the most significant discoveries was made in October 1985 when Drs. Tsui and Manuel Buchwald of The Hospital for Sick Children and a team of scientists from Collaborative Research Inc. in Boston identified the chromosome on which the defective gene was located. (Extracted from New Biotech: Canada's Biotechnology Magazine, Vol. 3, No. 9, September 1989.

Immunex clones IL-4 receptor

Scientists at Seattle-based Immunex have announced the successful cloning, and isolation in soluble form, of the mouse Interleukin-4 (IL-4) receptor molecule. The discovery could hold promise in preventing organ rejection following transplant surgery and in treating allergies and asthma.

The IL-4 cytokine promotes the production of certain antibodies, including IgE which is involved in allergic and asthmatic reactions. IL-4 is also known to activate T cells to kill tumour cells or infected or transplanted tissue.

Like other cytokines, IL 4 works by binding to matching receptors on the surface of immune cells. When bound, the receptor triggers a signal from the cytokine to the cell, promoting the immune response. A free floating, or soluble, receptor can act as a decoy. It retains the ability to bind to the IL-4, but is unable to trigger the immune response, thereby suppressing the specific immune reaction.

Soluble IL-4 receptors are widely held to be produced naturally in humans as the body's way of turning off an immune response. The Immunex scientists now suggest the cloned receptors might be of use in eliminating a variety of disease-causing auto-immune responses. (Source: European Chemical News, 13 November 1989)

Research on animal genes

The use of genetic engineering to boost wool and meat productivity

A small team at the Waite Agricultural Research Institute in South Australia is developing the technology to genetically manipulate micro-organisms living in the forestomach of cattle and sheep. The team has been working on the project for five years and believes that commercialization is still another five years in the future. Funding comes from the Australian Wool Corporation and the Australian Meat and Livestock Research and Development Corporation.

The biological make-up of cattle and sheep is obviously very different from that of humans, particularly in the way that foods are digested. Inside the rumen lives an enormous population of about 60 major bacterial species and many other minor species. These bacteria are anaerobic, surviving only in the absence of oxygen.

Once cellulose and protein are entirely broken down in the rumen, bacteria and a small quantity of plant nutrients are passed through to the small intestine, where secondary digestion occurs. Nutrient benefit to the animal is mainly gained in this stage, when the small intestine breaks down the bacteria swept through from the rumen. In this sense, ruminants obtain their nutrition from the digestion of rumen bacteria, not directly through pasture plants. The bacteria break down the cellulose into glucose, which they then convert into volatile fatty acids. Some of these fatty acids are used by the bacteria - and the rest are absorbed by the animal.

Agricultural scientists now argue that with today's pressure for increased food production the rumen is not as efficient as it could be.

In this view, dairy, meat and wool production may all be limited by the efficiency of the ruminant digestive system. Dr. J. Booker and his colleagues are looking into the genetic engineering of rumen bacteria in order to increase the supply of required amino acids directly to the animal. The modified bacteria, it is hoped, will supply proteins that contain higher levels of sulphur-containing and other essential amino acids than normal bacterial protein.

A previously undiscovered rumen bacteriophage has been isolated so that purified bacteriophage DNA can be experimentally introduced into the genetic pool of rumen bacteria.

An environmental impact study will be conducted, although the researchers believe that harmful effects are unlikely because of the anaerobic nature of the bacteria. Details from: Dr. John Booker, project leader, Department of Animal Sciences, Waite Agricultural Research Institute, Waite Road, Urrbrae, South Australia 5064. (Source: Biotechnology Bulletin, December 1989)

Rhino DNA mix and match

After a two-year study, Columbia University biologists have discovered that one black rhino is - genetically speaking - pretty much like another. That is important because it means that animals from different parts of Africa could be gathered together for breeding purposes, were that needed as a last ditch effort to save the species.

Don Melnick, associate professor of biological anthropology at Columbia, delved into the DNA of rhinos from three distinct regions: Kenya, Zimbabwe and South Africa. He discovered that despite being separated now by hundreds of miles, animals from the three populations are as similar as if they were still all living and breeding in one big group.

So conservationists, in their efforts to save the few remaining black rhinos, can potentially gather scattered animals together into havens and encourage the beasts to breed. Pooling dispersed rhinos into sanctuaries would make them easier to protect from poachers and give males and females a better chance of meeting during the two-day estrous period. If the rhinos had been genetically more distinct, interbreeding might have been ruled out. (Source: Science, Vol. 246, 24 November 1989, p. 1001, Briefings. Copyright AAAS)

Down's syndrome discovered in monkey

Researchers in Wisconsin have reported the first known case of a monkey with Down-like syndrome. The monkey's behaviour betrayed the inherited abnormality, and analysis of her chromosomes confirmed it. Down-like syndrome has been diagnosed already in chimpanzees and gorillas, but never before in a monkey. The monkey's condition is similar, both behaviourily and genetically, with those of humans with the disease.

Azalea, a female rhesus monkey, was born to a 21-year-old mother (quite elderly for this species) on 29 June 1988. Frans de Waal, a primate behaviour expert at the Wisconsin Regional Primate Research Center, says that "we knew within several days that she wasn't completely normal. She's healthy and well-accepted by the group, but she is also much slower at learning and she is much less active socially than other monkeys." (Source: New Scientist, 28 October 1989.

Ant antibody fights fungal infections in humans

Biologists in Australia have discovered that ants produce antibiotics to control diseases in their colonies. Trials in a Sydney hospital have already shown that these antibiotics are effective against a wide range of organisms, especially fungi, that cause diseases in humans. In particular, they kill the fungus Candida albicans, which is common in humans and causes "thrush", an infection of the mucous membranes.

Andrew Beattie of Macquarie University in Sydney studied more than a dozen species of ant. He was interested in discovering why it is that ants play almost no part in pollinating flowers, while bees and wasps, their close relatives, do such an important job. Beattie found that pollen dies when it touches an ant's body. In every species he studied, it was secretions from metapleural glands, at the rear of the ant's thorax, that killed the pollen.

Beattie found that the secretion is an antibiotic, called metapleurin, which the ants use to prevent the fungi and bacteria from growing in their bodies. The substance is a lipid molecule, which is quite different from other antibiotics. Apart from protecting the ants, metapleurin has the side efffect of making pollen less viable and able to germinate, so it dies.

When Beattie realised that the secretions of the metapleural glands had antibiotic properties, he took them to chemists to be analysed. He also asked medical colleagues at Westmead Hospital in Sydney to test how effective they were against bacteria that cause disease.

The hospital's initial screening tests against more than 300 of these bacteria have produced both good and bad results. Unfortunately, most of the bacteria are unaffected by the antibiotics. The good news is that metapleurin is highly effective against several strains of a common bacterium, Staphylococcus aureus, that are resistant to other antibiotics. These bacteria can be a major problem, sometimes preventing wounds from healing for many months after surgery.

Recently, it was discovered that a component of metapleurin had proved highly effective against C. albicans. Metapleurin also worked for the treatment of infections of the skin and internal tissues. Tests against other fungal organisms are under way. (Source: New Scientist, 18 November 1989)

Research on plant genes

Plant biotechnologists unveil breakthroughs

Plant biotechnology looks increasingly promising as a low-cost route to high value products.

Scientists at Mogen International in the Netherlands have succeeded in producing the protein human serum albumin (HSA) in potatoes. They claim it is the first time such a complex protein has been genetically engineered in a plant.

As part of a feasibility study funded by the Dutch Government, the Mogen scientists have succeeded in expressing the human gene in the potato plant by replacing the human signal sequence with a plant-derived signal.

"The purified albumin appears indistinguishable from HSA sourced from human blood plasma", says Andre Hoekema, senior scientist at Mogen.

The company has filed a patent application on the production method and is now teaming up with the Dutch potato-starch processing concern, Avebe, to scale up to semi-technical production.

Meanwhile, scientists at the Research Institute of Scripps Clinic, La Jolla, California, have introduced versions of mouse gamma and kappa immunoglobulin genes into tobacco cells. These have been cultivated into healthy plants, opening the possibility of an agricultural route to basic biotechnical building blocks.

Kappa and gamma immunoglobulins combine naturally to form antibody molecules. The Scripps researchers' processes can cross plants containing the gamma gene with those containing the kappa gene to produce a plant that expresses both. The antibody represents 1.3 per cent of the tobacco leaf protein.

Andrew Hiatt of Scripps explained that a commercialized process making antibodies as an

agricultural product would find uses hitherto unavailable because of the high cost. Hiatt believes the cost of producing antibodies could fall from millions of dollars per kilogram to less than $100/kilogram. He speculates antibodies could be used for purification in industrial processes or as environmental detoxificants. (Source: European Chemical News, 6 November 1989)

PGS unveils seeds breakthrough

Plant Genetic Systems (PGS) of Ghent, Belgium, has announced what it claims is a breakthrough in hybrid seed production. The discovery could lead to the creation of new and more efficient hybrids.

Working in collaboration with Professor Robert Goldberg of the University of California at Los Angeles, the Belgium agrobiotechnology company has constructed and expressed a gene that prevents pollen development in crop plants, specifically oilseed rape. The result is a male sterile plant, an essential component in the creation of hybrid seed. Traditional methods for instilling male sterility in plants can be costly and inefficient, claims PGS.

The scientists say they have succeeded in isolating a promoter that allows the expression of a gene exclusively during the development of a plant's anthers (the male reproductive organs).

According to Jan Leemans, research director of PGS, this anther-specific promoter has been used to express in the plant a gene conferring male sterility. Through the promoter, a protein encoded by the gene is expressed only during the critical few days when pollen would normally develop in the plant, suppressing its production. The protein then disappears after rendering the plant male sterile, allowing it to continue normal development.

Apart from the economic significance to oilseed rape, which accounts for some 2 million hectares of plantation in Europe, PGS claims the introduction of a gene in only a small part of a plant for only a few days is "unique in genetic engineering".

Further, the company claims the new system is "universal", except for cereals. Work is continuing on a wide range of crops from vegetables, such as brussels sprouts, to soya bean and cotton.

PGS has filed worldwide patents and plans to market the new technology to major seed companies. It is in "serious discussion" with a number of companies on possible licensing and joint venture arrangements which it expects to set up on a case-by-case basis. The new hybrids could be on the market by 1992. (Source: European Chemical News, 30 October 1989)

Ethylene gene cloned

The gene for ethylene in plants has been cloned, making possible the development of plants engineered to allow fruit ripening at the convenience of farmers, according to researchers at the Agricultural Research Service (Albany, CA). The work might also make possible the mass-production of ethylene for chemical use from sources other than petroleum. Ethylene helps control fruit ripening, seed germination and flower maturation, so its production in plants is tightly regulated. It is made from 1 aminocyclopropane 1 carboxylic acid (ACC) in a process mediated by ACC synthase. This enzyme is present in extremely small amounts, so cloning the gene was difficult. But now that it has been identified, it may be possible to block the gene in fruits so that they will not ripen until grocers expose the fruit to ethylene.

Inserting the gene into photosynthetic bacteria or algae could allow solar driven production of ethylene, of which 50 billion lb yr is used to make plastics, antifreeze and fibres. (Extracted from Science News, 16 September 1989)

Extract from stinging nettles fights off fungi in the soil

Scientists in Belgium have found that stinging nettles have a second defence mechanism in addition to the one familiar to country walkers. The plants contain a protein that protects them from fungi that cause disease.

Willem Broekaert and his colleagues at the Catholic University, Leuven, have studied lectins, proteins that recognise and bind to specific sugar molecules. Some lectins are toxic and are abundant in seeds, helping to deter animals from eating them. But why should the adult plant make lectins?

Scientists know that a lectin found in wheatgerm binds to the polysaccharide, chitin. Chitin is a component of the thick cell wall of many types of fungi. For this reason, scientists have suspected that the chitin-bonding lectin in wheatgerm might protect wheat seedlings that are germinating from attack by fungi.

Unfortunately, the earlier experiments designed to test this idea used a lectin preparation contaminated with traces of an enzyme, chitinase. This substance attacks the chitin molecule and breaks it down into its component sugars.

Now Broekaert and his colleagues have managed to extract from the common stinging nettle another lectin that bonds to chitin. They have purified it to remove all traces of chitinase enzyme. In the laboratory, this pure lectin did indeed block the growth of several types of fungus. Encouraged by this result, they measured the lectin in the nettle plant. They found that in the rhizome, or the underground stem of the plant, the protein is present at about 10 times the level needed to block the growth of fungi in the laboratory.

Broekaert and his colleagues found that the lectin is concentrated in the outer layers of the rhizomes and roots, not in stems or leaves. This suggests that it helps to defend parts of the nettle that are exposed to fungi in the soil.

The scientists suggest that the nettle lectin may be able to penetrate deep into the cell wall of invading fungi and interfere with the continuous remodelling of the fungal wall that happens as the fungus grows. The small size of the lectin molecule makes it particularly attractive to genetic engineers working to devise new strains of crops. Biotechnologists may be able to create crops resistant to some fungi. (Source: New Scientist, 4 November 1989)

Plants may produce antibodies

Plants could be used to mass produce antibodies, according to researchers at the Research Institute of Scripps Clinic (La Jolla, CA), who have inserted genes for mouse antibodies into tobacco plants. Antibodies to protect against plant diseases might also be engineered into important crop plants. Since antibodies consist of two

separate chains, researchers put the gene producing each chain into separate plants. When the plants were cross-fertilized, however, some progeny had both genes, and were able to produce complete antibody molecules. If the technique can be adapted for other plants, the cost of producing antibodies might be greatly reduced. Plants with antibodies to pollutants could be grown in polluted soil, and the antibodies in the roots would bind to the pollutants, removing them from the soil. The technique might be used to grow genetically engineered grass that would be dried to hay, which could then be used to soak up pollutants in lakes and streams. Plants might also produce antibodies to be used against human diseases. (Extracted from New Scientist, 11 November 1989)

Technology developed to produce haploid wheat

The National Institute of Agrobiological Resources has developed a practical technology for producing haploid (single chromosome set) wheat. The method will allow scientists to produce new varieties of wheat with genetically pure characteristics more rapidly than with normal diploid (paired chromosomes) wheat plants. The new technique can produce genetically pure seeds of a new wheat strain in three to four months. (Extracted from: New Technology Japan, December 1989)

Research on bacterial genes

PCB-degrading bacteria's gene cloned

Scientists at the Industrial Research Council's Research Institute for Industrial Microbiology (Tsukuba, Japan) have isolated the genes that allow certain bacteria to degrade polychlorinated biphenyls (PCBs), toxic chemicals that are a common component of industrial waste. Keitsuke Furukawa's research group determined that there are four PCB degradation genes, contained within a seven-kilobase segment of DNA from a pseudomonad they isolated from soil. (Source: Bio/Technology, Vol. 7, November 1989)

Antibodies to work faster

Scientists at the Medical Research Council in Cambridge, UK, have reported a cheap method of making new types of antibodies, which could replace some drugs, pesticides and diagnostics.

The key factor is that the cloned bacteria-produced antibodies attack antigen molecules very specifically, and binding activity is much faster than the process of monoclonal antibody manufacture.

The new molecules, called single domain antibodies, also have size advantages - they should penetrate tissues more quickly and attack tumours and clear toxins more efficiently. The research work is now concentrating on increasing the binding activity.

Human antibodies are made of four linked proteins, two heavy chains and two light chains, and each has "variable domains" for recognizing antigens. These fragments produced by the genetically engineered bacteria are made up of heavy chains only, yet still show the binding properties of intact molecules. (Source: Manufacturing Chemist, November 1989)

Mab advance seen

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

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

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

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

Research on viral genes

MPI unveils vaccine advance

Researchers at the Max-Planck-Institut für Biologie in Tübingen, Federal Republic of Germany, believe they have discovered a technique that will enable production of "designer vaccines". The scientists reported a system of stimulating cytotoxic T lymphocytes (CTLs), essential in the immune response, as effectively as if they had been exposed to infectious viruses.

Normally, CTLs recognize fragments of virus proteins so it was thought that synthetic peptides could mimic this response. Researchers discovered, however, this approach does not work.

The group, led by Hans-Georg Rammensee, claims to have found a way round this problem. By attaching parts of an E. coli protein to synthetic influenza virus peptides, CTLs were effectively stimulated. "This technique shows particular promise in the design of vaccines".

Nevertheless, Rammensee remains cautious in his optimism claiming further work on other viruses is required as well as proof that it will work in humans. He believes the technique may be extended to provide protection against non-viral pathogens such as malaria. (Source: European Chemical News, 4 December 1989)

Virus blamed as cause of multiple sclerosis

A researcher in Western Australia claims that a virus causes multiple sclerosis. The evidence accumulated by Bob Cook from Murdoch University contradicts the orthodox view that MS is an autoimmune disease.

Cook claims to have isolated the virus from the brain tissue of eight patients with MS. He points

out that a similar virus has been found in 17 of 265 domestic cats in Western Australia, Iceland and in the New York area. The virus has been isolated and cultured from five cats in Western Australia.

It is possible, according to Cook, that cats could be carriers of MS, but he stresses that other factors are probably also at work. These include stress and genetic susceptibility to the disease. Cook says that the virus he has isolated is similar to one that causes canine distemper and measles. It comes from a group of viruses called morbilliviruses.

Cook, an associate professor of histology from the School of Veterinary Sciences at Murdoch, has been working on MS for 17 years.

Cook is to present evidence for his claim at a seminar organized by the National Multiple Sclerosis Society at the Walter and Eliza Hall Institute in Melbourne.

MS occurs when the myelin sheath - an insulating layer - around nerve fibres decays away. According to those who say MS is an autoimmune disease, lymphocytes from the body's immune system attack the myelin sheath. But Cook says that the disease is caused when the virus attacks the cells which form the myelin sheathing. These are called oligodendrocyte cells. The cells send out strands to form the sheath but when attacked by the virus these same cells withdraw the strands.

Cook believes that it would take less than two years and about A$500,000 (250,000 pounds sterling) to produce a diagnostic kit to detect the virus in carriers. Cook also believes that it may be possible to develop a vaccine for multiple sclerosis. (Source: New Scientist, 18 November 1989)

When is a virus not a virus?

When Shyi-Ching Lo and his colleagues at the US Armed Forces Institute of Pathology isolated a new organism from an AIDS patient, they hedged their bets. Instead of saying definitively what the new agent was, they described it as a "virus-like infectious agent", or VLIA. Lo and colleagues now report that VLIA is not a virus at all but a mycoplasma: a prokaryotic organism that resembles a bacterium without a cell wall.

From the beginning VLIA aroused both interest and skepticism among AIDS researchers.

Earlier this year rumours began circulating that VLIA is a mycoplasma that had contaminated Lo's cell culture. Lo agrees that VLIA is a mycoplasma but contends it is a previously undiscovered specimen that "infects many AIDS patients, produces fatal systemic infection in experimental monkeys, and causes infection in healthy non-AIDS patients with acute fatal disease".

In recognition of the agent's apparent novelty Lo has dubbed it Mycoplasma incognitus. But M. incognitus bears a strong similarity to M. fermentans, a known mycoplasma, and Joseph Tully, who has worked extensively with mycoplasmas, says more work will be needed to ensure that M. incognitus is not simply M. fermentans travelling incognito. (Source: Science, Vol. 246, 8 December 1989)

Research instrumentation

Genomic sequencing by STM is possible

Direct sequencing of nucleic acids by scanning tunnelling microscopy (STM) may be feasible, say David D. Dunlap and Carlos Bustamante of the departments of chemistry and anatomy/pathology at the University of New Mexico, although a number of problems must first be overcome. Images they obtained of polydeoxyadenylate molecules aligned in parallel, with their bases laying flat on a surface of pyrolytic graphite, show that STM could be used to sequence DNA. However, before STM sequencing becomes a reality, scientists will need to improve their ability to form monolayers of single-stranded DNA containing other sequences and to control the deposition process. In addition, current microscopic resolution only allows one to differentiate purines from pyrimidines, so sequencing will require either improved resolution or prior labelling of bases. However, they write, "Direct sequencing would require far less material and would be more rapid than is possible at present." (Reprinted with permission from Chemical Engineering News, 13 November 1981, p. 21. Copyright (1989) American Chemical Society)

New instrumentation to speed DNA sequencing

A major concern of organizers of the human genome project is that the expensive and complex effort to map and sequence human DNA will not be completed on time and on budget. However, instrumentation and integrated circuit chips currently under development promise to allay some of these worries.

Applied Biosystems Inc. (ABI) has developed a prototype robotic pipeting workstation that automates a number of chemical sequencing reactions that currently must be done by technicians. The device also minimizes use of expensive reagents. Adaptable to different sequencing chemistries and usable as a front end for different types of sequencers (not just ABIs), the instrument is scheduled for delivery in late 1990.

Also under development at the California Institute of Technology is an integrated circuit chip called the Biological Information Signal Processor (BISP). BISP, like the similar Fast Data Finder chip announced earlier this year and currently being developed jointly at ABI and TRW Inc., detects similarities and patterns in sequence data much faster than previously possible, even with access to supercomputers. According to Michael W. Hunkapiller, ABI vice president of science and technology, the company hopes to come out with a Fast Data Finder-based product next year. The firm also will look at incorporating the BISP chip into the same genetic engineering work station that will use the Fast Data Finder technology. (Abstracted with permission from Chemical Engineering News, 13 November 1989, p. 6. S. Borman. Copyright (1989) American Chemical Society)

PCR technology leads to advances in AIDS research

In presentations at the Fifth International Conference on AIDS, Cetus Corporation's Gene Amp polymerase chain reaction PCR technology provided the basis for significant new developments in differentiating certain retroviruses and in estimating the number of cells infected with HIV in a given blood sample.

Researchers showed that with the PCR procedure they could differentiate between human T-cell lymphoma/leukemia virus type-I (HTLV-I) and type-II (HTLV-II) infections, a distinction that has proven very difficult with existing diagnostic methods. Antibody (ELISA) and antigen (Western blot) tests often cannot detect a difference because the antibodies and antigens for both viruses are so

similar. The researchers also demonstrated the potential value of PCR as a confirmatory test for HTLV-I and HTLV-II infection.

The ability to differentiate between the two viruses is important because HTLV-I can cause adult T-cell leukemia, a serious form of cancer that has been associated with chronic progressive myelopathy, a neurological disorder that causes paralysis of the lower limbs. It is not known whether HTLV-II causes disease.

The research is part of a larger study that includes New York area drug abusers in which 11 per cent of the samples were shown to be infected with HTLV-II. The findings have also been extended to a group of drug abusers in the New Orleans area. (Source: New Biotech: Canada's Biotechnology Magazine, Vol. 3, No. 9, September 1989)

General

Smaller but smarter

Monoclonal antibodies, a fairly recent development and one of the mainstays of biotechnology, are already in danger of becoming obsolete. The development of "mini-antibodies" was announced by a group of scientists from the Laboratory of Molecular Biology at Cambridge, where the original monoclonal antibody (mAb) technique was developed.

