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UNITED NATIONS INDUSTRIAL DEVELOPMENT ORGANIZATION

Genetic Engineering and Bio-technology Monitor

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Dear Reader,

Many of you may have heard by now via the media that UNIDO has been converted to a specialized agency of the United Nations system. At the General Conference of the newly independent organization, held during August at the historic Hofburg in Vienna, Mr. Domingo L. Siazon Jr. was elected Director-General of UNIDO for a four-year term. Mr. Siazon, who is well-known to Vienna's international community, had for many years served as Ambassador of the Philippines to Austria and Permanent Representative of his country to the United Nations Office in Vienna, the International Atomic Energy Agency and UNIDO. Mr. Siazon succeeds Dr. Abd-El Rahman Khane who had been Executive Director of the former UNIDO for more than ten years.

In this issue of the Genetic Engineering and Biotechnology Monitor you will find a brief report on the International Workshop on Biotechnology in Agriculture which was held in September in New Delhi, India. This was the first of a series of workshops on specific research areas of the work of the International Centre for Genetic Engineering and Biotechnology as had been recommended by the Panel of Scientific Advisers. The purpose of these workshops is to give a sharper definition to the research needs in broadly specified areas and particularly those pertaining to the needs of developing countries. The next workshop is scheduled for 3 to 7 March 1986 to be held at Trieste, Italy, and will cover enzymes, including protein engineering, pharmaceuticals, vaccines, hormones and other synthetic polypeptides, bioprocessing, polysaccharides and hydrocarbon-microbiology.

In this issue you will also find an index of the various items included which may make it easier for readers to locate their areas of specific interest. While on the subject of readership, we would greatly appreciate hearing from our readers whether they have any suggestions as to its further improvement bearing in mind that the Monitor's purpose is purely to inform on latest developments.

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A. POLICY, NEWS AND OTHER EVENTS

Unido News - The ICGEB Workshop on Biotechnology in Agriculture 17-22 September, New Delhi, India

The first ICGEB workshop was held on 17-22 September 1985 in New Delhi, India. Scientific papers were presented by 38 invited scientists following a keynote address given by Dr. M.S. Swaminathan, a member of the PSA. Several representatives from ICGEB member countries (Italy, Pakistan, Cuba) and from international agencies (FAO/IAEA Joint Programme, UNEP, UNESCO) also attended and took part in the discussion.

The workshop schedule that the participants faced upon arrival in New Delhi was very full, permitting too little time for discussion and the drafting of recommendations. However, the logistic problems that prevented the attendance of several of the invited scientists, also permitted the programme to be relaxed and rearranged, so that three half-days, on consecutive days, were devoted to the discussion and drafting of the workshop's recommendations for a research agenda in plant biotechnology for the ICGEB.

The participants divided into four working groups, each addressing a different technical area (gene transfer and vectors, genes of agricultural interest, nitrogen fixation, and culture and propagation). The morale and the enthusiasm of the participants in addressing the task they were asked to perform was very high. Some of the participants had spent a lot of time before coming to New Delhi thinking about how to set up meaningful programmes in plant biotechnology at the ICGEB with so little resources and manpower. The laboratories of most of the participants, who work only on a single project usually have 10 or more Ph.D. level scientists. The scientists, confronting the ICGEB for the first time, made a number of general observations and set forth certain criteria necessary for the ICGEB to achieve its objectives in addition to making specific technical recommendations.

The recommendations, in addition to certain general requirements set forth for the ICGEB, examine both the biotechnological tools that the ICGEB should try to