Mini-antibodies, or single domain antibodies (dAbs), are said to have several advantages over the older technology. They are easier to produce, they provide a wider selection and are smaller (hence mini) which gives them more flexibility. One other group, at the Research Institute of Scripps Clinic in La Jolla, California, is also working on dAbs.

Traditional mAbs are produced by fusing an antibody-producing cell, obtained from a mouse injected with antigen, with a cancerous cell. The monoclonal antibody is then harvested from this hybridoma. That process can take up to several weeks; dAbs, on the other hand, can be produced in just three days. They consist of just the binding site of the original antibody and are produced by injecting the relevant genes, taken directly from the mouse, into bacteria. The small size of dAbs allows them to be used for such delicate tasks as destroying cancer cells inside a solid tumour, penetrating tissue quickly and blocking specific active sites on a virus.

The Medical Research Council has moved to patent the dAb technology in an effort to avoid repeating the mistakes made with mAbs, where the MRC failed to capitalize on an expected market by 1992. The MRC now hopes that the new technique will completely replace traditional mAbs. It has plans to commercialize dAbs as soon as possible and intends to ask royalties in return for licences. The La Jolla group also says it has applied for patents for the technology and has mentioned Wellcome and Behringwerke of the Federal Republic of Germany as interested parties. The two groups may try to come to a financial agreement, in order to achieve better protection of their patents. (Source: Chemistry & Industry, 6 November 1989)

Complex stabilizes N2-fixation intermediate

A complex in which the extremely unstable molecule diazene (HN=NH) is stabilized by co-ordination to two iron atoms has been prepared for the first time by Federal Republic of Germany chemists. The complex is important because it is the first that can serve, both functionally and structurally, as a model complex for enzymatic nitrogen fixation. The first two-electron reduction step in this process converts N_2 into diazene. Scientists had wondered how this highly energetic intermediate could be stabilized. In the new complex, diazene is stabilized in three ways: by co-ordination to iron, by the "steric shielding" effect of each iron's bulky ligand (derived from 2,2'-bis [2-mercaptophenyl-thio]diethylamine), and by strong hydrogen bridges between each diazene hydrogen and two nearby sulphurs of the ligand. Stabilization by hydrogen bridges is "of major significance" because such bridges would not be expected for a precursor N_2 complex and they have never been seen in isolable N_2 complexes, say the researchers, Dieter Sellmann and colleagues at the University of Erlangen-Nürnberg, Federal Republic of Germany. (Reprinted with permission from Chemical Engineering News, 16 October 1989, p. 23. Copyright (1989) American Chemical Society)

DNA fingerprinting

DNA analysis of biological evidence has been successfully introduced in over 100 US and 50 UK criminal cases, and settled thousands of paternity disputes. The US FBI began widespread use of the technique in December 1988 after one year of practical tests.

The various genetic markers comprise blood group antigens, polymorphic proteins and DNA polymorphisms in biological fluids, dried or wet. Making sense of the results requires population statistics describing the frequency of each of the marker types. DNA profiling, or DNA fingerprinting, can link a suspect to a particular piece of evidence. It can be used in cases of rape, homicide, paternity and even animal poaching.

Some 25 US states have now accepted DNA typing as evidence, and appellate courts in Florida and Maryland have affirmed DNA profiling as evidence in criminal trials. Of greatest concern to forensic chemists, the judiciary and defence bar is a false identification in which one DNA type will be mistaken for another. While environmental conditions can degrade and alter DNA, as they do most other biochemical materials, experts at the FBI laboratory and at other DNA profiling laboratories say adverse treatment of DNA simply renders it unreadable; it does not cause it to mimic another DNA sequence. However, human error is possible, as with other techniques. In addition, forensic samples may have been scraped off a sidewalk, from soil or other dirty surfaces, so they may be contaminated with bacterial DNA, and the sample may be very small. (Abstracted with permission from Chemical Engineering News, 20 November 1989, pp. 18-30. Copyright (1989) American Chemical Society)

D. APPLICATIONS

Pharmaceutical and medical applications

New test identifies legionella rapidly

A three hour test for all 14 sero groups of Legionella pneumophila is available to customers of Nalfloc, a UK water treatment company jointly owned by ICI and Nalco Chemical, Chicago. By comparison, culture tests for the organism, which causes Legionnaires' disease and other ailments, can take two weeks. The new method uses monoclonal

antibodies specific for the bacterium, tagged with a chemical that fluoresces under ultraviolet light. The rod-shaped bacterium has a fluorescent green hue when viewed through a microscope. The test is based on studies at University Diagnostics in London, which in turn developed from work at Genetic Systems in Seattle. Although the sero group 1 form of L. pneumophila is the main one that causes Legionnaires' disease, current thinking is that other sero groups may mutate to sero group 1. Thus, it is important that they also be identified in water samples, the company notes. (Reprinted with permission from Chemical Engineering News, 30 October 1989, p. 19. Copyright (1989) American Chemical Society)

Limiting heart attack damage

A drug called a complement blocker, from T Cell Sciences (Cambridge, MA), has been found to reduce heart damage in rats by 40 per cent following a heart attack. After a heart attack occurs, the complement protein part of the immune system identifies and destroys damaged heart tissue, sometimes unnecessarily. The resultant damage is known as reperfusion injury. The T Cell drug, a modified natural protein, said to block the action of the complement proteins, was produced with help from the Johns Hopkins University School of Medicine (Baltimore) and Brigham and Women's Hospital (Boston). The company says it is negotiating with SmithKline Beecham (London) and Yamanouchi Pharmaceutical (Tokyo) over development and world marketing. (Source: Chemical Week, 6 December 1989)

Skin as drug deliverer

Technology that produces skin cells engineered to produce therapeutics has been awarded US patent 4,868,116. The cells' modified DNA causes them to produce such therapeutics as hormones, enzymes, or drugs, with potential applications in chronic disorders like haemophilia and diabetes. The cells can be made in transplantable patches or sheets to deliver drugs locally or systemically. Scientists at The Whitehead Institute for Biomedical Research (Cambridge, MA), an affiliate of the Massachusetts Institute of Technology, developed the technology, and Somatix (Cambridge, MA) holds an exclusive license to it. (Source: Chemical Week, 13 December 1989)

BMS joins hunt for new platinum-based drugs

US pharmaceutical firm Bristol-Myers Squibb (BMS) has concluded a collaboration and licensing agreement with the UK company Johnson Matthey (JM) to develop a range of platinum-based anti-cancer drugs. The collaboration will build on an existing partnership between the two firms marketing Cisplatin and Carboplatin platinum-based drugs effective against a range of human genito-urinary and head and neck cancers.

The initial work will be divided between JM and the UK's Institute of Cancer Research (ICR); the groups will be responsible for the chemistry and pharmacology of the compounds respectively. BMS will conduct toxicological and clinical studies on the most promising compounds and eventually formulate any drugs.

Chairman of the ICR drug development section Professor Ken Harrap reports that researchers had stumbled on a new class of compounds whilst looking for alternatives to Carboplatin. He believes there could be a clinical candidate in 2-3 years.

Harrap explained that platinum ions from these organometallic complexes bind to the DNA in cells undergoing rapid development, preventing further reproduction. The platinum ions either link two DNA strands together or form cross-links within a single strand.

However, these drugs are not specific to cancerous cells and can damage any rapidly dividing cells. The first platinum-based drug, Cisplatin, is exceptionally toxic and causes nausea and the other side-effects associated with chemotherapy. Its use is restricted by the kidney damage it causes. Carboplatin, introduced in 1986, has the same scope of clinical activity, but is much better tolerated by patients.

Harrap and the ICR research team would like to develop a third-generation drug for use against tumours which are resistant to the present treatments. They are also developing a candidate which can be administered orally. This compound has a theoretical bioavailability of 90 per cent, compared to 15 per cent for Carboplatin. The lower dosage required and easier administration would significantly reduce the total patient treatment cost. (Source: European Chemical News, 11 December 1989)

Anticancer strawberries

Department of Agriculture scientists are working to increase the content of an organic acid in strawberries, which according to some medical studies, inhibits the start of cancer caused by some chemicals. A purified, commercially made version of the acid has been used by medical researchers in cancer studies of rats.

John L. Maas, a plant pathologist for USDA's agricultural research service, tested 40 strawberry varieties and found "considerable amounts of ellagic acid" in them. He estimates that there would be about an ounce of ellagic acid in 25 pounds of strawberries.

Mr. Maas and his colleagues at the agricultural research service fruit laboratory in Beltsville, MD., are also testing several varieties of apple for ellagic acids content. He says the compound is also found in blackberries, raspberries, blueberries, cranberries and grapes and in various nuts.

Purified ellagic acid, used medically to slow blood clotting time, appears to be effective against four classes of chemical carcinogens: polycyclic carcinogens: polycyclic aromatic hydrocarbons, nitrosamines, aflatoxin and aromatic amines.

Experimental evidence indicates that the acid keeps a hydrocarbon found in tobacco smoke and in the atmosphere (benzo[a]pyrene-diol) from inducing skin and lung cancer in animals and genetic damage in cultured human lung cells.

It reduces aflatoxin-induced genetic damage in cultured human and rat lung tissue. Aflatoxin is a natural toxin found in mouldy foods like corn and peanuts.

It also inhibits the ability of a nitrosamine (n-nitrosobenzylmethylamine) found in mouldy foods from causing esophageal cancer in rats and genetic damage in cultured human esophagus cells. (Source: Chemical Marketing Reporter, 27 November 1989)

Chemical of immune system relieves diabetes

Interleukin 1 seems to have a beneficial effect on diabetes - in mice, at least. The discovery by scientists in Switzerland is significant because the mice that the researchers studied suffered from a

type of diabetes resembling the most common form of the disease in people.

The discovery of the antidiabetic properties of interleukin-1, by Adriana Del Rey and Hugo Besedovsky at the University Hospital, Basel, may provide clues to the causes of the disease. They wanted to know whether interleukin 1 might have an effect on normal metabolism as well. To test this idea, they injected low doses of the chemical into normal mice. They found that it lowered the levels of sugar in their blood.

The next step was to try injecting interleukin-1 into mice with various types of artificially induced diabetes. One group of mice, called db/db mice, was of particular interest because they inherit the disease and develop insulin resistance - a good model for non-insulin diabetes in people. The two researchers found that blood glucose fell to levels slightly below those of normal mice for a period of more than six hours. The discovery may, one day, lead to better treatment for diabetes. (Source: New Scientist, 28 October 1989)

Cold vaccine

Nippon Kokan, as part of its move into the medical field, is to join forces with the Battelle Memorial Institute in Columbus, Ohio, to develop a vaccine against colds and other respiratory viruses. The plan is to commercialize a new vaccine by the mid-1990s, a new vaccine that is not only safer than conventional ones but will have an almost indefinite shelf-life.

The developers intend to use either a coliform bacillus recombinant DNA technique or organic synthesis using amino acids to overcome the problems of conventional raw vaccines.

NKK will provide funds and some researchers, then as work progresses, will bring the products back to Japan for clinical testing. Battelle has several achievements in the field. (Source: Manufacturing Chemist, November 1989)

UK firm unveils protein delivery breakthrough

Scientists at a UK research company have developed a technique that could abolish the need to inject protein therapies such as insulin. Cortecs, a London-based developer of sophisticated drug delivery systems, believes it has found a way of administering insulin orally.

By wrapping the insulin molecule in an envelope of fatty acid and fat molecules, the protein is protected from gut enzyme attack. The envelope degrades in the small intestine releasing insulin where it is absorbed intact into the bloodstream.

Preliminary trials with 100 patients in Europe and Asia show the technique does work. But, a company spokesman added, a lot more work is still required. Nevertheless, Cortec's chief executive, Dr. Michael Flynn, has said the firm is already talking to other companies about the possibility of an oral insulin.

The technique has potential for other therapeutic proteins which at the moment must also be injected. Cortecs already has an R&D arrangement with US pharmaceuticals group Rorer to develop delivery "capsules" for calcitonin and DAVP.

Although these are the only other therapeutic proteins being studied, the spokesman does not rule out the possibility of collaborations to develop delivery capsules for other potentially lucrative protein therapies. Drugs based on proteins with potentially massive markets include tpa, erythropoietin, the interleukins, the interferons and blood factors. (Source: European Chemical News, 11 December 1989)

IFN offers hepatitis C respite

US researchers have reported results from trials of recombinant alpha interferon that show the drug has promise in treating damage caused by hepatitis C. In two papers in the New England Journal of Medicine, scientists report that about half of the hepatitis C sufferers responded to interferon in a placebo-controlled test. Dr. Adrian Di Bisceglie of the US National Institute of Diabetes and Digestive and Kidney Diseases studied the level of this enzyme in a trial of hepatitis sufferers.

Di Bisceglie found the enzyme level returned to normal in about half of the interferon-treated patients and reduced in a further 15 per cent, but remained high in all the patients who received the placebo. He also found the effect wore off after the treatment ended.

The results suggest that while patients respond to the drug they may need higher doses or longer periods to obtain a permanent cure, said Di Bisceglie. Similar results were reported by researchers at the University of Florida. (Source: European Chemical News, 11 December 1989)

New diagnosis method for mycobacterial infections

A rapid diagnosis of tuberculosis and other infections due to mycobacteria has been developed in France. Scientists from the Institut Pasteur, Hôpital Pasteur and Institut de la Santé et La Recherche Médicale (Inserm) claim new in vitro amplication technology allows diagnosis within 2-3 days instead of the 6-8 weeks typically required through culture of bacillus taken from the patient. The new method has been successfully tested on 35 people and is already being used to diagnose viral infections such as HIV and hepatitis B. (Source: European Chemical News, 13 November 1989)

European HIV drug trials continue

The Anglo-French placebo-controlled trial of zidovudine (AZT) on individuals in the early stages of HIV infection is to continue, despite the halting of a similar trial in the US.

In the US trial, zidovudine has shown positive short-term results in slowing the progression to AIDS and advanced AIDS related complex in individuals with a CD4 lymphocyte count of less than 500. Following the apparent success, the US National Institute of Allergy and Infectious Diseases (NIAID) ordered a halt to the trial in August. Since then the drug has been approved by the US Food and Drug Administration (FDA) for use with individuals in an early stage of HIV infection.

The Anglo-French trial, run jointly by the UK Medical Research council and the French Institute National de la Santé et de la Recherche Medicale, was set up in 1987 and involves some 2,000 patients. Working party chairman Ian Weller said patients, who are randomly allocated either a placebo or zidovudine, were free to leave the trial and take the drug if they wished.

In a further move, the FDA has approved a programme granting access to zidovudine for children with advanced symptoms of AIDS. The action comes

two years after the drug became provisionally available to adults. The programme provides the drug at no charge.

Meanwhile, from Australia come reports of encouraging results for the use of thalidomide in treating some of the symptoms of AIDS. Doctors at Melbourne's Fairfield Infectious Diseases Hospital have used the drug to treat severe mouth ulcers, making eating much less painful for AIDS suffers. (Source: European Chemical News, 6 November 1989)

New yardstick for success

Using a "surrogate endpoint" should allow promising drugs to be identified more quickly than at present. This could be important because early treatment for HIV infection has recently been shown to postpone the development of symptoms.

Counts of CD4 lymphocytes - white blood cells of tne type infectd by HIV, the virus causing AIDS - have long been used by people with AIDS as a rough indicator of the progress of their disease. But the counts must be made using laser cell-sorting, a technique whose results differ from one laboratory to another, making the data from various medical centres participating in a clinical trial difficult to compare. Measurements taken by centres conducting trials under the aegis of the US National Institute of Allergy and Infectious Disease are now being standardized.

CD4 counts also vary broadly in an individual according to the time of day. Ratios of CD4 to CD8 lymphocytes are often a more useful indicator than absolute numbers of CD4 cells. But increases in the amount of CD4 cells are usually short-lived even when a given drug is having a positive effect.

Assays for the p24 core protein of HIV and tests using the polymerase chain reaction to estimate the proportion of infected CD4 cells may be useful in monitoring the status of individual patients, but their use as endpoints in clinical trials is distant. Levels of HIV core protein in the blood rise when the virus is actively reproducing, but the protein can be detected only in roughly two-thirds of those infected with HIV. The polymerase chain reaction is used extensively in research, and it can be used to determine if a baby born to an HIV-infected mother has been infected. But it is sensitive to contaminating DNA from sources other than HIV, and results from different laboratories may vary.

The shortcomings of individual tests may be overcome by using several together. But measurements of CD4 cells may be the first surrogate endpoint to be used as a means of obtaining drug approval. (Source: Nature, Vol. 341, 21 September 1989)

Synergen begins ulcer drug trials

US concern Synergen has begun evaluation of its basic fibroblast growth factor in patients with topical ulcers. The Phase II trials, to be conducted at six medical centres in the US, are designed to evaluate the efficacy of the human protein in the treatment of diabetic ulcers and venous stasis ulcers.

Basic fibroblast growth factor is a potent stimulator of angiogenesis (the formation of new blood vessels). Synergen also claims it induces the multiplication of certain cell types, including fibroblasts and vascular endothelial cells, which are required for tissue repair.

The protein is being produced using recombinant DNA techniques in pilot plant facilities at Boulder, Colorado.

Earlier this year, Synergen licensed European marketing rights for topical applications to Ciba-Geigy's Zyma subsidiary. Zyma will be responsible for conducting trials for product registration in Europe.

Synergen has also announced that its anti-inflammatory drug IL-1i has demonstrated therapeutic activity in animal models of rheumatoid arthritis. If the results are confirmed in anticipated clinical trials, Synergen believes the IL-1i protein could form the basis for the next generation of anti-inflammatory drugs.

The IL-1i protein acts as a receptor antagonist for IL-1i, preventing intercellular signal molecules from initating inflammatory cellular processes. (Source: European Chemical News, 30 October 1989)

Genentech begins clinical trials of insulin-like growth factor

Genentech Inc. has begun human clinical trials of insulin-like growth factor (IGF-I). The company plans to investigate the activities of IGF-I in a variety of nutritional and growth disorders, as well as in tissue repair.

Studies in animal models have shown that IGF-I facilitates the transport of protein building blocks, known as amino acids, into cells where they are used and that IGF-I further inhibits protein breakdown in cells. These results indicate that IGF-I may be able to preserve and restore muscle mass even in severely malnourished patients.

Since IGF-I is the chemical mediator of growth hormone action, it may also be useful for the treatment of growth retardation due to growth hormone resistance, although this effect needs to be established in clinical trials. Details from: Genentech Inc., 460 Point San Bruno Boulevard, South San Francisco, CA 94080, USA or on +1(415) 266-1000. (Source: Biotechnology Bulletin, Vol. 8, No. 9, October 1989)

Anti-rotavirus antibodies

Scientists at Taiyo Kagaku (Tokyo) - collaborating with Takuzaburo Ebina's group at Tohoku University (Sendai) - are developing two new methods to treat and prevent rotavirus-induced diarrhea.

The first method employs anti-rotavirus antibodies, which the researchers produce in chicken eggs. Using eggs is a much less expensive route than using animals to generate the antibodies. Twenty-two-and-one-half micrograms of antibody were sufficient to protect six-day-old mice against rotaviral infection.

The second approach uses a polyphenolic compound extracted from green tea. This substance inhibits viral growth; it prevents rotaviral infection of monkey cells in vitro.

The safety of the antibodies and the tea-derived compound are currently being tested as a first step towards using them as medicines and food

supplements. The scientists are also exploring means for mass-producing both compounds. (Source: Bio/Technology, Vol. 7, November 1989)

Tree may hold the key to curbing Chagas' parasite

A chemical extracted from a tropical tree seems to "immunise" insects against parasites which use them as hosts, according to scientists from the Federal Republic of Germany and Brazil. The discovery may point the way to a method of controllong Chagas' disease, a major health problem in Latin America. It may also help to fight other diseases spread by insects, such as malaria.

Chagas' disease is caused by a parasitic flagellate, Trypanosoma cruzi, which invades the human body through abraded skin. The parasite lives and reproduces inside nerve and muscle cells, particularly in the heart. About 20 million people in Latin America are infected and may develop the chronic, debilitating disease that cripples the cardiovascular system and often leaves its victims unable to work.

Chagas' disease is spread to humans by insects similar to large bedbugs. These insects live in cracks and crevices in the walls and roof of poor houses in rural areas of Latin America. They emerge from their cracks at night to suck the blood of people and domestic animals sleeping in the houses.

The bug does not pass the parasite to victims through its bite, but through its excrement. It often defecates while feeding. In the morning, a victim scratches the itchy bump and so transports the excrement, together with the parasites, into the wound.

Near Munich, Heinz Rembold has been raising one species of the bug, Rhodnius prolixus, at the Max Planck Institute for Biochemistry in Martinsried. He uses the bugs as a model to study the effects of a "natural" pesticide, known as azadirachtin. The substance comes from the seeds of the neem tree, which grows wild in India and Africa.

Azadirachtin shows promise as an insecticide because it affects the bug's hormone systems but is not toxic to humans. Researchers have shown that the chemical can prevent young bugs from moulting or pupating, and so stop them from reaching maturity. In adults, it interferes with reproduction.

The Federal Republic of Germany Government is sponsoring research into R. prolixus at the Oswaldo Cruz Institute in Rio de Janeiro, which keeps both "germ-free" and infected bugs in its laboratories. Eloi Garcia, the head of the Brazilian team, fed blood laced with azadirachtin to a group of infected bugs, and made a surprising discovery: 20 days after the feeding, the bugs were free of parasites.

The bug is an intermediate host for the parasite. It normally becomes infected with the parasite when it feeds on the blood of an infected animal. The bugs bite any warm-blooded animal, but only mammals can become infected with T. cruzi. The parasites develop and reproduce within the bug's gut, ready to be transmitted in the bug's faeces when it feeds again.

Rembold and Garcia believe that azadirachtin somehow disrupts this carefully synchronised arrangement. They found that even a few micrograms of the chemical prevented the parasite from developing in the bug's gut, and that even 20 days after a meal laden with parasites, the bugs were still free of infection.

While azadirachtin does not kill the parasites, it does disrupt the host-parasite relationship in a lasting way.

Rembold and his colleagues intend to pursue their research into the effects of the neem extract to see if it can help them to understand the basis of relationship between host and the parasite. They already know that azadirachtin affects the bug's corpus cardiacum, an organ similar to the human pituitary, and which controls the secretion of hormones. That may be the key to how the parasite lives and reproduces in the gut, and how it can synchronise its life cycle with that of its host. Azadirachtin may, therefore, be useful as a research tool in the future. (Source: New Scientist, 28 October 1989)

New weapon in the war against schistosomiasis

The US Army is to start testing an antipenetrant to keep the schistosomiasis parasite out of the human body. It may keep troops healthy in infested areas of the world, but many experts believe it is unlikely that the Army's new medication will help those who need it most - the hundreds of millions of people in the third world who are exposed to Schistosoma, public enemy number two on the World Health Organization's list of top ten scourges.

The compound, niclosamide, has a long track-recod as a killer of the snails that harbour Schistosoma and, taken internally, as a drug that kills parasitic worms. Army research has indicated that when used in a lotion it effectively blocks Schistosoma from entering a human host. The lotion prevents cercariae, the microscopic swimming stage of Schistosoma, from penetrating the skin. Since cercariae are the only stage in the parasite's life cycle capable of getting through the body's defenses, if you stop them, you prevent infection.

So far, the preparation works perfectly in mice and monkeys. Next stop, man. A niclosamide lotion is about to enter phase I trials at Johns Hopkins University Medical School to determine whether it causes any adverse reactions. Phase II trials, slated to start in Egypt and Brazil in 1990, will establish the lotion's efficacy at preventing infection.

Schistosoma is a blood fluke that generally lives in the veins of the gut and liver of its human host. Adult worms can survive up to 20 years, and heavy infestations block blood vessels. The mere presence of even a few adults acts as a focus of inflammation and infection. Worse, the females release thousands of eggs each day, which often find their way to tissues such as liver, brain and lung, where they cause considerable damage by stimulating the body to form cysts and scar tissue around them.

Most eggs, however, pass through the bladder or wall of the gut. Once outside, they hatch and infect water snails. The parasite multiplies inside the snail, giving rise to thousands of cercariae that exit the snail and swim free in search of a mammal in which to complete their life cycle. When the cercaria makes contact with skin it releases enzymes that dissolve the protein of the skin, affording easy entry.

The WHO estimates that some 200 million people world-wide suffer one or another of the forms of schistosomiasis. Only malaria causes more sickness and debility.

In 1982, Captain Robert E. Miller recognized that the most promising compounds were all so-called salicylanilides. Miller's search of the Army's data base of chemicals revealed that niclosamide was also a salicylanilide, and in animal tests a single application proved able to block penetration by cercariae for 7 days or more.

Other salicylanilides were even more effective antipenetrants, but the army chose not to pursue them.

The long lasting protection is thought to be the result of niclosamide binding chemically with the outer layers of the skin. Researchers speculate that the enzymes that the cercariae secrete to get through the skin sever the bond between niclosamide and skin, releasing the compound which then kills the cercariae.

Field trials will probably take place among rice growers in the Nile delta and farmers in the Bahia region of Brazil who spend much of their time in infested waters. The trials will measure re-infection among people who have been treated to eliminate the disease. They will be given either niclosamide or a placebo to apply to the skin.

Army researchers are confident that niclosamide will come through the trials as a safe and effective lotion to prevent infection by cercariae. That will suit the military need to keep troops healthy. But will it help the 600 million people who live with the threat of schistosomiasis?

Gerald Webbe, professor of applied parasitology at the London School of Hygiene and Tropical Medicine, who discovered in 1975 that concentrations of niclosamide too low to kill snails nevertheless killed cercariae, thinks that lotions and creams will not be made available because there is no market among the desperately poor people who are most exposed. And even if they were available, Webbe says local people would not use them.

Miller, who discovered the topical antipenetrant, concedes that the lotion might be impractical because it has to be applied carefully and regularly. But his colleague Reynaldo Dietze, associate professor at the School of Medicine of the Federal University of Espirito Santo in Brazil, is working on a niclosamide soap that Miller thinks could be the answer. The Brazilian farmers he has been working with are very hygienic and a soap containing 0.1 per cent niclosamide would be effective and cheap. (Extracted from Science, Vol. 246, 8 December 1989, p. 1242-3, J. Cherfas. Copyright AAAS)

Allelix and BRI collaborate to develop new pharmaceuticals for migraine and psychiatric disorders

Allelix Biopharmaceuticals Inc. and the Biotechnology Research Institute (BRI) of the National Research Council of Canada are collaborating on a Canadian research and development programme to develop new pharmaceuticals for central nervous system (CNS) disorders such as migraine, schizophrenia, anxiety and depression. The cost-shared R&D venture commits $1.5 million over two years and focuses on serotonin.

Serotonin has long been known as an important compound in the body. It functions through a precise interaction with specific molecules called serotonin receptors which are found on the surface of certain nerve cells in the body. The amounts of serotonin and its receptors are normally very precisely controlled, but abberations may lead to such debilitating disorders as depression, severe anxiety, schizophrenia and migraine headaches.

The collaborative programme, which will be co-ordinated by Drs. Michael Wosnick of Allelix and Michael Dennis of BRI, takes particular aim at the serotonin receptors. (Source: Company News Release, 23 November 1989)

G-CSF may help chemotherapy

Granulocyte colony stimulating factor (G-CSF) could aid chemotherapy for small cell lung cancer, according to P Dexter of the Paterson Institute for Cancer Research. G-CSF produces a significant increase in neutrophil counts, but does not significantly affect platelets, lymphocytes, monocytes, eosinophils or haemoglobin. G-CSF reduced the period of neutropenia 80 per cent, and neutrophil counts returned to normal within two weeks after chemotherapy began. No episodes of infection were reported in chemotherapy patients while G-CSF was being administered, against six episodes, requiring 30 days of hospitalization, while the 12 patients were not on the G-CSF. G-CSF might allow for more intensive chemotherapy, and if animal models are valid for humans, the more intense chemotherapy may be able to produce 100 per cent cures, rather than the total failure often experienced now.

Work in Australia has also shown G-CSF to halve the duration of neutropenia in patients with lymphoma and acute lymphatic leukemia, according to G. Morstyn of the Royal Melbourne Hospital. Phase 3 clinical tests are now underway. (Extracted from Medical World, 9 October 1989)

Gelatine as drug carrier

Gelatine could be used as a drug carrier to deliver immunomodulators to macrophages, according to researchers at Kyoto University. The macrophages ingest gelatine, and so the drugs are delivered right to the macrophages. The technique has been tested using interferon and mouse colony stimulating factor (M-CSF), producing macrophage stimulation several hundred times the effect obtained when the drugs are administered in conventional dosage forms. The tests also showed that interferon dosages 1/500th those normally given were able to curb tumour growth in mice. (Extracted from Japan Chemistry, 5 October 1989)

New CF diagnosis test

A new test can reliably and simply diagnose cystic fibrosis in newborns, according to F.J. Accurso of the University of Colorado School of Medicine (Denver). A five-year study indicates that the disease can cause abnormalities before any obvious symptoms appear. Many children with the disease are hospitalized several times before an accurate diagnosis is made. The new test costs only about $2. It measures immunoreactive trypsinogen (IRT) in a dried drop of blood. Trypsinogen is normally converted to trypsin for digestion. In CF patients, some trypsinogen enters the blood stream. Of 280,000 babies tested, 78 had the disease, as confirmed by a second IRT test and "sweat test" that is the conventional diagnostic tool. Only five CF cases went undetected by the IRT test. Early diagnosis can allow doctors to give supplemental digestive enzymes. Parents unanimously agreed that the early diagnosis and treatment were preferable to waiting until the child was older. (Extracted from Science News, 7 October 1989)

Japanese team latches onto an antibody that shows promise against HIV

Research in Japan has raised hopes that an experimental technique for killing cancer cells may also work against AIDS. It relies on a monoclonal antibody, which, the researchers say, seems to kill cells infected with AIDS but leave healthy cells intact.

Monoclonal antibodies are pure, identical copies of a cultured antibody that is specific to a particular antigen.

A joint research team from Yamaguchi University and Tokyo Metropolitan Institute of Medical Science announced the finding at a meeting of the Japanese Cancer Association in Nagoya.

The researchers said that they have succeeded in producing a monoclonal antibody specific to the Fas antigen on the surface of cells infected with the HIV virus. The team tested the antibody on cultures of human T-cells infected with HIV, the virus that causes AIDS. Three days after treatment 98 per cent of the infected cells were dead.

Shin Yonehara of the Tokyo institute said the next stage in the research will be to investigate the side effects of the treatment of normal T-cells, before going on to perform animal tests and then trials in people. Yonehara could not say when this would happen.

Researchers still face many problems before they can turn the Japanese discovery into a drug for patients with AIDS. They do not know how the antibody works, although previous research at the Tokyo Metropolitan Institute of Medical Science suggests that it follows a similar pattern to tumour necrosis factor, a natural substance that kills cancer cells in experiments. Another problem is that the Fas antigen may not appear on all cells that are infected with AIDS. Japan still has relatively few people suffering from AIDS or carrying the HIV virus. (Source: New Scientist, 4 November 1989)

Battling AIDS

Drs. Ron Kennedy and Tran Chanh at San Antonio's Southwest Foundation for Biomedical Research have developed a potential AIDS vaccine, which appears to have slowed the progress of the deadly disease in four trial patients in the UK. The vaccine, which uses antibodies produced in mice, has a two-fold effect when injected into the human bloodstream. The antibodies attach to receptors on white blood cells, preventing AIDS viruses from attacking them, and at the same time, produce a second generation of themselves, called anti-idiotypes, which bond with individual AIDS viruses and inactivate them. The vaccine's potential has led to a three-year extension of a $2 million international AIDS research programme, encompassing a five-year effort that will hopefully lead to breakthrough advancements in the battle against AIDS. For more information, contact Ken Slavin or Dee Dee Donohue, Dublin-McCarter & Associates - 512/227-0221. (Source: Biobytes (San Antonio Biotechnology News & Information, produced by Dublin-McCarter & Associates), November 1989)

Second AIDS drug available to patients in the USA

DDI has become the second AIDS drug to be officially available to patients. The drug, produced by Bristol-Myers and developed by US National Cancer Institute scientists, has been approved by the US Food and Drug Administration for use in patients who do not tolerate the only approved AIDS drug, AZT. Patients at very advanced stages of the disease and who do not respond to AZT can also receive DDI. Phase II clinical trials of the drug have just started, after phase I trials showed higher intoxicity than had previously been expected.

Phase I trials indicated that DDI can be tolerated by "the vast majority of patients", according to Robert Yarchoan, one of the scientists who developed the drug, together with Samual Broder and Hiroaki Mitsui. However, nerve damage in the feet and, less commonly, damage to the pancreas can result from high doses of or long-term treatment with the drug. The symptoms were reversible, though, if detected early. Maximum doses of DDI have been set at 750 mg/day per patients over long periods and at 1 g/day for a short time.

Three different phase II trials have started recently. Two of the studies will compare DDI's effectiveness to AZT's and one is designed for patients who cannot tolerate AZT. About 2,600 patients will be involved in the trials, conducted by the AIDS clinical trials group of the US National Institute of Allergy and Infectious Diseases together with Bristol-Myers.

- Results from Dutch trials show that AZT helps prevent dementia, one of the most common neurological disorders in AIDS patients.

- Compound Q, a drug derived from Chinese cucumber root, has been shown to be effective against AIDS in unofficial clinical trials in the USA. However, it is unlikely to be a cure in itself. The nature of the trials was condemned by many researchers. (Source: Chemistry and Industry, 16 October 1989)

Test finds defects in unfertilized human eggs

Women who carry a genetic defect can now have their eggs tested for the mutation. The test, developed by scientists in the US, can be applied to ova from women who are attempting in vitro fertilization (IVF). Because it is done before the egg and sperm fuse, there is no need to sample the genetic material of embryos which might then have to be discarded. The researchers believe that this aspect of their test will make it more acceptable to anti-abortionists.

Yuri Verlinsky of the Illinois Masonic Medical Center announced the test at the annual meeting of the American Society of Human Genetics, held in Baltimore, Maryland. He and his colleagues thought of the idea when they were obtaining eggs from the ovaries of several women attempting IVF.

Normally, says Verlinsky, scientists destroy ova when they extract material from them. But he saw an opportunity to circumvent this during meiosis, the stage in the development of an egg when it halves its complement of chromosomes. (The sperm restores the other half after fertilization). At meiosis, half the egg's chromosomes are packaged in a nodule that forms at the cell wall called the first polar body, and which is subsequently discarded.

Verlinsky and his colleagues at the centre's Reproductive Genetic Institute were able to extract the DNA of the polar body with a micropipette. They then multiplied sections of it to find a mutation

that causes a rare disorder known as alpha-1-antitrypsin deficiency. This affects the alveoli, or air sacs, of the lungs, and sufferers usually contract emphysema by the age of 40.

The new diagnostic technique relies on the fact that people have their chromosomes in pairs, acquiring one chromosome of a pair from the mother and one from the father. In so-called recessive disorders, a person who inherits a faulty gene on one chromosome and a normal gene on the other will merely carry the disorder, remaining healthy themselves. If both chromosomes are defective for the gene, however, the person will suffer from the disease.

If Verlinsky finds the mutant gene in the polar body, he knows that its counterpart in the egg is in good order, and vice versa. He worked with a couple in which both partners were carriers, and he was able to select an egg that had expelled the faulty gene. He fertilized it and returned it to the woman's womb. Verlinsky rejected eggs in which the polar body carried the intact gene.

Although the pregnancy failed for other reasons - IVF fails in a high proportion of cases - Verlinsky considers the diagnostic process to be a success. He says that the method could be applied to any recessive disorder in which scientists know the mutation or a DNA marker. These include thalassaemia, Tay-Sachs disease and cystic fibrosis.

So far, Verlinsky's attempts to extract DNA from sperm have failed. Other researchers, too, have been unsuccessful. But in recessive disorders, if one version of the gene is intact, the worst that can happen is that the child is a carrier.

Verlinsky says that the new procedure is only practical during IVF and suggests it should be restricted to couples with a family history of recessive disorders. It is preferable to sampling material from an eight-celled embryo, a current technique for pinpointing genetic defects. (Source: New Scientist, 25 November 1989)

Monoclonal antibody for tetanus toxin

Morinaga Institute of Biological Science has developed a human monoclonal antibody that neutralizes tetanus (lockjaw) toxin. This monoclonal antibody, available in six types, can be used in combination for added effects and for completely neutralizing the toxin even with a low concentration. As compared with globulin tetanus antitoxins currently used clinically, its neutralization is 10-100 times greater and there is also the possibility of preventing infections of blood disease. The company has already established a system for mass producing the antibody.

The researchers, with the co-operation of the Research Institute for Microbial Diseases of Osaka University, endeavoured to produce antibodies using tetanus toxoid as the antigen. Lymphocytes were extracted from the peripheral blood of healthy volunteers immunized with tetanus toxoid and cells were fused by using human-mouse heteromyeloma and polyethylene glycol, which revealed that several types of human monoclonal antibodies are produced with respect to tetanus toxin. Further examination of these monoclonal antibodies showed that there are six types which react with the three fragments of tetanus toxin, each of which was reported as serving to adhere onto cells and generate toxins.

Examining the activities of these six types of monoclonal antibodies revealed that they neutralize over 0.001 IU/100 μg, with one of these types having an exceptional neutralizing capability of 5.7 IU. Using the six types in combination and comparing their effects with existing serums and the state of progress of maladies showed that their neutralization activity was 10-100 times greater.

Whereas conventional tetanus anti-toxin sera accompany the hazard of viral infection since they use blood as the raw material, the new antibody, being a monoclonal antibody, completely prevents infection. The company used a special culture medium with insulin and other substances added, and succeeded in producing 40 mg/d of antibody having a concentration of about 50 μg/ml. Further information available from Morinaga Institute of Biological Science 1-1, Shimo-Sueyoshi 2-chome, Tsurumiku, Yokohama City, Kanagawa Pref. Tel: 045-572-8247. Fax: 045-571-5042. (Source: JETRO, January 1990)

Livestock applications

US researchers unveil SIV vaccine success

Researchers in the US have unveiled results that are being hailed as a breakthrough in the search for an AIDS vaccine. The team, led by Michael Murphey-Corb at Louisiana's Tulane University Medical Centre, reports that Rhesus monkeys immunized with whole inactive simian immunodeficiency virus (SIV) were protected from infection and disease caused by a live version of SIV, a monkey equivalent of the AIDS virus.

A vaccine was produced by killing SIV with formalin. When given to nine Rhesus monkeys, the inactive SIV was able to stimulate antibody production. Treated and untreated monkeys were then exposed to live SIV.

Murphey-Corb's team has reported that it was able to fully protect eight Rhesus monkeys from a challenge SIV injection. A ninth monkey was also clinically normal one year after the challenge, but blood cell tests indicate viral infection had occurred.

However, the challenge infection caused infection in all 17 unvaccinated monkeys. Moreover, more than three quarters of these monkeys were dead within seven months of infection.

Commenting on the results, Murphey-Corb claims they may prove useful in the search for a human AIDS vaccine. (Extracted from European Chemical News, 18/25 December 1989)

New oral vaccine immunizes chimpanzees against hepatitis B

Wyeth-Ayerst Research scientists say that chimpanzees can be successfully immunized against hepatitis B with a new oral vaccine. The vaccine uses a genetically altered virus in a gelatin capsule. The researchers attach the major surface antigen of the hepatitis B virus to adenoviruses. Oral vaccines against adenovirus are very safe, based on military records. When the altered adenoviruses were given to three chimpanzees, two developed immunity and resisted a challenge with hepatitis B virus given eight weeks later. The third did not develop antibodies, and so developed hepatitis. A stronger antibody response might be elicited in humans, since adenoviruses do not normally infect chimps, but they do infect humans. The next step may be human trials. (Extracted from Science News, 23 September 1989)

Using antibodies to increase yields

Agricultural and Food Research Council (AFRC) researchers are evolving two novel strategies for increasing milk yield and carcass weight in cows and other livestock. Exploiting the animals' own immune systems, the techniques may offer more convenient and acceptable alternatives to using anabolic steroids (now banned from animal husbandry in the European Community [EC]) or bovine somatotropin (BST, subject of an 18-month EEC moratorium imposed in September). Both approaches hinge on introducing anti-idiotypic antibodies that remain in the bloodstream for long periods, thus obviating the need for the repeated injections necessary with BST.

Working at the Hannah Research Institute (Ayr, Scotland), David Flint and his colleagues have learned how to induce animals to make antibodies that mimic the structure and action of BST. By injecting BST into rabbits, they have generated anti-BST antibodies which, injected back into cows, provoke the formation of anti-idiotypic antibodies resembling BST in shape (if not in detailed chemistry). These antibodies are specific to BST: They bind to its receptors, but not to those for other hormones such as insulin and prolactin. Flint and his co-workers also report that both the mimics and BST itself promote growth when injected into rats deficient in their own growth hormone.

Meanwhile, at the AFRC Institute for Grassland and Animal Production (Hurley, Berks), Isabel Forsyth and colleagues have found that monoclonal antibodies directed against BST can enhance, rather than impair, its biological action. In one series of experiments, lactating sheep given growth hormone increased their milk yield. When given an identical dose of hormone complexed with monoclonal antibody, however, they produced nine per cent more milk over the same treatment period. Presumably, the antibody promotes the action of BST by altering its binding to the BST tissue receptor.

The researchers next set out to identify the epitope of growth hormone associated with the enhancement, and to raise antibodies against it. Such antibodies may derive from more than one B lymphocyte and thus not be strictly monoclonal, but may behave as such. Their presence in an animal's circulation should thus enhance the biological activity of its own hormone. Preliminary results indicate that this will be feasible. In sheep, Forsyth and co-workers have raised an antibody against an epitope of growth hormone, and given a partially purified version of it to another group of sheep. They found that the antibody combined with circulating, endogenous growth hormone and increased it bioactivity. Compared with untreated controls, the animals showed reduced fat synthesis.

The Hurley team believes that a strategy based on one or two injections of small amounts of hormone epitope, where both hormone and enhancing antibody are produced by the animal itself, offers practical and regulatory advantages over repeated injections of large quantities of exogenous hormone. (Source: Bio/Technology, Vol. 7, November 1989)

Agricultural applications

Micropropagation of Cedro by tissue culture

The Forestry and Forest Product Research Institute of Japan has cultured the tissue of Cedro, a useful tree of the Peruvian Amazon Region. Eucalyptus, acacia and other imported trees have been used for reforestation in the tropical forests of South America, but the tissue culture of cedro is expected to clear the way for afforestation with native species having high added values.

Shoot-tips of 5-month-old cedro seedlings were used for the tissue culture. Shoot-tips cut from the young seedlings and cultured in an agar medium propagated seedlings at a rate of four times every six weeks. The propagated seedlings were then transplanted to a separate culture bed for rooting. The rooting rate was 90 per cent.

Cedro is an important forest tree and its wood is highly valued for its quality. It is used for high-class domestic furniture and doors, however Cedro has been severely decimated by the Meliaceae borer Hypsipyla and only a few good quality trees for high-class interior decorative materials are available from a hectare of forest. Morever, the fact that cedro bears fruit only once very three years is another reason why large-scale afforestation by seed cultivation is difficult.

The greatest advantage of tissue culture is the mass propagation of seedlings having the same genetic quality as that of the good quality original tree. Thus, mass propagated seedlings are expected to have resistance against the Hypsipyla borer. Moreover, tissue culture can supply seedlings in bulk irrespective of the number of seeds. Further information available from Forestry and Forest Products Research Institute, Ministry of Agriculture, Forestry and Fisheries, 1, Matsunosato, Kukizaki-cho, Inashikigun, Ibaraki Pref. Tel: 0298-73-3211. Fax: 0298-74-3720. (Source: JETRO, November 1989)

In search of wild rice

Rice is a very old grass, scattered since early geologic periods in the tropics. According to Dr. T.T. Chang, head of the International Rice Germplasm Centre (IRGC) at the International Rice Research Institute in the Philippines, the genetic diversity of cultivated rice, especially those in Asia, has been enriched by thousands of years of natural and human selection by countless rice farmers and by dissemination by rice-eaters, even before scientific plant-breeding intensified in the 1960s.

When high-yielding semi-dwarf rice varieties became popular in the 1960s scientists were concerned the new varieties might lead to the loss of traditional rice in a "genetic wipe-out". The concern was understandable. In tropical Asia, the area planted to modern varieties increased from 2.6 million hectares in 1967 to 28 million ha. in 1977.

Rice workers worldwide responded in a massive collection of land rices and wild species of rice. Between 1972-1985, over 40,000 samples of rice seeds were gathered and sent to the IRGC which now stores over 80,000 distinct types of rice.

This genetic material has been used by researchers to help stabilize rice production in areas where crops face disease, insect, soil, low temperature, excess water or drought problems. Newly-opened areas in Africa and Brazil can now be planted to rice because of the genetic materials pooled from diverse habitats. (Source: Development Forum, November/December 1989)

Quantifying potato pathogens by immunoassays

Traditional methods of quantifying fungal pathogens in plants are tedious and one commonly used method, based on chitin determination, is inappropriate for studies on potato late blight

because that compound is not a component of the cell walls of Phytophthora spp.

Enzyme linked immunosorbent assays (ELISA) have been used at the Scottish Crops Research Institute for detecting viruses in plants and the expertise was applied to developing an ELISA to measure the amount of P. infestans in potato leaves.

Success in detecting P. infestans with ELISA stimulated the development of a similar technique for detecting Spongospora subterranea, the cause of powdery scab. However, because this fungus is an obligate pathogen, it was necessary to use infected tuber tissue as the antigen. The resulting antiserum reacted with scabbed tuber tissue and with healthy tissue, but the affinity with the host tissue was removed by absorbing it with healthy tuber tissue.

The purified antibodies detected a low disease incidence in peelings from lightly-infected tubers using ELISA. Symptomless tubers selected from a bulk of potatoes with the disease also gave a positive result, presumably due to the presence of contaminating spore balls. Details from: Bob Exley, Scottish Crops Research Institute, on (0382) 562731. (Source: Biotechnology Bulletin, Vol. 8, No. 9, October 1989)

Food and food processing applications

Diagnostic kit for beer

An innovative diagnostic kit for brewers has been developed at the South Australian Institute for Technology (SAIT) and is now undergoing field trials. Funded by S.A. Brewing, CSIRO and SAIT, the kit is designed to assay the minute quantities of enzyme which is added to beer to prevent clouding. Priced at around $200, its designs assure brewers that this new method of assaying is cost effective because it is more accurate, easier, more convenient and far quicker than the traditional, labour intensive method. Strong interest has already been shown by one brewing consultant who plans to take the kits to the UK for trials. (Source: ABA Bulletin, Vol. 4, No. 5, October 1989)

Crisper tinned vegetables

An enzyme that prevents tinned vegetables from getting soft has been discovered by M. Bourne of Cornell University (Ithaca, NY). Pectin methylesterase produces molecular bridges of calcium atoms, and so can restore the pectin polymers that are responsible for a vegetable's firmness. The pectin is degraded by heat during the blanching and sterilization processes. Blanching at 60-65° C, and then allowing 30 minute for the enzyme to work, makes the canned vegetables much crisper. Adding some calcium and citric acid lowers pH and makes the vegetables even crisper. (Extracted from New Scientist, 23 September 1989)

Low-cost route to L-alanine

Mitsubishi Petrochemical has developed a low-cost route to the amino acid L-alanine from fumaric acid using fungi. The company plans to commercialize production in Japan for use as a food additive. Costs should be as low as one-third those of conventional enzymatic processes.

Central to the new process are two fungi, Brevibacterium flavum and Pseudomonas dacunkae, which contain high concentrations of the enzymes aspartase and aspartate β-decarboxylase, respectively.

The fumaric acid is first reacted with L-aspartic acid in the presence of the aspartase, and the product is then converted into L-alanine by means of the aspartate β-decarboxylase. The reaction is reported to occur at temperatures of around 45° C.

L-alanine is involved in the body's metabolism as a nitrogen carrier. High process costs in Japan have restricted its use to intravenous solutions. Mitsubishi is now optimistic its new route will cut the price to open up opportunities for use as a food additive. (Source: European Chemical News, 11 December 1989)

Odour detector

Scientists at Hokkaido University (Sapporo) have developed an ultra-sensitive odorant detector using liposomes. The detector measures subtle changes in the physical properties of liposomes after they have absorbed small amounts of lipid-soluble compounds. According to Kazumi Kurihara, the sensitivity of the liposomes depends on their chemical composition. For instance, Kurihara says that amylacetate (a compound with a fruity odour) can be detected at a concentration of one microgram per litre by liposomes composed of 90 per cent lecithin and 10 per cent phosphatidylserine. By contrast, liposomes composed entirely of lecithin are one-million-fold less sensitive. Moreover, says Kurihara, individual odourants produce different perturbations in liposome structure.

The liposome sensor is 50,000-fold more sensitive than humans at detecting odours. If scientists can develop a practical sensing device, it could be used for detecting everything from industrial pollutants to illegal drugs. Such devices could also be used to monitor the quality of perfume and processed food. (Source: Bio/Technology, Vol. 7, November 1989)

Chemical applications

Fermentation butanol?

Researchers from Michigan Biotechnology Institute and Michigan State University have developed a fermentation route that produces n-butanol directly from carbon monoxide, a process they feel could be commercially attractive.

The discovery, using Butyribacterium methyloltrophicum, is called the first evidence of a direct biological pathway from carbon monoxide to butanol and is thought to indicate potential for one-step butanol production based on syngas.

The one-step conversion can operate at ambient pressure and temperature and produce butanol in the presence of sulphur contaminants, unlike commercial syngas-based catalytic processes, such as the oxo route, which are sulphur sensitive.

Mark Worden, an assistant professor in MSU's department of chemical engineering, says the fermentation is currently yielding butanol concentrations of 0.5 grams per litre; the process will begin to look economically attractive only at concentrations about ten times that, but he believes such yields obtainable.

Research is now focusing on increasing yield. The micro-organisms used can metabolize hydrogen, so the scientists are looking at using H_2 to reduce butyric and other acids formed in the fermentation to the corresponding alcohols. Also possible is

incorporating other commercial fermentation processes to carry out the reduction.

While cost of production has yet to be determined, the researchers think the process could offer distinct advantages for traditional butanol markets as well as fuel additive uses. (Source: Chemical Marketing Reporter, 20 November 1989)

Energy and environmental applications

New environmental research organization

Research into the fate of pollutants in the environment and their effects on ecosystems, and developing biotechnologies to remove toxic chemicals from effluents and waterways, are among the principal objectives of the new European Environmental Research Organization (EERO). Established as an analogue to the European Molecular Biology Organization (Heidelberg, FRG), the non-profit, tax-exempt foundation is "entirely non-political, and consists solely of scientists renowned for their contributions to environmental science and other individuals active in the promotion of environmental research".

EERO's initial support comes from a grant from the Volkswagen Foundation (Hannover, FRG), and contributions from the Dutch, Swiss, and Spanish Governments. It will organize fellowships, workshops, and advanced laboratory courses designed to promote research on environmental problems and to train scientists in appropriate techniques.

Over its first five years, the organization plans to sponsor 70 long-term postdoctoral fellowships (up to 24 months, with a possible 12-month extension) and 60 short-term fellowships (up to three months). Recipients will work in the laboratories, and under the guidance of established experts. The availability of the first EERO fellowships is being publicized, and in April EERO will sponsor a five-day symposium on Environmental Biotechnology in Braunschweig in association with the Gesellschaft für Biotechnologische Forschung. The symposium will encompass biomonitoring, waste treatment and biodegradation pathways, strain improvement, the environmental impact of bioremediation processes, and the rapid containment of environmental catastrophes.

During the second phase of its activities, EERO will establish a network of training centres, begin publishing manuals on modern techniques in the environmental sciences and create a central assessment unit to evaluate and compare different national and international regulations, recommendations, and monitoring data. (Extracted from Bio/Technology, Vol. 7, December 1989)

New pulp mill effluent treatment

Lund University researcher Thomas Welander has detailed a novel anaerobic method of detoxifying pulp mill effluent. In his process, pulp effluent is pre-treated by addition of a number of undisclosed micro-organisms and aluminium ions, and then transferred into an anaerobic reactor where lack of oxygen results in the formation of methane. Welander claims tests have shown the anaerobic treatment primarily reduces acetate, methanol and carbohydrates, while wood extracts can be removed by an aerobic post treatment. The byproduct methane can be used as fuel for the plant. The method has been on trial for two years treating some 2,800 m^3 of toxic effluent/day at a pulp mill in Timara, north Sweden. (Source: European Chemical News, 11 December 1989)

ICI to market Biopol biodegradable plastic bottle in the Federal Republic of Germany

ICI is planning to spend 10 million pounds sterling to double the capacity of its pilot fermentation plant at Billingham, used to produce Biopol - made by Alcaligenes eutrophus. Federal Republic of Germany consumers will shortly be able to buy cosmetic and toiletry products in bottles made from Biopol, the plastic polyhydroxybutyrate (PHB). PHB-V is similar to polypropylene and can be used for films and bags. ICI hopes that the growing interest in environmental issues will translate into substantial Biopol sales. (Source: Biotechnology Bulletin, Vol. 8, No. 10, November 1989)

New biodegradable plastics

Researchers at the Tokyo Institute of Technology have developed an easy-to-process biodegradable plastic that is manufactured by bacteria. Previously the bacteria produced an optically active polyester P(3HB) that was readily decomposed by soil microbes, but was extremely brittle. The Tokyo Institute researchers changed the carbon feedstock given the bacteria causing them to synthesize a co-polymerized polyester P(3HB) -co-(4HB), which is highly elastic and can be processed into threads or films. The threads have strength comparable to nylon threads and are very transparent and pliable. Materials made from the new co-polymer decomposed completely in three-four months when buried in the ground. The bioplastic is optically active, piezoelectric, biocompatible and hydrolytic.

Meanwhile, researchers at the Laboratory for Renewable Resources Engineering, Purdue University have developed a biodegradable plastic that retains its properties on the shelf. Most biodegradable plastics are moisture sensitive and do not retain their strength or flexibility when stored, but the new material has good shelf-life while biodegrading in the presence of soil or ocean water. The material combines a cornstarch/styrene co-polymer graft mixed with natural starch acetates. The co-polymer was achieved by use of an emulsifying agent. (Extracted from New Technology Japan, October 1989 and Design News, 4 September 1989)

Biodegradable plastic from lactic acid

A process to make bio- and photodegradable plastics from lactic acid has been developed by researchers at Argonne National Laboratories. The degradable films are 85-100 per cent lactic acid. The other ingredients can include compounds to make the plastic more sensitive to light or to water hydrolysis. The researchers produced the lactic acid from potato starch. The lactic-based films could be used in agriculture. The plastic may be produced completely with lactic acid or by a blend of 90-95 per cent of lactic acid with polymers that are petroleum-based. Heretofore, biodegradable plastic that incorporated corn starch usually was not strong enough for use in such items as shopping and garbage bags.

Lactic acid might also be used to decontaminate meat and poultry. A process developed by Purac awaits US Department of Agriculture approval. A study indicates that a 2 per cent lactic acid solution at 140° F kills 94 per cent of Salmonella bacteria.

Lactic acid can also be used in ethyl and butyl lactate solvents. (Extracted from Chemical Marketing Reporter, 16 October 1989)

Enzyme developed to degrade lignin

Oji Paper (Tokyo, Japan) has developed an enzyme capable of biodegrading non-fibrous lignin that could form the basis of a non-polluting wood pulp processing technology. Current pulp processing methods involve the use of polluting chemicals and generate malodorous waste streams. The new enzyme, a phenol oxydase, was discovered in a white-lot mushroom, Coriolus hirgutus, and has been successfully gene transferred to bread yeast colonies. The Coriolus enzymes differs from previously discovered lignin degrading enzymes in that it is selective toward lignin and does not attack wood pulp cellulose. Thus far, Oji Paper has only been able to get a few milligrammes of enzyme per litre of culture medium, which is inadequate for commercial production, but the company is actively working to achieve commercial quantities. (Extracted from New Technology Japan, September 1989)

Progress made on PCB biodegradation

Recent progress makes it possible to test natural biodegradation of polychlorinated biphenyls (PCBs) in the Hudson River within the next two years, according to General Electric Co. researchers. GE researchers have found that adding small amounts of nutrient medium (basically nitrogen, phosphorus, and minerals) to the naturally occurring culture of aerobic and anaerobic bacteria can cut the degradation time for the most heavily chlorinated PCBs by 50 per cent. In laboratory tests lasting 23 weeks, concentrations of the most highly chlorinated PCBs in Aroclor 1242, the most common type in the upper Hudson River, were reduced more than 90 per cent. Anaerobic bacteria in the river sediment attack the more highly chlorinated PCBs, stripping the chlorine atoms. This makes the molecules more susceptible to attack by aerobic bacteria. Daniel A. Abramowicz, manager of the environmental technology programme at GE's corporate R&D centre in Schenectady, N.Y., says GE plans to develop a two-step process that can completely eliminate PCBs in river sediment. (Reprinted with permission from Chemical Engineering News, 13 November 1989, p. 21. Copyright (1989) American Chemical Society)

Mobile pesticide cure

A new technique to decontaminate pesticide waste water produced in agricultural communities is being developed by the US Department of Agriculture (USDA) and Ciba-Geigy Corp. The aim is to develop a portable method of destroying pesticides in water such as those used in spraying equipment.

The treatment uses a combination of chemical and biological attack. The waste water is first oxidized in a tank, by the introduction of ozone, followed by percollating through a soil bed innoculated with Pseudomonas A.

The bacteria, which is naturally occurring, was discovered and patented by Ciba-Geigy and breaks the otherwise resilient ring structures found in most pesticides. The byproducts of the process are ammonia and urea, which if discharged, are converted by soil bacteria into nitrogenous compounds. (Source: European Chemical News, 20 November 1989)

Muck, metals and microbes

Of the potentially toxic elements in sewage sludge, zinc and cadmium are most readily absorbed. Zinc is generally present in greater amounts than other metals and is toxic to plants at concentrations that are too low to cause toxicity in animals. Zinc contamination is, therefore, a problem for crop production; and since plants die if an excess of zinc is absorbed they act as "barriers" preventing too much zinc from being consumed by animals.

By contrast, concentrations of cadmium in plants can become dangerously high for their use as food, without any obvious effects on growth. Also, cadmium accumulates in the kidneys of mammals over long periods where it can eventually disrupt them. Most concern over the build-up of heavy metals in food chains is focused on cadmium.

Guidelines for environmental protection are based on evidence which scientists use to infer upper concentrations of metals in soil that are not directly toxic to most plants and are unlikely to be toxic to animals or people. But there is growing evidence of damaging effects on microbial processes in the soil at metal concentrations close to these guidelines, which may cause serious problems for agricultural production in the future.

It was research done at the Woburn Experimental Farm which raised the alarm on the toxic effects of heavy metals on micro-organisms in soil. Thanks to a long-term field experiment begun there in 1942, Woburn has both uncontaminated plots of soil and plots contaminated with metals at concentrations close to the limits laid down by the current guidelines.

Some leafy vegetables grew less well on metal-contaminated plots than on uncontaminated plots, but no visible effects on growth were seen in other crops. But when white clover was sown in 1984, there were alarming differences in yield between the high- and low-metal plots. Yield was reduced by more than 40 per cent where heavy metals had been added, and the plants were yellow and stunted.

These effects were reproduced in glass-house experiments where clover was sown in soil taken from the field, but feeding the plants with nitrogen eliminated the difference in growth. This suggested that the metals were not poisoning the plants directly.

Clover plants grown in uncontaminated soil had root systems with pink nodules containing the nitrogen-fixing bacteria Rhizobium. Root systems of the stunted plants grown on metal-contaminated soil were covered in small white root nodules which could not fix atmospheric nitrogen. So the metals were affecting the growth of plants by depriving them of nitrogen.

Large concentrations of metals are directly toxic to Rhizobium and the small white nodules are formed by the only strain of Rhizobium which can survive in metal-contaminated soil. As this strain of Rhizobium can tolerate larger concentrations of metals than most others, it may be possible to engineer strains which can tolerate metals and fix nitrogen.

In fact, nodules can be made to fix nitrogen even in metal-rich soil by inoculating the soil with a normal strain of Rhizobium. Once the Rhizobium bacteria are within the tissue of the root nodule, they are protected from the metals in the soil. But if no clover plants are grown on the soil, even for just a few weeks, the effective rihzobia will be killed.

Other research has shown that in the soil with a high concentration of metals, the biomass of free-living microbes is halved, and blue-green algae (cyanobacteria) are effectively eliminated.

What are the questions raised by these findings? The first need is to pinpoint which of the cocktail of metals in the original London sewage sludge used at Woburn is responsible for the toxic effects. Cadmium, zinc, copper and nickel are probably the most toxic of the elements normally found in large amounts in sewage sludge, as they are more soluble in the soil.

It is particularly alarming that these effects occur at concentrations of metals that are close to the current guideline limits of the European Community. As yet no one can say what are "safe" concentrations of metals in the soil for the microbes.

Clearly the accumulation of cadmium in food chains is serious, as it is toxic and readily absorbed from the soil by plants. The direct effects of other metals toxic to animals, such as lead, are less of a worry, although animals may absorb more by eating soil while grazing.

The underlying problem is that we are storing up trouble for generations to come, since the metals will remain in the soil indefinitely. As agriculture moves towards systems based less on fertilizers and other agrochemicals, we are likely to become increasingly dependent on soil microbes to fix atmospheric nitrogen and to maintain efficient cycling of nutrients from organic manures.

The obvious way to avoid these problems of pollution is to prevent contamination of sewage sludges at source, by imposing more stringent controls on industry to stop discharges of metals into the sewage system.

But this will not be cheap. How effective the new private water authorities will be in minimizing contamination of sewage sludges with heavy metals remains to be seen. (Extracted from New Scientist, 4 November 1989)

E. PATENTS AND INTELLECTUAL PROPERTY RIGHTS

Plant patent faces new legal challenge

A Swedish political group has decided to mount a legal challenge to a decision by the European Patent Office in Munich to grant the first European patent on a genetically engineered plant.

The Swedish group claims that the EPO's decision conflicts with the European Patent Convention of 1973, which states that patents cannot be granted on "plant or animal varieties".

Conflicting interpretations of this clause in the patent convention have been at the centre of disputes over whether or not applications should be granted on genetically engineered plants and animals. For example, the EPO earlier this year quoted the clause as its reason for rejecting an application from Harvard University for a patent on a genetically manipulated mouse.

The Swedish group says several thousand patent applications covering the use of recombinant DNA techniques to alter the genetic characteristics of both plants and animals are awaiting the EPO's verdict.

The outcome of the Swedish challenge, which is likely to be supported by environmentalist organizations, various farmers and plant breeders' groups, and other public interest organizations throughout Europe, will therefore be of considerable importance for the future of Europe's biotechnology industry.

The EPO awarded the controversial patent to the American company Lubrizol in March this year. The patent covers both a method for inserting into plants genes that boost the ability to store proteins, and the cells obtained using this method. Plants derived in this way are also included; the company has applied the technique to the fodder plant known as alfalfa, but almost any plant could be altered in the same way, and would be covered by the patent. (Extracted from New Scientist, 16 December 1989)

Genetics Institute gains US patents

Genetics Institute has obtained two US patents for new biotechnological products: human blood cell growth factor, Interleukin-3; and BMP-1, an agent which can induce the formation of new cartilage.

The Cambridge, Massachusetts-based company has patented the materials and methods for Interleukin-3 (IL-3) using recombinant DNA technology, and has licensed rights to Sandoz, which is conducting preclinical studies.

The US company claims IL-3 acts earlier in the pathway of blood cell development than other growth factors and may be used in combination with similar products such as GM-CSF. It is likely to prove valuable as a treatment for blood cell deficiencies associated with cancer treatment, bone marrow transplantation and other blood cell disorders.

The second patent covers BMP-1 type proteins and methods for treating bone and cartilage defects. Bone morphogenetic proteins (BMPs) act by recruiting bone forming cells, initially producing cartilage which by further development and mineralization forms bone. BMP may be useful in fracture healing and treating bone loss following periodontal disease and certain cancers. (Source: European Chemical News, 13 November 1989)

New plant hybridization method patented

DNA Plant Technology (Cinnaminson, NJ) has patented protoplast fusion, a new plant hybridization method for tomatoes that works even for very different varieties. The method was patented (4,863,863) for DNA Plant by D. Evans, J. Bravo and T. Concaing from the University of Nottingham (UK). The method involves growing new plants from cells made by fusing cells of two different tomato varieties in a test tube. The cell walls are removed from cells from two varieties and are placed in a test tube to fuse and produce a hybrid variety that has attributes from each plant. The fused cells are placed in a petri dish, grown into shoots and transplanted in soil to be grown into mature plants. Cross pollination, the traditional hybridization method, will not work if the plant varieties are too different. (Extracted from New York Times, 7 October 1989)

Patent for making "transgenic" animals

Patent protection has been granted (US 4,873,191) for DNA microinjection, a basic and widely used process for making "transgenic" animals - those incorporating a new gene in their

genetic makeup - by injecting a DNA segment into the nucleus of a mammalian embryo shortly after fertilization. The patent was granted to Thomas E. Wagner, head of Edison Animal Biotechnology Center at Ohio University, and Peter C. Hoppe, a researcher at Jackson Laboratories in Bar Harbor, Me., who assigned their rights to Ohio University. The university has licensed exclusive rights to DNX Inc., a small, privately held biotechnology firm based in Princeton, N.J. Critics contend the patent may prove difficult to enforce, and may be challenged as "obvious" and widely used. DNX responds that the patent applications was filed in 1981, when the process was not commonly used, and the firm considers the patent strong and enforceable. DNX plans broad commercial licensing, but says it will not hinder non-commercial basic research using the technology. (Reprinted with permission from Chemical Engineering News, 23 October 1989, p. 12. Copyright (1989) American Chemical Society)

New Zealand Patent Office to review practice regarding biotechnology

The New Zealand Patent Office has set up a Committee of Principal Patent Examiners in order to formulate a biotechnology manual of practice. This will comprise a glossary of terms, and guidelines for examination. A list of topics for such guidelines has been circulated to members of the patent profession in New Zealand for comment, so that the Patent Office can develop a policy.

The establishment of the Committee follows submissions requested by the Patent Office and the Ministry of Commerce in relation to the report of the New Zealard Industrial Property Advisory Committee (IPAC) which was released during 1988. That report recognized that some of the practices of the New Zealand Patent Office were not in line with the practices of the Patent Offices in many of New Zealand's major trading partners. The New Zealand profession was also concerned with an apparent lack of consistency among examiners. The IPAC report also canvassed the possibility of New Zealand joining the Budapest Treaty. (Source: ABA Bulletin, Vol. 4, No. 6, December 1989)

Supreme Court of Canada rejects application for plant variety on grounds of insufficient disclosure

In the case of Pioneer Hi-Bred Limited versus Commissioner of Patents, the Supreme Court of Canada has held that the description of the invention contained in the specification was insufficient to satisfy the disclosure requirements of the Canadian Patents Act, even though a deposit of seed had been made. The application was for a new variety of soybean, and the specification described the cross-breeding step only by the statement "soybean varieties 0877 was developed from the cross (Clark X Chippewa 64) X Corsay which was made in 1967". The Court concluded that this disclosure was insufficient to enable performance, but commented upon the fact that it did not have before it affidavit evidence by a skilled person stating that he or she had been able to arrive at the invention claimed without other instructions than the specification itself. It is therefore possible that the Court would have ruled otherwise if such an affidavit had been available. It was held that the disclosure did adequately describe the selective reproduction step. The Court stated that Section 36 of the Patents Act requires a description of how a third party can make the invention, even if a deposit has been made. This implies that in cases involving a deposit of a micro-organism, such deposit may only serve to complete the description of the invention contained in the specification, and may not itself function to satisfy the disclosure requirements. Therefore applicants in Canada should include as complete a description as possible of the micro-organism in the specification, even if a deposit has been made.

The Court did not rule on whether a new variety of soya bean resulting from artifical cross-breeding represents an invention within the meaning of Section 2 of the Patent Act, since the application was being refused on other grounds. However, the Court characterized genetically engineered life forms as falling within two classes, the first being a cross of different species or varieties by hybridization, and a second involving a change of the genetic material itself through biochemical processes. The new soybean variety claimed fell within the first class, and the genetic intervention by the applicant was merely the artifical crossing of different plant varieties, in which the reproductive processes of the plants proceeded according to the laws of nature. Although the Court declined to rule upon the effect of the differences between the two classes, the decision at least arguably implies that the first class of life forms in unpatentable as being directed to creations following the laws of nature. (Source: ABA Bulletin, Vol. 4, No. 5, October 1989)

US Patent Office to train examiners to handle biotechnology patents

The United States Patent and Trademark Office is establishing a special institute in order to train examiners to handle biotechnology patents, so that it can keep up with the rapidly growing demand for patents in biotechnology. The US Patent Office presently has a backlog of approximately 7,000 biotechnology applications awaiting examination. The new institute will be assisted by a board comprising government, trade association and academic representatives, which will help the PTO to foresee new trends in biotechnology, so that it can ensure that appropriately qualified examiners are available. (Source: ABA Bulletin, Vol. 4, No. 5, October 1989)

F. BIO-INFORMATICS

International Biotechnology Directory 1990

The Biotechnology Directory 1990 provides quick access to information on more than 8,000 companies, research centres and academic institutions involved in new and established technologies.

This new 1990 edition offers more than 650 new organization listings including more than 300 new entries for North America. There is a greatly expanded buyers' guide with more than 500 product codes to help locate the products and services quickly and easily. In addition, for easy access, Part III (Companies and Organizations) combines non-commercial and commercial organizations under each country heading and has an index alphabetized by organization at the end.

The Biotechnology Directory is compiled by Dr. J. Coombs, a consultant for the EEC for the UK Department of Energy; he is editor of Biomass, and Vice Chairman of BABA, and Dr. Y. Alston of CPL Scientific Ltd. and Secretary of BABA, the trade association of the British biomass industries. 800 pp., November 1989. ISBN: 0 333 49782 1, 95 pounds sterling. Further information available

from Globe Book Services Ltd., Stockton House, 1 Melbourne Place, London, WC2B 4LF, UK.

Canadian Biotechnology Directory 1990
(Edited by Peter Winter and Dr. Hans Giese)

The Canadian Biotechnology Directory 1990 is the first edition of what will be an annual publication which reviews the state-of-the-art in Canadian biotechnology. It examines the characteristics of the federal and provincial programmes, research and development in the public and private sector, the nature of the companies involved in the industry, Canadian products under development, R&D funding, and the infrastructure required for the commercialization of a biotechnology industry. This infrastructure includes an appropriate investment environment, government policies in taxation incentives and grants, and an efficient regulatory environment, and adequate intellectual property protection.

The directory provides a qualitative and quantitative overview on the scope of Canadian biotechnology to the present. As such it will be an invaluable reference tool for researchers and executives involved in biotechnology as well as those interested in learning about the nature of the industry and its participants. In addition to invaluable articles and contact names and addresses of leading decision-makers in government departments, a comprehensive listing of Canadian biotechnology firms, biotechnology suppliers and product listings will be provided.

Additional information and documentation is available from New Biotech, Directory 1990 Offer, P.O. Box 7131, Station J, Ottawa, Ontario, Canada K2A 4C5.

Biotechnology Guide Japan

As Japan evolves into a leading contender in the biotechnology field, it has become essential for companies to keep abreast of the biotechnology industry in Japan. Far more than a simple directory, this Guide provides a detailed analysis of what is happening in Japanese biotechnology today.

Compiled by the publishers of the leading biotechnology newsletter in Japan, the Guide is a direct translation from the latest edition of the directory compiled in Tokyo by the publishers of Nikkei Biotechnology, the most influential newsletter covering the field of biotechnology in Japan.

In addition to complete coverage of 500 companies, the Guide also provides exhaustive analysis of the largest 100 companies that comprise the core of the Japanese biotechnology industry. Leading experts from Nikkei Biotechnology discuss the key strategies and characteristics of these companies. 350 pp., March 1990. ISBN: 0 333 51805 5, 95 pounds sterling. Further information available from Globe Book Services Ltd., Stockton House, 1 Melbourne Place, London, WC2B 4LF, UK.

Biotechnology Guide USA - Companies, Data and Analysis by Mark D. Dibner, PhD

Following the explosive growth of the biotechnology industry in the United States, there has been a demand for information about the hundreds of new companies that work with biotechnology. The need for information comes from a variety of areas, including potential clients, suppliers, partners and competitors, as well as those wishing to monitor growth in the industry or a particular sector. This book focuses on the 360 key firms working directly with the new technologies, and gives details of each company and an analysis of the whole industry and its many sectors.

The heart of the Guide consists of listings and rankings, which analyse the companies by:

- Financing and equity;
- Revenues;
- R&D budgets;
- Personnel;
- Areas of interest - animal agriculture, plant agriculture, biomass conversion, biosensors/bioelectronics, bioseparations, biotechnology equipment, biotechnology reagents, cell culture, commodity chemicals, specialty chemicals, clinical diagnostics, energy, food productions/processing, mining, production/fermentation, therapeutics, vaccines, waste disposal/treatment, aquaculture, marine natural products, veterinary areas, research, immunological products, toxicology, biomaterials, fungi, drug delivery, medical devices, testing/analytical services;
- Nature of incorporation (public/private);
- Partnerships;
- Patents;
- Subsidiaries;
- Founding and founders;
- State activities.

In addition to the analysis of the 360 core companies, the Guide describes the involvement of large corporations in the biotechnology industry, and offers information on the work of the State biotechnology centres. In all, almost 500 organizations are represented.

Mark D. Dibner, PhD, is director of the Biotechnology Information Program at the North Carolina Biotechnology Center. He is also a Professor at Duke University's Fuqua School of Business, where he teaches Management of Technology. 389 pp., August 1988. ISBN: 0 333 48551 3, 80 pounds sterling. Further information available from Globe Book Services Ltd., Stockton House, 1 Melbourne Place, London, WC2B 4LF, UK.

Resources and Applications of Industrial Biotechnology edited by R. N. Greenshields, Director of the Biotechnology Centre, Wales, and editor of Industrial Biotechnology

Written by some of the UK's foremost biotechnologists, this book:

- Introduces some of biotechnology's basic biological processes;
- Looks at major applications in pharmaceuticals, agriculture, food-processing, biosensors, etc.;

- Considers the future of biotechnology and its progress in countries other than the UK.

The book has been especially designed to help improve communication and increase co-operation between academic researchers and industrial biotechnologists. 456 pp., October 1989. ISBN: 0 333 44358 6, 60 pounds sterling. Further information available from Globe Book Services Ltd., Stockton House, 1 Melbourne Place, London, WC2B 4LF, UK.

Intellectual Property Rights in Biotechnology Worldwide by S. Bent, R. Schwaab, D. Jeffery, D. Conlin

An invaluable guide to protecting a broad range of applied biological inventions in different countries, the book:

- Presents a theoretical and historical overview of proprietary rights in biotechnology;

- Provides a detailed analysis of pertinent case law, statutes and regulations for all countries with a significant market for biotechnology products;

- Examines all relevant international treaties including the Paris Convention, the Budapest Treaty, the Patent Co-operation Treaty and the European Patent Convention;

- Explains Patent Laws for all major countries and emphasizes how legal principles differ from country to country; and

- Covers trade secret laws world-wide.

700 pp., 1987. ISBN: 0 333 39288 4, 80 pounds sterling. Further information from Globe Book Services Ltd., Stockton House, 1 Melbourne Place, London, WC2B 4LF, UK.

Biotechnology and the Environment: International Regulation by Jeffrey Gibbs, Iver Cooper, Bruce Mackler

This work guides scientists, managers and lawyers on the issues which arise as the US Environmental Agency - EPA - uses its statutory authority to regulate the manufacture of biotechnology products and the disposal of waste products characteristic of the biotechnology industry. Countries outside the USA are also looking at regulations although they will be influenced by the EPA since the US has taken the greatest steps so far. Thus, UK, Japan and Continental Europe are discussed in the international scene. 354 pp., 1987. ISBN: 0 333 42934 6, 85 pounds sterling. Further information from Globe Book Services Ltd., Stockton House, 1 Melbourne Place, London, WC2B 4LF, UK.

Animal Patents - the Legal, Economic and Social Issues, edited by William H. Lesser, PhD

In 1987, the US Patent Office declared animals to be patentable. The following year the first such patent was granted. Since that time, the patenting of animals has become a major issue of international scope for business, science and the public sector. Animal patents are a very new and complex area, making it difficult for individuals and companies to determine policy and practical implications. This new book is the first to address the broad implications of patenting animals. Beginning from the legal perspective, experts report on research developments, economic implications for agriculture and the broader perspectives of farmers, agribusiness and opponents. Implications are extended to other countries, including the European Community. A series of appendices contain pertinent primary documents. 380 pp., November 1989. ISBN: 0 333 49012 6, 55 pounds sterling. Further information from Globe Book Services Ltd., Stockton House, 1 Melbourne Place, London, WC2B 4LF, UK.

Patenting Life from the Office of Technology Assessment, Washington, DC, USA

In 1980 the US Supreme Court ruled that a living micro-organism could be patented. Subsequently the US Patent and Trademark Office held that certain types of plant and animal life constituted patentable subject-matter.

This special report by the OTA (Office of Technology Assessment of the US Congress) reviews US patent law as it relates to the patentability of micro-organisms, cells, plants and animals, as well as specific areas of concern including deposit requirements and international considerations.

One inherent difficulty in examining the patenting of living organisms is determining which are novel and directly related to patent issues as opposed to those questions that would exist independently of patent considerations (e.g., environmental aspects, the welfare of the animal, the morality of such work, etc.).

Thus the primary focus of this report is on subject-matter patentability - what can and cannot be patented, as enacted by Congress under the patent statute and interpreted by the courts. 208 pp., November 1989. ISBN: 0 333 53465 4, 35 pounds sterling. Further information from Globe Book Services Ltd., Stockton House, 1 Melbourne Place, London, WC2B 4LF, UK.

The US market for biosensors

In an era of major biotechnology expansion, the field of biosensors will have great appeal as a compatible technology addressing important applications ranging from health care to process engineering. The biosensor market, still in its start-up phase, generated only about $10 million in US sales revenue in 1988, but the real excitement is in the research activities being conducted on a world-wide basis by universities and private firms. This is mainly driven by the ability of biosensors to address very large or socially important markets led by health care, food and environmental monitoring. Further, there are new product introductions anticipated over the next five years which should enlarge the market for biosensor devices themselves to some $70 million by 1993 (measured in constant 1988 dollars), a 47 per cent average annual growth rate from the small current base. Added to this are sales of disposable items (such as replacement membranes) and contract R&D, which will bring the total US market to roughly $115 million in 1993. Reaching this goal would indicate that biosensors had overcome market resistance and that the devices will enter volume production thereafter.

For the study of this market, a biosensor device is tightly defined as one which incorporates both a biodetector (a biological component whose function is to detect specific substances within complex mixtures) and a transducer in intimate contact. The latter converts the chemical or

physical change occurring in the biodetector to a useful signal proportional to the activity being monitored. An understanding of developments in each of these areas is vital in assessing the product outlook in this field. Such biological materials as enzymes, antibodies and receptors are being developed as biodetectors.

Research is being conducted within large private firms, often with government agency support, as well as many leading university laboratories and medical institutions. On the other hand, manufacturers of biosensor products in the US are commonly small, privately held companies, many of which were founded by university researchers. The larger companies, a few of whom have entered only tentatively, are naturally attracted to the large volume health care and environmental monitoring applications of the future. Larger foreign firms are playing a major role in research and product development. The smaller, high technology firms currently struggling to broaden the market tend to lack marketing strengths, especially distribution channels to the volume markets, opening the way to partnerships with larger drug or processing firms, and eventually technology-driven acquisitions.

Very importantly, biosensors makers are broadening their product lines, advancing from single analyte laboratory instruments to field and on-line monitoring types. Acceptance of these new devices is none the less quite dependent on their convincing established OEM suppliers to adopt biosensor technology for their product lines. These OEMs bring an established customer base, market reputation and applications knowledge to the battle for wide market acceptance. The required close working relationship among these firms is likely to lead to many strategic partnerships over the next few years.

Integrating biosensors into the public perception of the biotechnology era is likely to gain ground as this technology begins to address areas that touch our daily living. Applying biosensors to at-home medical or athletic self-testing can ease the cost and time burdens of health monitoring. Monitoring the safety and quality of air, food and water supplies clearly requires new and more cost-effective techniques. Thus, the overall impact of biosensor technology promises to be far reaching. It is important to understand the current state of this industry and its directions to be in a position to take advantage of future business opportunities.

Frost & Sullivan has completed an updated 312-page analysis of the Biosensor Market in the US which:

(1) Categorizes and discusses the characteristics, applications, advantages and disadvantages of biosensor devices;

(2) Brings the evolution of biosensor technology up to date;

(3) Identifies many examples of existing products and their suppliers and reviews world-wide product developments;

(4) Provides in-depth discussion of a wide range of targeted biosensor applications, particularly identifying those with high growth potential;

(5) Reviews the state-of-health and economic conditions in the five major customer end markets for biosensors and the opportunity for selling biosensors into each;

(6) Sizes the current market and forecasts, through 1993, dollar demand for biosensors by product type, by end-use markets and by a matrix of products versus markets;

(7) Examines this embryonic industry's competitive structure in terms of research as well as product sales, indicating market leaders in several categories;

(8) Offers possible marketing and distribution strategies for each of the end-use segments; and

(9) Profiles US product suppliers including their sales (when known), products, market niches and other important information.

The report (No. A2139) costs $2,400. Further information from Sullivan House, Department RE-1, 4 Grosvenor Gardens, London, SW1W ODH, UK.

In the series World Employment Programme Research of the International Labour Office (ILO) several "Working Papers" on biotechnology have been published, of which the following are a few. ILO publications can be obtained directly from ILO, CH-1211 Geneva 22, Switzerland.

Industry-University Relationship and Biotechnology in the Dairy and Sugar Industries: Contrast between Mexico and the United States by Gerardo Otero

This study analyses: (1) the emerging biotechnology industry within the US economy, university research and the role of the North American State in the "commoditisation" of science; (2) biotechnology and university-industry relations in Mexico; and (3) prospects for the sugar and dairy industries in the United States and Mexico.

Mexico faces several severe dilemmas. Because of the weakness of university-industry links in Mexico (it has no more than 200 biotechnologists, most of them doing basic research) and of the financial strength of Mexican industry, the tendency is that (foreign) multinational enterprises are the ones who will capitalize the few Mexican efforts.

The following example may illustrate Mexico's "milk-dilemma". It seems that many developing countries are facing similar dilemmas.

Mexico faces a large milk deficit (in 1988: 12.5 million litres per day) and the temptation of adopting BGH (the American patented Bovine Growth Hormone that can generate a 30-40 per cent increase of milk per cow) is therefore very big. Firstly, BGH might help to make the Mexican dairy industry more cost efficient, and secondly, the drainage of foreign exchange on imports of dairy products may be reduced. However, the introduction of BGH might have very problematic effects. Especially large-scale farms will profit from the use of BGH for milk production (as the US example proves), thus generating a polarizing effect in the current production structure of dairy farmers. Small farmers in relatively poor regions will have a hard time competing on local markets, because BGH milk will become cheaper than normal milk. Another problematic aspect is that BGH makes Mexico dependent on importing a technology that is patented and privately owned. The tragic side of the dilemma is that Mexico has to pay anyway: whether by importing milk to cover the internal deficit or by increasing the local supply with an expensive foreign-owned technology. January 1989, 41 pp. [WEP 2-22/WP 192.] ISBN 92-2-106963-X.

New Biotechnologies for Rural Development by Pablo Bifani

Dr. Bifani explores obstacles to the growth of agriculture and food supplies, and the possible role of new biotechnology in reducing or overcoming such obstacles. He examines in a rather detailed manner some concrete cases of biotechnology applications for productivity increase, fertilization, rapid micropropagation of plant varieties, pest control and production of microbial pesticides. In the last chapter negative effects on the third world countries are examined that are likely to arise from the application of the new technology by developed countries in their effort to substitute raw materials imported from developing countries. Special attention is among others given to tissue culture techniques. The cases of cassava and oil palm trees are elaborated. Cassava. the seventh largest agricultural product in the world, shows a rate of increase of 2.67 per cent per annum. Its production offers an interesting area for biotechnology application in developing countries as to: the inoculation of micorrhiza for the detection of diseases, production of disease-free plant material through in-vitro cloning, for biological pest control, for the processing of cassava for industrial purposes, and in particular its conversion to alcohol or microbial proteins through single-cell protein systems. They can also be used for the upgrading of traditional food processing based on fermentation like gari and foo-foo. Both CIAT in Colombia and IITA in Nigeria developed new, high-yielding varieties of cassava. For instance, with the new varieties cloned at IITA, yields ranging from 20-50 ton/hectare have been achieved in Rwanda, Liberia, Seychelles and Cameroon.

The case of the palm oil tree is quite another one: Unilever, the Dutch-British multinational initiated as early as 1968 the tissue culture technology for the improvement of Malaysian plantations. Unilever has about 60,000 hectares dedicated to oil palm trees in developing countries. "The main concern with rapid propagation of palm oil tree is that it will displace from the market the product of the coconut palm which is grown mainly by small farmers in Kerala (India) and the Philippines. In the case of the Philippines, it is estimated that about 25 per cent of the population depends on coconut palm", Dr. Bifani writes. This study shows clearly (with elaborated examples) that biotechnology innovation and diffusion is an irreversible scientifically-based process that can have negative or positive effects on the economies of developing countries, depending upon the economic and institutional mechanisms that each country will adopt for the application of these innovations. However, Bifani concludes, developing countries have to face the fact that at the international level the developed countries and their multinational enterprises are making an effort to solve their particular problems and to secure their markets for their production. January 1989, 95 pp. [WEP 2-22/WP 195.] ISBN 92-2-107015-8.

The socioeconomic impact of agricultural biotechnology on less developed countries by Harold H. Lee, Frederick E. Tank

The authors propose as policy suggestion for developing countries that distribution, food processing and transportation and other related industries need to be upgraded, or created, to handle the anticipated surpluses emanating from output-enhancing biotechnology. They emphasize the educational need for both biotechnology development and for the spin off the new biotechnology-based agriculture will generate. As the labour/output ratio will decrease, the macro-economic, theoretical and sometimes speculative analyses focus on the distribution of surplus farm workers. They also emphasize that in order to reduce undesirable consequences of assessment of biotechnology, the imported biotechnologies should be examined for cultural appropriateness, responsiveness to people's needs and desires, and consistence with both available resources and the governments' broad social goals.

Two illustrations of a potential commercial application of biotechnology at the firm level are worked out: micropropagation industries and embryo engineering for animal husbandry. January 1989, 41 pp. [WEP 2-22/WP 199.] ISBN 92-2-106990-7.

Innovation and sovereignty: the patent debate in African development by C. Juma and J. B. Ojwang

One of the major issues analysed relates to intellectual property rights for innovations generated by the so-called informal sector. These innovations account for a large share of the indigenous industrial activities of the African countries. The book stresses the need for a comprehensive law that would protect and promote these innovations and recommends the introduction of utility models or certificate system. The main purpose of utility model protection is to make available, in addition to patents, a system of protection of inventions that do not necessarily fulfil all the requirements of patentability.

The eight chapters fall into four main areas: (a) technological change and national sovereignty with emphasis on the need for a new legal régime that would protect local innovations, (b) emerging international trends in intellectual property protection (including the impact of biotechnology), (c) sectoral issues (intermediate and biological innovations and the legal issues of technology regulation), (d) policy review for a relevant intellectual property protection régime for African countries, including a proposal for a Kenyan patent law. (ACTS research series, No. 2, 1989, 252 pp., US$18.99, 10.50 pounds sterling, African Centre for Technology Studies, P.O. Box 45917, Nairobi, Kenya, Tel. 505920.)

Monokines, lymphokines and growth factors are some immune hormone products likely to enjoy huge markets

Alpha interferon products have been on the market since 1986 and researchers keep finding new areas of clinical utility. It has to be noted, however, that immune hormone products make up what is still an embryonic market. This is clear from Frost & Sullivan's new 412-page study The US Market for Monokines, Lymphokines and Growth Factors (No. A2025). But the study also notes that the quickening pace of research activity and the fact that given the kinds of medical problems addressed (from hepatitis to cancer), the market is bound to be extremely large.

The greatest impact of the new products is expected to be in cancer treatment, mainly because of inadequacies in current treatments using chemotherapy or radiation. But the potential does not by any means stop cancer. The interferons, for instance, seem to have broad utility in treating viral diseases from herpes to the common cold.

Immune deficiency syndromes, arthritis and degenerative nerve diseases are also likely to be targets for new treatments. EPO is an example of what makes the products exciting. In clinical

trials, 256 anaemic transfusion-dependent dialysis patients were treated. Of these, 255 responded to the extent that they no longer required transfusions. Side-effects were minimal and easily controlled.

Details of the report, priced at $2,600.00, from: Frost & Sullivan Ltd., Sullivan House, 4 Grosvenor Gardens, London, SW1W ODH, or on 01-730 3438. In the USA, Frost & Sullivan Inc., 106 Fulton Street, New York, NY 10038, USA or on +1(212) 233-1080. (Source: Biotechnology Bulletin, Vol. 8, No. 9, October 1989)

Biotechnology in future society

Sub-titled "Scenarios and Options for Europe", this book has been edited for the European Foundation for the Improvement of Living and Working Conditions by Edward Yoxen (Department of Science and Technology Policy, University of Manchester) and Vittorio di Martino (European Foundation for the Improvement of Living and Working Conditions). It, too, is based on a seminar, organized by the Foundation. Details of the book, priced at 29.50 pounds sterling, from: Gower Publishing Co. Ltd., Gower House, Croft Road, Aldershot, Hampshire GU11 3HR or on 0252-331551. (Source: Biotechnology Bulletin, Vol. 8, No. 10, November 1989)

Biotechnology is interbreeding disciplines in Europe

Several of Europe's scientific disciplines are mutating into a new form due to biotechnology, according to a new study from Frost & Sullivan, Research Biochemicals in Western Europe. The 370-page report says that "the major feature in the 1980s is the removal of specializations such as cell biology or molecular biology. These do still exist, particularly in the universities, but the majority of research workers use the disciplines as tools to solve their problems".

The four fundamental biological approaches now merging into biotechnology research are immunology, biochemistry, cell biology and molecular biology. This clustering of research and product development will cause the European market for the relevant biochemicals to rise from $329 million in 1988 to $480 million by 1993.

Nationally, France is "actively trying to ensure that it does not miss the economic advantages of having a strong industry", the report says. It predicts that, along with Spain, France will post the top growth rates in Europe. With $25.7 million in 1988 purchases of research biochemicals, the French market is "much more academically directed than the Federal Republic of Germany market is, though the emphasis is on establishment of biotechnology institutes rather than expanding the university role".

The FRG constitutes the largest national market in 1988. The central Government has set up gene research centres, which also have industrial backing, and a central biotechnology research centre.

"The overall attitude is application-directed" in the UK, the report concludes, where the Government is examining privatization of central laboratories. The UK market amounted to $37.2 million in 1988. The Italian market represented $27.4 million in 1988 research biochemical demand.

On an organizational basis, Frost & Sullivan predicts that the specialized biotechnology institutes will grow fastest in the years ahead, with sales to them doubling between 1988 ($71 million and 1993 ($140 million). Universities will remain the largest product purchasers, however, with demand from them climbing from $121 million to $184 million in the same years.

Industry, meanwhile, will increase its spending from $105 million in 1988 to $156.5 million by 1993. Details from: Frost & Sullivan Ltd., Sullivan House, 4 Grosvenor Gardens, London, SW1W ODH or on 01-730 3438. In the USA, Frost & Sullivan Inc., 106 Fulton Street, New York, NY 10038, USA or on +1(212) 233-1080. (Source: Biotechnology Bulletin, Vol. 8, No. 9, October 1989)

Biotechnology in Europe and Latin America

"The accession of Spain and Portugal to membership of the European Community in January 1985 not only brought new vitality to the European initiative", say the editors of a new book, "but served as a powerful reminder of the broader dimensions of the Spanish- and Portuguese-speaking worlds."

Edited by Bernardo Sorj, Mark Cantley and Karl Simpson, Biotechnology in Europe and Latin America is sub-titled "Prospects for Co-operation". The book is based on "SOBELA", a Seminar on Biotechnology in Europe and Latin America held in Brussels in April 1987. Details from: Kluwer Academic Publishers Group, PO Box 322, 3300 AH Dordrecht, the Netherlands. No price is given. (Source: Biotechnology Bulletin, Vol. 8, No. 10, November 1989)

The International Federation of Institutes for Advanced Study (IFIAS) is launching a new publications series - the IFIAS Biopolicy Series. The series emerges from the IFIAS International Diffusion of Biotechnology Programme and is edited by Dr. Calestous Juma, the director of the IFIAS Biotechnology Programme.

The first two papers already available in the series are:

- Biotechnology in China: Institutional Reforms and Technological Innovation, by Xu Zhaoxiang and Zhou Yongchun; and

- Biotechnology and Culture: The Impact of Public Debates on Government Regulations in the United States and Denmark, by Eric Baark and Andrew Jamison.

The next two papers in the series will be available shortly. A complete list of other publications planned in the series are as follows:

- Biotechnology and the Mining Industry: The Bacterial Connection, by Rohini Acharya and Ralph Spencer;

- Bio-pesticides in Developing Countries: Prospects and Research Priorities, by R. Gerrits and E. B. J. van Latum;

- Biotechnology in Mexico: Opportunities and Constraints in the Agroindustrial Sector, by Rosalba Casas;

  Biotechnology in Brazil. Institutional Trajectories for the 1990s, by Bernardo Sorj and John Wilkinson.

For those interested in obtaining further information about the series or the programme or ordering any of the other publications in the series, please contact either:

Dr. Calestous Juma, Executive Director
African Centre for Technology Studies
Nairobi, PO Box 45917
Kenya, or

Ms. Rohini Acharya
IFIAS-Maastricht
Witmakersstraat 10
6211 JB, Maastricht
The Netherlands.

IFIAS would also like to welcome those interested in submitting manuscripts for publication in the series to contact the editor, Dr. Juma, in Kenya.

The International Federation of Institutes for Advanced Study (IFIAS) is an association of 44 leading research institutes which collaborate to address major global problems of long-term importance in environment, economy and science and technology. IFIAS research programmes are interdisciplinary, seeking to advance understanding of complex systems for the improved management in a rapidly changing world with an uncertain future. IFIAS stands for the more effective and consistent use of scientific understanding in world councils, and for the adoption of long-term strategic thinking.

The African Centre for Technology Studies (ACTS) is a non-partisan, not-for-profit institution established to conduct policy and practical research in technological innovation and natural resource management. The Centre promotes the view that technological change, natural resource management, and institutional innovation are crucial to sustainable development and should be at the core of all development efforts. ACTS has a national focus and a regional view and collaborates with United Nations, governmental, intergovernmental, private, academic and other research institutions with similar objectives.

World human vaccine markets to reach $3.7 billion by the year 2000

In a report entitled Genetically engineered vaccines II - A worldwide study on new opportunities in human vaccines, Technology Management Group (TMG) predicts that world-wide markets for human vaccines will reach $3.7 billion by the year 2000.

A significant part of the vaccine market in the year 2000 will be for developing countries. After 2000, market growth in the developing countries will accelerate, both because new vaccine products will have been developed and because more of these countries will then be able to afford them.

Numerous diseases are common in the developing countries. Of these, the most prevalent is malaria. At least 17 companies and 34 other organizations are developing vaccines for the disease. Among other parasitic diseases, the most common are schistosomiasis, leishmaniasis and filariasis.

Diarrhoeal diseases also affect large numbers of people in developing countries. At least four companies and 15 other organizations are developing vaccines against rotaviruses, which account for many diseases in this group. Other tropical diseases include cholera, which is being studied by at least four companies and five other organizations, typhoid fever (three companies and 12 other organizations) and leprosy (two companies and nine other organizations).

Seven new vaccines are expected to be commercialized by 1999, targeted against: chicken-pox, cholera, typhoid fever, cytomegalovirus, encephalitis, herpes, malaria and pneumonia. Over 208 companies and 456 other organizations are involved with human vaccines, with the greatest activity found in relation to hepatitis B. At least 46 companies and 48 other organizations are involved in this area. Details of the report, priced at $2,350.00, from: Technology Management Group, 25 Science Park, New Haven, Connecticut 06511, USA or on +1(203) 786-5445. Fax: +1(203) 786-5449. (Source: Biotechnology Bulletin, Vol. 8, No. 9, October 1989)

Recombinant DNA molecule drawing software

Plasmid Artist from GeneSystems Computer Software allows biologists to construct publication-quality diagrams (plasmid maps) detailing their recombinant DNA molecule binding strategies and results by using Macintosh computers. With a mouse and pull-down menus, users can draw linear or circular restriction map diagrams containing a virtually unlimited number of restriction sites and fragments. The program shows the map with correct scaling on screen and prints a high-quality image with any PostScript printer.

New biotech directory data base available

BioCommerce Data's international directory data base on the biotechnology industry is now available on two on-line systems, Dialog and Data-Star, as part of the file BioCommerce Abstracts and Directory.

The data base expands and complements BioCommerce Data's business news abstracting activity to provide detailed background information on over 1,400 organizations world-wide. There are mainly companies but also included are universities, government agencies, research institutes and venture capital funds. The entire industry is covered - research-based biotechnology companies, equipment suppliers and service providers. Each entry includes address, telephone/telex/fax numbers, keywords for areas of activity, a description covering founding date, investors, products, staff numbers, 1989 turnover and research expertise, plus the names and job titles of senior employees.

The on-line format of the BioCommerce Data directory data base means that the information is revised and expanded every two weeks, making it much more up-to-date than printed products. It is also possible to retrieve just a few selected entries, a very cost-effective way to obtain the needed information. However, for those who prefer this type of information in a handy "off-the-shelf" package, the UK directory information from the data base is also available in book form, as the UK Biotechnology Handbook. The second edition of this will be published in January 1990 and includes strategic review articles on the British market as well as profiles of over 550 organizations (price 85 pounds sterling/US $150)..

These new directories will be valuable marketing tools for anyone working in biotechnology. For further information or to order the UK Biotechnology Handbook '90, contact BioCommerce Data Ltd., 95 High Street, Slough, Berkshire SL1 1DH, UK. Tel. (0753) 511777 (Int. +44 753 511777), Fax: (0753) 512239 (Int. +44 753 512239).

New journal

Human Gene Therapy, a new quarterly journal, answers the need for a central forum dealing with all aspects of gene transfer in mammals. Original scientific contributions will include:

- Techniques for gene transfer into mammalian cells;
- Construction and testing of retroviral vectors;
- Examination of the life cycle of retroviruses where it is applicable to the use of retroviral vectors;
- Regulatory mechanisms for controlling gene expression;
- Animal models for human diseases;
- Studies evaluating gene transfer and expression in animals;
- Results of pre-clinical safety and efficacy studies;
- Results of clinical studies.

Other topics in Human Gene Therapy will include ethical, legal, regulatory, social, and commercial considerations.

Human Gene Therapy will address itself to all aspects of this specific field including broader social issues; additionally, this new publication will serve as a resource for current information as well as a repository for future reference. Further information from Editor-in-Chief: W. French Anderson, MD, Laboratory of Molecular Haematology, Bldg. 10, 7D-18, National Heart, Lung and Blood Institute, National Institutes of Health, Bethesda, Maryland 20892, USA.

G. MEETINGS

APRIL 1990

1-2 April	Savannah, Georgia, USA. Symposium on Growth Factors in Reproduction. Details from L. Lisa Kern, Serono Symposia, USA, 100 Longwater Circle Norwell, MA 02061, USA.
3-4 April	University College Swansea, Swansea, UK. Advances in Separation Processes. Details from R.K. Sinnott, Chemical Engineering Department, University College Swansea, Swansea SA2 8PP, UK.
3-5 April	Cambridge, UK. SCI Biotechnology Group: Opportunities in Biotransformations. Details from Society of Chemical Industry, 14 Belgrave Square, London SW1X 8PS, UK.
5-6 April	University of Birmingham, Edgbaston, UK. Stability of Recombinant DNA. Details from Dr. S.C. Thomas, School of Biological Science, University of Birmingham, Edgbaston, Birmingham B15 2TT, UK.
7-8 April	Royal Agricultural College, Cirencester, UK. Molecular Mechanisms in Host-Infective Agent Interactions. Details from Mrs. F. Perrin, Dept. of Cellular and Molecular Sciences, St. George's Hospital Medical School, Cranmer Terrace, London SW17 ORE, UK.
9-11 April	Palazzo dei Congressi, Florence, Italy. BIOTECH RIA '90. Biotechnology of Plasma Proteins: Haemostasis, Thrombosis and Iron Proteins. Details from Clas International, Via Pace 5, Brescia 25122, Italy.
9-11 April	Sestri Levante (Genoa), Italy. The Identification of the CF Gene: Recent Progress and New Research Strategies. Details from Ms. Silvia D'Agostino, Laboratorio di Genetica Molecolare, Istituto Gaslini, Largo G. Gaslini 5, 16148 Genoa, Italy.
18-20 April	Orlando, Florida, USA. First International Conference on Human Antibodies and Hybridomas. Details from S.L. Patterson, Butterworths, 80 Montvale Avenue, Stoneham, MA 02180, USA.
22-25 April	Kyungju and Seoul, Korea. Asia-Pacific Biochemical Engineering Conference '90. Details from Prof. Paul Greenfield, Australian Convenor, Dept. of Chemical Engineering, University of Queensland, St. Lucia, 4067, Queensland, Australia.
22-25 April	Malmo, Sweden. BioScience (biotechnology exhibition and fair). Details from Malmo Massan, Box 19015, S-20073 Malmo 19, Sweden.
23-26 April	Heidelberg, Federal Republic of Germany. Oncogenes and Growth Control. Details from Dr. T. Graf, EMBL, Meyerhofstrasse 1, 6900 Heidelberg, FRG.
23-27 April	Eilat, Israel. 34 OHOLO Conference: Novel Strategies in Production and Recovery of Biologicals from Recombinant Micro-organisms and Animal Cells. Details from OHOLO Biological Conference, P.O. Box 19, Ness-Ziona 70450, Israel.
29 April to 7 May	Kilymbari, Crete, Greece. Molecular and Development Biology of Drosophila. Details from Dr. S. Artavanis-Tsakonas, Crete Workshop, Department of Biology, Yale University, P.O. Box 6666, New Haven, CT 06511-8112, USA.
30 April to 1 May	Michigan State University, USA, Commercialization of Biotechnology. Details for Michigan Biotechnology Institue, Michigan, USA.
30 April to 1 May	Michigan State University, USA. Commercialization of Biotechnology. Details from Michigan Biotechnology Institute, Michigan, USA.

MAY 1990

4 May	London UK. Probiotics - fact or fiction? Details from Society of Chemical Industry, 14 Belgrave Square, London SW1X 8PS, UK.
4-7 May	Athens, Greece. Cell Differentiation/ Oncogenesis. Details from Professor Demetrios A. Spandidos, National Hellenic Research Foundation, 48 Vas. Constantinou Ave., Athens 116 35, Greece.
6 9 May	Seoul, Korea. 2nd International Biotechnology Conference. Details from Organizing Committee, 2nd International Biotechnology Conference, Korean Institute of Biotechnology and Bioengineering, Nam Seoul P.O. Box 33, Seoul 151, Korea.

13-18 May — Anaheim, California, USA. Ninetieth Annual Meeting of the American Society of Microbiology. Details from R. A. Bray, ASM, 1913 I Street NW, Washington DC 20006, USA.

14-17 May — Monterrey, California, USA. 11th International Symposium on Capillary Chromatography. Details from P. Sandra, Laboratory of Organic Chemistry, University of Ghent, Krijgslaan 281, (S4) B-9000 Ghent, Belgium.

20-25 May — Boston, USA. International Symposium on Liquid Chromatography. Details from Ms. Shirley Schlessinger, 400 E Randolph Street, Suite 1015, Chicago, Illinois 60601, USA.

21-23 May — East Lansing, Michigan, USA. Mathematical Aspects of Microbial Ecology. Details from Ms. Rebecca Murthum, College of Natural Science, Michigan State University, 103 Natural Science Building, East Lansing, MI 48824.

22-25 May — Dijon, France. Bio-chromatography and Molecular Affinity. Details from Groupe Française de Bio-chromatographie, Unite d'Immuno-Allergie, Institut Pasteur, 28 rue du Docteur Roux, F-75724 Paris Cedex 15. France.

23-26 May — Florence, Italy. First International Congress ISNIM (4th International Workshop on Neuro-immunomodulation). Details from UP Service s.r.l., P.O. Box *336, 60100 Ancona, Italy.

23-26 May — Osaka, Japan. Bio Japan '90 (part of Expo '90). Details from Bio Japan '90 Osaka Secretariat, c/o Inter Group Corp. Shiroguchi Building, 2-15 Kakuta-cho, Kita-Ku, Osaka 530, Japan.

24 May — Hilton Hotel, New York, USA. Cytokines and Cell Motility. Details from Ms. Ann J. Boehme, Office of Continuing Education, Long Island Jewish Medical Center, New Hyde Park, New York, NY 11042, USA.

28 May to 1 June — Florence, Italy. 7th International Conference on Prostaglandins and Related Compounds. Details from Pondazione Giovanni Lorenzini, Via Monte Napoleone 23, 20121 Milan, Italy.

JUNE 1990

2-5 June — Vienna, Austria. Fourth International Conference on Arabidopsis Research. Details from Ms. Kathrin Peuker, Institute of Botany, University of Vienna, Rennweg 14, A-1030 Vienna, Austria.

6-7 June — Munich, FRG. Oral Immunisation using Recombinant Bacteria. Details from P. Schödel, Max Planck Institut für Biochemie, D-8033 Martinsried, FRG.

11-14 June — Arlington, Virginia, USA. 4th Annual Seminar on Analytical Biotechnology. Details from Mrs. J. Cunningham, Barr Enterprises, P.O. Box 279, Walkersville, MD 21793, USA.

14-16 June — Lake Buena Vista, Florida. Second International Symposium on Immunotoxins. Details from Dr. Arthur E. Frankel, Florida Hospital Cancer Center, 500 East Rollins Street, Suite 305, Orlando, FL 32803, USA.

18-22 June — Vienna International Centre, Vienna, Austria. FAO/IAEA International Symposium on Contribution of Plant Mutation Breeding to Crop Improvement. Details from Joint Symposium Secretariat, c/o IAEA Conference Service Section, P.O. Box 100, A-1400 Vienna, Austria.

25-29 June — Amsterdam, the Netherlands. Amsterdam Biotechnology '90 Exhibition to be held in conjunction with the 7th Congress of the International Association for Plant Tissue Culture. Details from RAI International Exhibition and Congress Centre, Europaplein, 1078 GZ Amsterdam, the Netherlands.

24 June to 5 July — Cape Sounion Beach, Greece. Vaccines: Recent trends and Progress. Details from Dr. G. Gregoriadis, School of Pharmacy, University of London, 29-39 Brunswick Square, London WC1 1AX, UK.

JULY 1990

1-6 July — Kiruna, Sweden. 8th International Conference on Methods in Protein Sequence Analysis. Details from Hans Jörnvall, Department of Chemistry I, Karolinska Institutet, S-104401 Stockholm, Sweden.

8-13 July — Copenhagen, Denmark. 5th European Congress on Biotechnology. Details from ECB-5, Spadille Congress Service, Sommervej 3, DK-3100 Hornbaek, Denmark.

19-20 July — London, UK. 25th Anniversary Symposium - Research in Arthritis. Details from Mr. C. Boden, General Secretary, The Kennedy Institute of Rheumatology, 6 Bute Gardens, Hammersmith, London W6 7DW, UK.

22-27 July — Chichester, UK. Phytochrome Properties and Biological Action. Details from Dr. Brian Thomas, Institute of Horticultural Research, Worthing Road, Littlehampton, West Sussex BN17 6LP, UK.

AUGUST 1990

8-10 August — Oulu, Finland. 5th International Symposium on Basement Membranes. Details from the Secretariat, 5th International Symposium on Basement Membranes, Department of Biochemistry, University of Oulu, Finland, SF-90570 Oulu, Finland.

12-18 August — Strasbourg, France. 6th International Symposium on the Genetics of Industrial Micro-organisms. Details from the Symposium Secretariat, GIM 90, Société Francaise de Micro-biologie, 28 rue du Docteur Roux, 75724 Paris Cedex 15, France.

21-24 August — Bangkok, Thailand. First Conference on Biotechnology and Environment: Molecular Approach. Details from Dr. Skorn Mongkolsuk, Department of Microbiology, Faculty of Science, Mahidol University, Rama VI Road, Bangkok 10400, Thailand.

26-31 August — Vienna, Austria. Euroanalysis VII. Details from the Secretariat, Inter-convention, P.O. Box 80, A-1107 Vienna, Austria.

26-31 August — Berlin, FRG. 8th International Congress of Virology. IUMS Symposium on Development in Diagnosis and Control of Infectious Diseases. Details from Congress Secretariat, Institute for Clinical and Experimental Virology, Free University of Berlin, Hindenburgdamm 27 D-1000 Berlin 45, FRG.

28 August — Regensburg, FRG. 4th International Mycological Congress. Detai s from Prof. Dr. Andreas Bresinsky, Botanisches Institut der Universität, D-8400 Regensburg, FRG.

SEPTEMBER 1990

September — Beijing, China. Biotech Expo '90. 3rd Round of the International Exposition and Symposium on Bictechnology and Life Sciences. Details from Commedia-CIGS Limited, 22/F Sing Po Building, 101 King's Road, North Point, Hong Kong.

2-5 September — Island of Spetsai, Greece. Global Regulation of Gene Expression in Micro-organisms. Details from the Spetsai Summer School Secretary, Institut de Biologie Physico-Chimique, 13, rue Pierre et Marie Curie, 75005 Paris, France.

2-22 September — Abbaye de Solignac, France. Structures and Functions in Biological Organizations. Details from Dr. A. Kretzschmar, INRA, B.P. 91, 84140 Montfavet, France.

3-4 September — Budapest, Hungary. The New Biology of Steroid Hormones. Details from Ares-Serono Symposia, Via Ravenna 8, 00161 Rome, Italy.

4-7 September — Prague, CSSR. Symposium on Bioanalytical Methods. Details from Symposium, House of Technology, Gorkéhonám, 23 CS-111 28 Prague 1, CSSR.

9-14 September — Interlaken, Switzerland. 5th International Symposium: Molecular Genetics of Plant-Microbe Interactions. Details from Dr. Hauke Hennecke, Mikrobiologisches Institut, ETH-Zentrum, CH-8092 Zurich, Switzerland.

11-13 September — Reading, UK. Second International Conference on Separations to: Biotechnology. Details from Prof. D.L. Pyle, Biotechnology Group, Dept. of Food Science and Technology, Reading University, Reading RG6 2AP, UK.

16-22 September — Osaka, Japan. IUMS Congress: Bacteriology and Mycology. Details from Dr. Yoshifumi Takeda, Secretary General, IUMS Congress, c/o the Institute of Medical Science, University of Tokyo, 4-6-1 Shirokanedai, Minato-ku, Tokyo 108, Japan.

24-27 September — University of Leeds, Leeds, UK. Biotech UK. Details from Biotech UK Information, c/o J.D. Bu'Lock, University of Manchester, Manchester M133 9PL, UK.

24-27 September — Gold Coast, Australia. 9th Australian Biotechnology Conference. Details from Prof. P. Greenfield, Dept. of Chemical Engineering, University of Queensland, St. Lucia, Queensland 4067, Australia.

OCTOBER 1990

1-3 October — University of Berne, Switzerland. First International Conference on DNA Fingerprinting. Details from Dr. G. Dolf, Institute of Animal Breeding, University of Berne, Bremgartenstrasse 109a, 3012 Berne, Switzerland.

12-14 October — Gainesville, Florida, USA. 3rd International Symposium on Molecular and Cellular Biology of Insulin and IGFs. Details from Dr. Mohan K. Raizada, Dept. of Physiology, University of Florida, JH Miller Health Center, Room M521, Gainsville, FL 32610, USA.

28-31 October — San Francisco, USA. Anabiotec '90. 3rd International Symposium on Analytical Methods in Biotechnology. Details from Shirley Schlessinger, Anabiotec '90, 400 E. Randolph Drive, Chicago, IL 60601, USA.

29-31 October — Florence, Italy. Plasminogen Activators: From Cloning to Therapy. Details from Department of Clinical Physiopathology, University of Florence, Viale Morgagni 85, 50134 Florence, Italy.

DECEMBER 1990

December — New Delhi, India. Biotek India '90. Details from Ms. Anu Kapor, Convex, 14-F Basant Lok, Vasant Vihar, New Delhi 110057, India.

1991

10-13 April — Boston, USA. International Symposium on Pharmaceutical and Biomedical Analysis. Details from Shirley Schlessinger, 400 E. Randolph Drive, Suite 1015, Chicago, IL 60601, USA.

9-15 June	Frankfurt-am-Main, FRG. ACHEMA 91. Details from DECHEMA, P.O. Box 970146, D-6000 Frankfurt-am-Main, FRG.
August	Jerusalem, Israel. 15th International Congress of Biochemistry. Details from N. de Groot, Dept. of Biological Chemistry, Hebrew University, Jerusalem 91904, Israel.
24-27 September	Leeds, UK. First Conference on UK Biotechnology. Details from Biotech UK Information, c/o J.D. Bu'Lock, Manchester University, Manchester M13 9PL, UK.

1993

1993	Italy. 6th European Congress on Biotechnology organized by Italian Member Societies.

B. ARTICLES

Biotechnology and the Developing Countries: Trends and Options*

BACKGROUND

In the last 15 years, unprecedented developments in bio-sciences have generated an immense interest in the industrial uses of living organisms. The term "biotechnology" has been coined to encompass applications in many diversified fields of economic activity such as the agrifood, chemical, biomedical, energy and environmental industries.

Even the most widely quoted definitions of biotechnology maintain an element of vagueness indicative of the fact that biotechnology is a generic rather than sectoral technology.

Although biotechnology is thousands of years old (fermentation of foodstuffs, brewing, crossing of plant and animal species), the discovery of new techniques such as recombinant DNA-technologies and cell fusion has led to an explosion of applications in almost all sectors of industrial activity. This technological advent distinguishes what is now called "new" from traditional biotechnology. The essential difference is the speed and specificity by means of which the tools of "new biotechnology" confer desired characteristics to organisms. Other differences include:

(i) "New" biotechnology's dependence on techniques across the spectrum of scientific disciplines and in particular:

Genetics/molecular biology
Microbiology
Chemistry
Biochemistry/biophysics
Immunology
Chemical and process engineering
Bio-electronics;

(ii) Integration of fundamental research in production processes;

(iii) Rapid transfer of research into the commercial domain relative to most other technologies;

(iv) Commercialization of biotechnology is dependent on a capacity to manage complex systems, e.g. access, processing, interpretation and exchange of a vast number of data from diversified sources. To acquire this capacity, structural changes of the involved industries may be needed.

INDUSTRIAL APPLICATIONS

1. Health care and pharmaceuticals

The production of therapeutic agents by genetically modified micro-organisms is gradually replacing more traditional methods of production such as large-scale cell cultures and organic synthesis.

Applications in this sector are characterized by the nature of the products (low volume - high-value-added) and the long time lag between development and commercialization. Such applications are inevitably capital intensive. Initial activity has focused on the production of insulin, interferon, human serum albumin, antibiotics, and vaccines for viral, bacterial and parasitic diseases. Increasing activity is envisaged in the fields of endocrinology (hormones) and neurobiology (neurotransmitters).

Development of biotechnologically produced diagnostics is more amenable to accelerated commercialization. Technologies for the development of such products involve oligonucleotide probes, monoclonal antibodies and a variety of immuno assays (RIAs, IRMAs, EIAs, ELIZAs, fluorescence, chemiluminescence, bioluminescence and turbidimetry).

2. Agriculture

The same trends are observed in animal husbandry as in the health care and pharmaceutical industries. The relative expense of developing "new" biotechnology products, however, limits their application to "high value" animals only. Nevertheless this field is attractive for further R&D since the regulatory framework is not as stringent as in the field of human health.

Green biotechnology is proceeding at a rapid pace. Short-term applications will include transferring of simple genetic traits such as stress, herbicide and pesticide resistances from plant to plant. Genetic engineering on symbiotic bacteria (production of pesticides, inhibition of frost formation) is also a short-term target. Long-term goals involve the transfer of complex genetic traits such as increased growth rate, photosynthetic ability and the stimulation of nitrogen fixation. Reduction of fertilizer requirements not only conserves fuel in producing and applying the fertilizers but also minimizes adverse environmental effects from fertilizer accummulation.

Biologic control of plant pests is another major entry point of biotechnology in agriculture. Although the control of insect pests by bacteria (Bacillus thurigiensis) and viruses (baculoviruses) has been known for decades, new possibilities are now open by genetically modifying them to enhance their insecticidal properties. Transfer of bacterial toxins by genetic engineering to internal colonists of plants constitutes an alternative pesticidal strategy.

* This article is based on a paper by George T. Tzotzos (Ph.D), Science Co-ordinator, ICGEB, presented at the Third Conference on New Technologies and Development of the Muslim World, 2-5 December 1989, Kuwait.

3. Food and feeds

The use of micro-organisms with specialized properties in food production has been known since antiquity. Bread-making, brewing and the fermentation of milk products are cases in point. Genetic modification provides a new alternative strategy for confering desired characteristics to micro-organisms used in the food industry. For example, brewers yeast is not capable of degrading starch. Its improvement by the use of classical genetics is limited by the inability to cross yeast strains. Genetically engineered amylolytic (starch degrading) yeast is an attainable target.

The development of probiotic molecules as feed additives to enhance the digestibility of feedstuffs is also an area of intense R&D work.

The production of completely novel foods such as single cell proteins and "mycoprotein" are receiving attention despite presently unfavourable economic considerations.

4. Chemicals

Developments in the biotechnological production of commodity chemicals (acetone, glycerol, ethanol, propanol, etc.) from biomass feedstocks is at present hampered by the unfavourable techno-economic considerations governing the production of commodity chemicals.

Biotechnology has a role to play in the production of low-volume high-value-added chemicals such as amino acids and steroids as well as food additives. Improvement of bioprocesses and replacement of multistep processes by one- or two-step enzymic ones will greatly enhance biotechnology's penetration in this field.

5. Environment

The application of micro-organisms in domestic waste treatment has been known for several centuries. Sludge digestors, settling ponds and trickling filters depend on microbial processes.

Environmental applications of biotechnology will play an increasingly important role. The development of novel waste treatment methods by enhancing the catabolic activities of bacteria by genetic modifications will improve anaerobic and aerobic sewage and silage treatment.

The same is true in the case of biodegradation of pollutants in the environment by the use of genetically modified micro-organisms. Biodegradation, being environment friendly and less costly, is a valuable alternative to non-biological methods such as chemical degradation and incineration. The permanent removal, rather than the mere containment, of organic pollutants under a wide range of environmental conditions is an additional advantage of biodegradation. Furthermore, the combination of several degradative steps in the same micro-organisms is a definite possibility in pollution control.

6. Other industrial processes

Enzyme electrodes used as biosensors are subject to increasing research as are biological conducting devices (biochips). The so-called "bioelectronics" industry is in its infancy however.

Commercial bleaching operations are also beginning to find their way in the mining industry. Thiobacillus bacteria are used to extract metal from low grade ores, mainly copper and uranium. Recovery of precious and semi-precious metals such as silver from seawater by appropriately manipulated bacteria is also possible.

Oil recovery by use of genetically modified bacteria can improve the yield of oil wells by extraction of oil that cannot be recovered by conventional methods.

Biotechnology opportunities for developing countries

The introduction of "new" biotechnology to developing countries has a unique strategic significance in that it can contribute considerably to the quality of life by providing solutions to survival problems, such as disease, food and fodder, fertilizer and fuel. Failure to commit human and material resources to the sustainable introduction of biotechnology will inevitably lead to the broadening of the existing gap between North and South, as the requisite elements for the commercialization of biotechnology (i.e. academic and industrial infrastructure, funding of research, financing, etc.) offer developed countries significant advantages for the accelerated exploitation of living organisms.

In addition, developing countries cannot afford to miss the opportunities offered by "new" biotechnology in taking full advantage of the great wealth of their indigenous natural resources, hitherto unidentified and/or under-exploited. Screening and identification of natural resources, overlooked until recently, is now beginning to receive attention in industrialized countries. Genetic resources could offer solutions to a number of industrial process problems. For example, the understanding of the rapid turnover of vegetable life on the very thin topsoils of some developing countries and the genes responsible for this, locked in plants and micro-organisms, could play an important role in the energy and environmental industries. Sewage treatment is an obvious application, as the growing problem of urban sprawl in the developing world makes sewage control a major environmental and public health issue. In addition, the high turnover of waste organic matter provides exciting opportunities for conversion into useful products. These opportunities will, however, have to be seen in their global perspective.

UNIDO's role in biotechnology

The challenge is to impart a decisive momentum to activities involved in the sustainable development and application of biotechnology for developing countries and to avert any adverse side-effects such as loss of germplasm, displacement of exports, negative impact on the labour market, etc.

UNIDO's biotechnology programme

In industrialized countries, commercialization of biotechnology, as with all other innovative industrial activities, because of its capital-intensive nature, leads to ever-increasing dependence on private sector R&D investment. Securing returns on investment is conducive to privatization of know-how and to pressures for stringent regulatory mechanisms (patenting).

In developing countries, indigenous development of biotechnology is not only hampered by the inadequacy of financial resources but also from the insufficiency of mechanisms to analyse global technology trends, inadequate science base and trained manpower, and unfavourable legislative and

socio-economic frameworks. The equitable distribution of benefits arising through North to South collaboration to transfer biotechnology is likewise impeded by the same negative constraints.

The preceding short description of positive and negative considerations pinpoints the need for the adoption of innovative strategies and mechanisms to effect the introduction of "new" biotechnology to developing countries. Some of the considered strategy options are given below:

- Development and transfer of biotechnology through the creation of structures at the supranational level, with the necessary support and necessary social, political and economic authority from national governments to guarantee their role.

- Identification of products or processes where large spin-offs of research carried out in industrialized countries can be adapted to specific problems in developing countries. This may be the case where North and South objectives do not coincide. Results for example obtained in corn research may well find applications for millet.

- Establishment of international resource centres to address specific problems of the developing world and serve as focal points in the development and dissemination of biotechnology.

In so far as the first option is concerned UNIDO's role can be only promotional. The latter two, separately or combined, provide UNIDO's biotechnology programme with greater scope. The establishment of the International Centre for Genetic Engineering and Biotechnology (ICGEB), for example, is a key project in UNIDO's biotechnology programme. The activities of ICGEB are multivalent aiming not only at strengthening the basic research capability of its members but also at increasing awareness in biotechnology. Joint collaborative projects with affiliated laboratories provide stimulus to further expand the research activities of the latter. The various training programmes offered ensure that significant numbers of scientists from Member States are trained in the most modern techniques, bearing direct relevance to the agricultural and health problems of their countries. The Centre as a central resource of communication networks, specialized major equipment, journals and data bases etc. provides services which, more often than not, could not be afforded by its individual member countries. In addition, a wide network of affiliated centres in Member States serve as localized nodes in a network distributing information and material resources.

The above represented feasible options are in the light of the considerable volume of information that has accumulated through the involvement of UNIDO and ICGEB in a large number of activities in Muslim countries. Fourteen of the 41 members of ICGEB are Muslim countries. Three of its 12 affiliated centres are in Algeria, Egypt and Nigeria. A proposal from Iraq to host an affiliated centre is currently receiving attention. ICGEB scientists have visited all affiliated centres to identify areas for collaborative research and development. ICGEB, through interaction with its members, has built up data bases of R&D priorities, available human and material resources, needs etc. UNIDO has fielded expert missions to Egypt, Kuwait and Saudi Arabia. These, in the case of Egypt, resulted in the formulation of a project to support the Genetic Engineering and Biotechnology National Programme and in the establishment of a National Agricultural Genetic Engineering Laboratory. Of these, the former, still in the preparatory assistance phase, will address problems in plant biochemistry (drought and salt resistance factors in legumes), food industry (conversion of sucrose into cyclodextrins) and health (epidemiology and serotyping of pathogenic strains of E. coli). A bioinformatics unit will provide valuable support services to the teams involved in the above areas of research. The second project, already under way, addresses a spectrum of increasingly complex scientific challenges ranging from tissue culture technology to the use of Restriction Fragment Length Polymorphisms as molecular markers to increase plant breeding efficiencies and to the genetic transfer of genes controlling growth, maturity and quality. Research performance will determine the potential for future laboratory expansion and addition of new project goals. Both projects aim at building up R&D capability through pilot projects and extensive twinning arrangements with established international laboratories.

A National Plan of Biotechnology for Kuwait has been developed with UNIDO's assistance. The Plan comprises eight pilot projects grouped in four priority areas (health care, industrial, marine and agricultural biotechnology). Projects in DNA diagnostic probes for human diseases and mitochondrial DNA fingerprinting of marine organisms are intended to provide needed basic expertise in manipulating DNA. Similarly, screening and development of Kuwaiti microflora to develop de-emulsification systems, biosurfactants and chiral intermediates for the petrochemical and fine chemicals industries have been chosen as technologies of intermediate level of complexity that may lead to commercial applications. The same rationale led to the selection of advanced tissue culture as an adjunct to conventional methods of producing stress tolerant plants.

In Saudi Arabia, a preliminary mission of UNIDO consultants was followed up by a National Biotechnology Conference with contributions from international experts. The Conference aimed at defining priority R&D areas for the national academic and industrial laboratories.

The first phase of a collaborative research project for the development of industrial micro-organisms producing high levels of cellulases, between the University of Lahore and Trinity College, Dublin, has been concluded with very interesting results and will be followed up with the involvement of laboratories from China and Italy.

Common patterns have emerged through these UNIDO activities despite the fact that they were prompted by the specific needs of individual countries. They may be summarized in the following:

(a) National options focus on concentrating human and material resources on a small number of projects of national interest. These are meant to serve as pilot activities to introduce "new" biotechnology. Their longevity and impact is subject to being provided with adequate political support and financial backing.

(b) Networking with other national and international laboratories is an appropriate mechanism to broaden the scope of these activities, enabling research teams to reach critical mass levels and, in addition, reduce costs of research through the sharing of resources.

(c) Demand for training in all biotechnology related disciplines is great. The ensuing costs, estimated at $20,000 per man/year, can be substantially reduced if some of the training is provided at home. This can best be effected through the utilization of modern teaching aids and permanent courses with the participation of staff from the international twin laboratories.

With the above set in perspective, UNIDO is currently formulating two interrelated demonstration projects aimed at the establishment of an R&D centre of hydrocarbon microbiology acting as a central resource of a network of national academic and industrial laboratories dealing with problems of enhanced oil recovery, environmental pollution due to oil spillages and microbial conversion of wastes. The importance of the oil industry to many Muslim countries provides the necessary ground for such collaborative transnational R&D undertaking. In support of this initiative an inventory of advanced teaching aids, including audio-visual and instrumentation simulation software and hardware will be prepared and maintained with regular updates. A laboratory of the network may then be assigned a central training role servicing the needs of the collaborating national laboratories, organizing appropriate short- and long-term courses, both in-house and extramurally, and utilizing and developing appropriate teaching aids.

In addition to these initiatives, UNIDO's biotechnology programme and the services provided by ICGEB should be taken to full advantage. Established international structures are essential adjuncts for technology transfer and the strengthening of the national R&D capabilities. It is precisely this that led UNIDO to the establishment of ICGEB. The activities of ICGEB are multivalent, aiming not only at strengthening the basic research capability of its members, but also at increasing awareness in biotechnology. Joint collaborative projects with affiliated laboratories provide stimulus to further expand their research activities. The various training programmes offered ensure that significant numbers of scientists from Member States are trained in the most modern techniques, bearing direct relevance to the agricultural and health problems of their countries. The Centre as a central resource of communication networks, specialized major equipment, journals and data bases etc., provides services which more often than not, could not be afforded by its individual member countries. In addition, a wide network of affiliated centres in Member States serve as localized nodes in a network distributing information and materials.

UNIDO's biotechnology programme is not limited to ICGEB and includes other important elements such as:

A. Information acquisition and dissemination

Quantification of data and forecasting require expertise in the acquisition, processing and exchange of information on technology and market trends.

The mechanisms currently employed are:

(a) Inter-agency collaboration, such as the UNIDO/WHO/UNEP Working Group on biosafety.

(b) Collaboration with Member States to organize symposia, workshops and colloquia to enhance awareness, information exchange and to catalyze activities at the national and/or regional level;

(c) Sectoral meetings, convened to examine specific topics (for example animal vaccines, lactic acid fermentation, etc.);

(d) Monitoring international trends, by studying issues related to licensing in biotechnology and the changing structure of the technology market;

(e) Sectoral policy-oriented studies, such as enzymatic conversion of cellulose and marine biotechnology;

(f) Publications such as the quarterly current awareness bulletin, Genetic Engineering and Biotechnology Monitor and the Directory of Biomass Research Institutes; and

(g) Compilation and maintenance of a biotechnology roster of scientists and technologists.

Short-term objectives

- Continuation of promotional activities and preparation of information packages intended to introduce and increase awareness of government officials, policy makers and investors in developing countries in the potential applications of biotechnology.

Medium/long-term objectives

- Preparation of sectoral studies, e.g. analyses, forecast and assessment of developments in the various sectors of the bio-industries.

- Building up a bio-informatics network accessible to member countries.

B. Policy, programme formulation

UNIDO's role is focused on sensitizing and increasing the awareness of national governments in the all-pervasive impacts of biotechnological applications. It also assists member countries to analyse technology and market trends, identify sectors of application, and optimal entry points.

Current and short-term objectives

- Stimulation of awareness in biotechnology at the national level through seminars and advisory missions.

- Assistance in the formulation of national biotechnology programmes.

Medium/long-term objectives

- Identification of national and regional needs.

- Identification of sectoral priorities.

C. R&D capability building

R&D co-operation between institutions in developed and developing countries, joint collaborative programmes and provision of services by ICGEB have been initiated and constitute major activities in this programme element.

Current and short-term objectives

Setting up of an international service for the supply of bioreagents to researchers in developing countries.

Stimulation of product oriented R&D in the fields of starter cultures for the dairy industry and carbohydrate biopolymers.

Medium/long-term objectives

- Demonstration projects.

- Transfer of technology through technological co-operation at the enterprise level and through investment promotion.

D. Biotechnology industrial capability building (BICB)

The process of BICB and commercialization is largely independent of the industrial sector involved. In all cases certain prerequisites must be met including:

- Market research
- Product development
- Economic assessment
- Production
- Marketing
- Financial analysis

At this stage of the industrialization process, the need for financial resources increases exponentially.

Current/short-term objectives

- BICB project supervision.

- Process development and product adaptation to the needs of developing countries.

- Seeking new sources for financing BICBs other than through UNDP and ID funds.

Medium/long-term objectives

- Encouragement of licencing agreements between developed and developing countries.

* * * * *

COBIOTECH'S role in biotechnology world wide

The curious or skeptical often ask, "What and why is COBIOTECH? What is it doing?" Philipp Gerhardt* attempts here to provide information for the curious and allay concerns of the skeptics about COBIOTECH's emerging role in biotechnology internationally.

COBIOTECH is the acronym of the Commitee for Biotechnology, which is an interdisciplinary scientific consortium within the International Council of Scientific Unions (ICSU). ICSU is a world-wide non-governmental scientific umbrella organization of 20 international scientific unions, 75 national academies of science and councils of research, and 26 associate scientific organizations. Its goal is simply to encourage co-operation in international scientific activity for the benefit of humankind, with special concern for the less-developed countries of the world. ICSU pursues this objective through a network of scientific unions, scientific and special committees, inter-union commissions, working groups, and permanent services. It organizes joint international scientific programmes and projects in multi- or transdisciplinary fields, such as the current International Geosphere-Biosphere Program to study global change. It enjoys reciprocal working associations with numerous intergovernmental organizations, notably UNESCO (an acronym better known than its full name, the United Nations Educational, Scientific and Cultural Organization). ICSU has vigorously and rigorously enforced a policy of non-discrimination, so that scientists throughout the world can freely join in its scientific activities without regard to race, religion, political philosophy, ethnic origin, citizenship, gender, or language. In my years of association, I have come to admire ICSU as an effective, efficient, worthwhile organization that ably serves science in general and biotechnology in particular around the world.

As for COBIOTECH, its goals are to promote biotechnology in breadth for the benefit of humankind and to inform and advise the international community about biotechnology, reflecting ICSU's special concern for developing countries. COBIOTECH'S objectives boil down to initiation and co-operation with appropriate organizations within and outside ICSU, including the industrial community, for the advancement of research and education and for the transfer of information and resources in biotechnology.

COBIOTECH is led by an internationally representative steering group, newly comprising Ephraim Katchalski-Katzir, President (Israel); Konstantin G. Skryabin, Secretary (USSR); Isao Karube, Treasurer (Japan); Ronald E. Cape, (USA); Philipp Gerhardt (USA); K. C. A. M. Luyben (Netherlands); S. N. C. Okonkwo (Nigeria); Manfred Ringpfeil (GDR); and Carlos Rolz (Guatemala). The recently retired Secretary, Jorge E. Aliende of Chile, contributed greatly to establishing COBIOTECH as an effective organization. A general assembly is convened annually and is attended by representatives of the participating countries and organizations. Active participation and financial support have come from 21 countries, four unions (the International Unions of Microbiological Societies, Pure and Applied Chemistry, Biochemistry, and Biological Sciences), and several biotechnology companies. Written pledges continue to be received.

COBIOTECH overlaps and co-operates with other interdisciplinary committees within ICSU. The Scientific Committee on Genetic Experimentation (COGENE) is focused on research activities related to recombinant DNA technology, whereas COBIOTECH covers the breadth of biotechnology, including bio-engineering, and has a broad programme of activities and a wide constituency. The Committee on Data for Science and Technology (CODATA) is concerned with data management and use, with which COBIOTECH is becoming more involved. The International Biosciences Networks (IBN) is a joint ICSU-UNESCO programme that helps developing countries to build up their capacities in the biological sciences, including biotechnology.

COBIOTECH also interacts with regional biotechnology organizations, such as the European Federation of Biotechnologists, and with a wide range of intergovernmental organizations interested in biotechnology. These especially include UNESCO, UNIDO (the United Nations Industrial Development Organization) and its International Centre for Genetic Engineering and Biotechnology in Trieste, and UNDP (the United Nations Development Programme). As examples of these interactions, representatives of COBIOTECH served on an advisory panel for the generation of new biotechnology programmes to be implemented by UNESCO, and

---

* Philipp Gerhardt is the immediate Past President of COBIOTECH and a former President of the International Union of Microbiological Societies and of the American Society for Microbiology.

proposals are being submitted to UNDP for long-term substantial support for strengthening biotechnology training and research in the third world.

COBIOTECH was created in September 1986 by ICSU in response to a grassroots request from representatives of several unions meeting at biotechnology conferences for the formation of a transdisciplinary group that would co-ordinate all aspects of biotechnology internationally. COBIOTECH's first and organizing general assembly was convened at Amsterdam in June 1987, the second one at Paris in July 1988, and the third one at Kiev in September 1989. The next general assembly is scheduled at Copenhagen on 13-14 July 1990, after the 5th European Congress on Biotechnology.

In acting on ICSU's desire to develop links with industry, COBIOTECH included on its steering group several individuals having industrial affiliations, and convened industry panels at its general assemblies to provide direction. An effort was made recently to enlist participation from an extensive number of biotechnology companies and organizations, but relatively few of them have perceived COBIOTECH'S activities and plans as filling their immediate needs.

COBIOTECH's activities are in three general directions - research, education and information transfer. In each of these it seeks to avoid duplication of existing activities by other organizations and to join in co-operative efforts.

Research efforts are focused on conferences and workshops in selected areas. For example, early on COBIOTECH had identified marine biotechnology as an untended, important, burgeoning field and so asked its treasurer, Isao Karube, to lead an effort in Japan to organize an international conference on this subject. Within a year, a Japanese Society for Marine Biotechnology was formed, and international and local organizing committees were convened to plan the programme and raise funds. On 4-6 September 1989, in Tokyo, this first International Conference on Marine Biotechnology was attended by more than 400 scientists, including more than 100 from 25 countries, who participated in a wide-ranging stimulating programme. A second conference is scheduled for September 1991 in Washington, D.C. COBIOTECH is also looking forward to a series of focused workshops in 1990 on the degradation and utilization of lignocellulose, to be held at Trieste in co-operation with UNIDO's International Centre for Genetic Engineering and Biotechnology.

COBIOTECH's educational activities are managed by a co-ordinating panel (chaired anew by Arnold L. Demain), directed especially towards developing countries, and financed by multiple sponsors. A good example is a COBIOTECH-initiated training course on biogas production by thermophilic micro-organisms, which was held last August in Nigeria, staffed by GDR scientists, and co-sponsored by the African Biosciences Network and the African Microbiology Network. Also held recently, or soon, are training courses and workshops on microbial breeding (in Italy and Yugoslavia), next generation of vaccines (in Switzerland), yeast biotechnology (in Colombia and Nigeria), and engineering of biological reactions and processes (in Guatemala). Upcoming are other training courses and workshops: techniques for human genome research (in Chile); bio resources, processes, products and equipment (in Czechoslovakia); micropropagation of forestry species (in Venezuela); advanced plant biotechnology (in the USSR and Nigeria); environmental biotechnology (in Latin America); and protein engineering (in Latin America).

The main focus of COBIOTECH'S informational activities, managed by another co-ordinating panel, is a resource book Biotechnology Worldwide. It is being organized with James Coombs and Peter N. Campbell as editors. The book will contain reports on the state of biotechnology in more than 50 developing as well as developed countries, as viewed by selected internal correspondents. Each report will be written in a prescribed format and length, and will be subject to external review and editing. Provision is being made for inexpensive publication and for reproduction and wide distribution in developing as well as developed countries.

COBIOTECH'S steering group met recently in conjunction with a symposium, Human Genome Research: Strategies and Priorities, at Paris. There the new leadership aimed its sights on where and how to serve biotechnology internationally in the years ahead, and reset the stage for the useful role that COBIOTECH can play in biotechnology worldwide.

* * * * *

Seeds - breeding extinction

In this issue we highlight the rapid disappearance of the genetic diversity of seeds, especially those of grains and vegetables that have become essential foods for people everywhere. Ironically, the extinction of a growing number of traditional seed varieties is the direct result of major technological advances that have increased food production while seriously reducing the variety of plant species required for successful breeding. Compounding the problem, some corporations are more concerned about patenting new seeds than in ensuring their diversity and the very future of our food system. This article, prepared by the Rural Advancement Fund International,* stresses the importance of finding ways to conserve our priceless agricultural diversity.

Thousands of different and genetically distinct varieties of our major food crops are being cultivated by farmers around the world. These different types were developed over the years to be grown in different ecological conditions and for different purposes.

But today, much of this genetic diversity is being lost. Many of these unique varieties are disappearing and becoming extinct. The introduction of modern grain varieties in the Middle East has led to the widespread disappearance of traditional varieties. African rice is nearly extinct in its native West African homelands. It is estimated that three quarters of all vegetable varieties now grown in Europe will vanish in the next decade.

---

* The Rural Advancement Fund International (RAFI) is a non-governmental organization working for the conservation of genetic resources. Its activities include research, writing, lobbying, public education and consulting on both policy and technical matters.

RAFI, R.R. 1 (Beresford), Brandon, Manitoba, Canada R7A 5YI, or RAFI, P.O. Box 1029, Pittsboro, North Carolina 27312, USA.

The rapid disappearance of so many grain and vegetable varieties has been described as a botanical holocaust. A variety of hybrid rice called IR-36 now extends over 60 per cent of the rice lands of South-East Asia where, only a few years ago, thousands of varieties were common. Another strain, IR-8 rules from the cool of Taiwan to the heat of Benin. Where 30,000 different varieties of rice grew only a few years ago, Indian agronomists now expect that no more than a dozen will soon dominate three quarters of the land. The Detroit Globe beet (introduced to Turkey by a German company) has "mopped up" - or eliminated - its own gene pool in the Near East. Melons and watermelons brought by American companies are eroding the gene pool of native varieties in Africa, and the Black Beauty eggplant is single-handedly destroying its own diversity in the Sudan. From Malaysia to Rwanda, farmers sow Palmetto soybeans. In the Middle East, Beecher and OP25 barleys have claimed close to half the crop while Mexipak and Sonalika have shattered the kaleidoscope of wheats and now account for 70 per cent of the harvest. A vast sameness is descending like a curtain over the agricultural stage.

To some the replacement of old with new is part of the march of progress. But more and more people are realizing the importance of preserving the traditional crop varieties. In the field and garden, genetic diversity often thwarts the attempts of pests and diseases to inflict major damage. The third world farmer who plants several different kinds of seed in a field is often sowing insurance against crop failure if one variety succumbs to a disease or a period of bad weather.

Generally speaking, genetic diversity in a crop safeguards its adaptation to different environments and growing conditions. The ability of a certain plant variety to withstand drought, grow in poor soil, resist an insect pest, give higher protein yields or just produce a better tasting food is passed on naturally by the variety's genes. The genetic material from the world's thousands of distinct varieties of wheat or all the different potatoes constitutes the raw material plant breeders use to breed new crop varieties. Without this diversity plant breeding would cease. Pests and diseases would have a stationary target to attack. Crop evolution would come to a standstill.

The value of genetic diversity (the largest gene pool is in the third world) to modern crops in industrialized countries is difficult to exaggerate. Every wheat variety grown in Canada contains genes introduced in recent decades from up to 14 different countries. American cucumbers find the genes for disease resistance from as far away as Korea, Burma and India. Modern lettuce varieties include genes from Israel, Italy and Turkey. Tomatoes could not be grown commercially in North America were it not for genes from wild tomato species from Central and South America. The world's leading hybrid grain sorghums are based upon Zera-Zera sorghums from the Sudan and Ethiopia.

With world agriculture and millions of lives and livelihoods dependent on genetic diversity, common sense tells us that the loss of these resources imperils our very food supply.

It is important to realize why third world genetic resources are important to third world people. Traditional crop varieties are part of the whole agricultural system. They are interwoven with different farming practices, human cultures, ecologies and local histories. Old varieties have adapted over centuries to the local climate. The local farmers know how to nurture and sustain them and they have become embedded in the native culture and economy. When an old variety ceases to be planted and becomes extinct it is not a distant crop breeding programme that suffers the greatest loss but the local community and its people. The simple extinction of a traditional variety can sometimes so profoundly disrupt a native agricultural system that it can provoke economic calamity, even famine.

Natural gene banks

In the last 30 years efforts have been made to collect specimens of diverse crops and store them for safekeeping under conditions of low temperature and low humidity in facilities called seed or gene banks. But the promise of gene banks - to conserve genetic diversity - often goes unfulfilled. Technical inadequacies and equipment failures pose significant problems. More troubling is the fact that once stored, seeds are removed from the process of evolution. Literally frozen in time, the life of the variety will depend more on its ability to adapt to gene bank conditions than the characteristics that made it valuable enough to collect and store in the first place.

Not surprisingly, much diversity is lost inside the gene banks. William Brown, former president of Pioneer Hi-Bred, the world's largest maize seed company, asserts that more maize diversity is being lost within the gene banks than in the outside world today.

Ideally, the proper role for gene banks is as one component of a large system which includes farmers and gardeners preserving and cherishing the different varieties they grow. In these gardens our crops originated and diversity flowered. Here evolution continues. The best conservation system maintains the invaluable and historic role of people in creating and maintaining diversity. And it uses modern technology, like gene banks, to aid and supplement that endeavour.

Geographically, biological diversity is not evenly distributed. Perhaps one half of the world's plant and animal species are located in tropical moist forests. The tiny nation of Panama contains more species diversity than all of North America.

Agricultural scientists have long recognized that there are geographic "centres" where the diversity or richness of varieties of particular crops and their wild relatives are greatest. These are called "centres of diversity".

Usually, but not always, a crop's centre of diversity corresponds to where the crop originated. Potatoes originated in the Andes. It is in the Andes where potatoes have been cultivated for thousands of years that the crop has had the opportunity to develop the most diversity.

In early times, however, crops migrated with people. Often important "secondary" centres of diversity sprang up over the course of hundreds or thousands of years far away from a crop's original homeland. Maize, for example, comes from Central America. But valuable diversity can now be found in Asia. Apples are from Asia, but Americans have cultivated over 7,000 distinct varieties in the last 200 years.

Unlike the vast fields that modern agriculture has created with single crops stretching to the horizons, the family-sized gardens of traditional ethnic people tend to be a mosaic of different kinds of plants. Herbs, root crops, fruits, flowering vines and hedgeplants may all be intermingled. Perhaps this kind of garden evolved so that humans could satisfy their need for a diversity of tastes, sights and smells. In any case, such gardens provided the variety of foods needed for a balanced and nutritious diet.

Yet this diversity also plays an ecological function. Whenever various crops are grown together they tend to utilize the scarce resources available in their environment, such as water, nitrogen and light, more efficiently. One kind of plant may harbour a predatory wasp which preys upon the pest of another, neighbouring plant. One kind of flower may keep bees in an area until a second kind needs them to perform pollination. A mixture of plants may hide the most vulnerable one from pests that would easily destroy it in the open.

Crop evolution

Any variable population of a crop is co-evolving in relation to other organisms present in the area. The crop evolves new ways of fending off the animals and micro-organisms that attack it. In turn, the pests are always attempting to evolve new ways to neutralize the plant defences. The price for each to remain a contestant in the co-evolutionary race is to have available the genetic diversity on which this natural selection can act.

But crop evolution is not just about plants and bugs. It is also about people - all kinds of people.

Farmers notice things about their crops that others cannot see The scientist who proudly "discovered" that an Ethiopian sorghum he had collected had a high protein content and excellent baking qualities could have saved himself some time in the laboratory if only he had asked Ethiopian farmers about the variety. Their name for it was sinde lemine which translates as "why bother with wheat".

Farmers and gardeners often appreciate qualities in their crops that others do not. Sometimes these qualities are aesthetic. But they can be very practical.

The crop diversity we all depend on today was not created by people who were satisfied with having the exact same variety everyone else had. Differences in plants were noticed, encouraged and perpetuated by people who appreciated and valued those differences, often for reasons we cannot fully understand today. Different cultures and different needs played an important role in creating diversity.

Until recent times every farmer was a plant breeder. From the dawn of agriculture 12,000 years ago until the twentieth century, each farmer had to produce and save his/her own seed for sowing the next season. This necessity contributed to the development of genetic diversity and resulted in varieties remarkably well adapted to very specific conditions.

Today seeds are a $13 billion a year business, and plant breeding is a corporate activity. The number of plant breeders has been reduced from millions to a mere handful of specially trained scientists employed by a still smaller number of giant transnational corporations.

In the past 20 years government involvement in plant breeding has declined and giant petrochemical and drug companies have moved in to acquire hundreds of once family-owned seed companies all over the world. One of the largest seed companies in the world today is Royal Dutch/Shell. Other dominant plant breeders today are Ciba-Geigy and Sandoz of Switzerland, Atlantic Richfield, Upjohn, Occidental Petroleum, Pfizer, and ITT of the United States; Lafarge Coppee, Elf Aquitaine and Rhone-Poulenc of France; Volvo and KemaNobel of Sweden; and Dalgetty and British Petroleum in the UK.

Corporate takeover

These corporations have become involved in the seed business for several reasons. It is highly profitable; the distribution channels are identical to those of their crop chemicals; and, according to the current head of Pioneer Hi-Bred, because of the possibility of linking chemical and seed development and marketing. Ciba-Geigy, for instance, markets its own brand of sorghum seed which comes wrapped in three chemicals, one of which is to protect the seed from Ciba-Geigy's leading herbicide. The integration of these technologies into one marketing package allows the company to sell more seed and more chemicals.

Through sheer size and economic power, the transnationals have come to dominate the commercial seed market, especially in industrialized countries where laws give corporations patent-like control over new varieties they develop. Often called "Plant Breeders Rights", these laws allow corporations to own plant varieties and set the sale conditions for them. This has meant that the few companies big enough to have full-fledged plant breeding programmes obtain most of the patents, locking up the market on new seed varieties. Furthermore, these same companies often cease to offer traditional varieties because no patent-like control can be obtained over varieties that predate the laws, resulting in many traditional varieties falling out of use. If they - and the centuries of plant breeding work that went into them - are to be preserved, farmers and gardeners will have to do it.

The extension of patenting laws to the third world would mean that companies could control and market crop varieties in countries which had donated the genetic material used to breed those varieties. Increased imports of patented varieties to centres of crop diversity in the third world would result in the wholesale replacement and extinction of traditional varieties.

When traditional varieties become extinct, communities lose a bit of their history and culture, and the plant species loses some of its gene pool. Future generations lose some of their options and the present generation forfeits its self-reliance. The type of seed sown tends to determine the farmer's need for fertilizers, pesticides and machinery, and often the market for the crop and the ultimate consumer. Communities that lose traditional varieties, adapted over centuries to their needs, lose control and become dependent - forever - on outside sources of seeds and the chemicals needed to grow and protect them. The loss of a traditional quality like drought resistance can cause real hardship for farmers because seeds bred

for large farms in industrialized countries are rarely bred for drought resistance. Without an agricultural system (and seeds) adapted to a community and its environment, self-reliance in agriculture is impossible. Saving agriculture's genetic diversity does not guarantee self-reliance or development, but losing this diversity does reduce options and foster dependency.

The gene revolution

The widespread introduction of modern, high-yielding varieties since the 1950s has been called the "Green Revolution". Today, a new and more important revolution is beginning. It is the "Gene Revolution". Biotechnology and genetic engineering hold out the promise of significant alteration in virtually every crop.

We can expect yield increases as high as 500 per cent for some crops like oil palm and cassava. New coconut trees yielding over 1,000 per cent more coconuts annually are possible. Such developments will alter the structure of these industries, affecting supplies, price, the need for labour and land. Breakthroughs in one crop could seriously affect the fate of other similar crops overnight.

Disease and pest resistance may be enhanced by biotechnology. However, the widespread use of "clones" (produced by tissue culture) in the field may ultimately make the crop more vulnerable due to genetic uniformity. The breeding of crops more appropriate to the use of herbicides and other crop chemicals is a certainty.

Biotechnology will decrease the length of time needed to breed and commercially distribute new plant varieties, and this will probably accelerate the loss and ultimate extinction of presently used "primitive" and traditional varieties.

Genetic resources form the foundations for traditional plant breeding and the new biotechnologies. Ironically biotechnology may end up contributing to the loss of the very resources upon which it depends.

Biotechnology will certainly bring about startling increases in crop yields. It will produce new, previously unattainable pest and disease resistance for some crops, but perhaps at the cost of making the entire crop genetically uniform. It may totally eliminate the in-field production of some commodities. It will probably produce new organisms, plants and animals to do things we cannot currently imagine.

How biotechnology is used, what problems (and whose problems!) it is directed to solve, and who benefits from it will be decided by who controls the technology and how strongly those who do not control it can influence those who do. In any case our present genetic resources must be preserved to provide the raw material for the good things biotechnology can produce, to provide options and insurance against the negative effects it could have to give those presently without power (but with genetic resources) a greater voice in determining the direction biotechnology takes.

From millions of plant breeders to a few; from a public activity to a private one; from varieties owned by everyone or no one to varieties and even individual genes patented by corporations; from the common heritage of mankind to the raw material stockpiled in gene banks - the trend is one of lessening public ownership, control and participation in the conservation and breeding of plants.

Concerned about the loss of genetic diversity and the growing "privatization" of the resources, third world governments have begun important discussions at the United Nations Food and Agriculture Organization (FAO). Third world countries have called for an international agreement for the full and free exchange of all genetic resources and an international system of gene banks under FAO auspices. In 1983 they succeeded in establishing an FAO Commission on Plant Genetic Resources which for the first time has given governments the opportunity to sit down with each other and focus solely on the conservation, control and utilization of genetic resources.

There are also efforts to establish a World Gene Fund to support the conservation and development of seed resources within the third world.

The reasons for conflict over genetic resources are clear. Genetic resources are the only raw material in the world that is donated - largely by the poor to the rich. Over the last decade of intensified collection, more than 90 per cent of the seed has been gathered in the third world but almost the same percentage has either gone to industrialized countries (where plant patent legislation prevails) or to the International Agricultural Research Countries (IARCs) located throughout third world regions. In either case, it has escaped the sovereign control of the donating country and it is far out of reach of the farmers who created and sustained the diversity in the first place. (Reprinted from Development Forum, May-June 1989)

For new subscribers only

UNITED NATIONS INDUSTRIAL DEVELOPMENT ORGANIZATION

(UNIDO)

UNIDO MAILING LIST QUESTIONNAIRE

UNIDO MAILING LIST, INDUSTRIAL INFORMATION SECTION,
P.O. BOX 300, A 1400 VIENNA, AUSTRIA

	Type or print clearly (one letter per box) and leave a space between each word
NAME (underline family name)	
TITLE OR POSITION	
ORGANIZATION	
STREET AND No. (or P.O. Box)	
CITY AND STATE OR PROVINCE	
COUNTRY	

PLEASE DO NOT WRITE IN THESE SPACES

S/A ☐ DISP. CODE ☐ COUNTRY ☐☐☐

CITY ☐☐☐☐☐☐☐☐☐☐☐☐

T TYPE OF ORGANIZATION: Identify below the type of organization to which you belong, checking the box(es) as appropriate (e.g., for a research centre at a university, boxes 20 and 23 would be applicable)

01	☐	UN, specialized agency or other UN body	12	☐	Trade centre or association	23	☐ Research centre/laboratory
02	☐	Other intergovernmental organization	13	☐	Professional association/learned society	24	☐ Library/documentation centre
03	☐	International non-governmental organization	14	☐	Bank or financial institution	25	☐ Information centre
04	☐	UNIDO National Committee	15	☐	Industrial enterprise	26	☐ Publisher
05	☐	Embassy or Mission to UNIDO	16	☐	Public utility	27	☐ Bookseller
06	☐	Government body for development aid	17	☐	Trading concern	28	☐ News agency/press
07	☐	Ministry for industry	18	☐	Engineering organization	29	☐ Radio and television
08	☐	Other governmental department	19	☐	Consultant		
09	☐	Non-governmental aid agency	20	☐	University		
10	☐	Chamber of industry or commerce	21	☐	Vocational or technical institute/school		
11	☐	Manufacturers' association	22	☐	Industrial training or productivity centre		

F FIELD OF INTEREST: Check the appropriate box(es) which reflect your *main* field(s) of interest.

MANUFACTURING INDUSTRIES – PLANTS, PROCESSES AND PRODUCTS								
001	☐	Food processing	017	☐	Electrical machinery	030	☐	Industrial legislation
002	☐	Beverages	018	☐	Transport equipment	031	☐	Industrial property
003	☐	Tobacco	019	☐	Precision instruments	032	☐	Transfer of technology (licensing)
004	☐	Textile and garment	020	☐	Agricultural machinery	033	☐	Industrial research and development
005	☐	Leather	NON-MANUFACTURING INDUSTRIES AND PROJECTS			034	☐	Standardization
006	☐	Wood processing	021	☐	Mining and quarrying	035	☐	Industrial organization and administration
007	☐	Pulp and paper	022	☐	Utilities (including power plants)	036	☐	Industrial co-operatives
008	☐	Petrochemical and plastics	023	☐	Public services (transport, communications, tourism)	037	☐	Industrial information and documentation
009	☐	Industrial chemicals and fertilizers	024	☐	Construction (civil engineering) projects	038	☐	Industrial promotion
010	☐	Pharmaceuticals and other chemical products	SUPPORTING INDUSTRIAL ACTIVITIES			039	☐	Industrial training
011	☐	Rubber	025	☐	Industrial planning and programming	040	☐	Industrial management
012	☐	Non-metallic mineral products and building materials	026	☐	Industrial policies	041	☐	Industrial consulting services
013	☐	Iron and steel	027	☐	Industrial financing and investment promotion	042	☐	Development of small-scale industries
014	☐	Non-ferrous metal	028	☐	Promotion of export oriented industries	043	☐	Industrial estates
015	☐	Fabricated metal products	029	☐	Industrial development surveys	044	☐	Appropriate technology
016	☐	Machinery						

LANGUAGE: Indicate below in which language you wish to receive the NEWSLETTER

ENGLISH ☐ FRENCH ☐ SPANISH ☐ RUSSIAN ☐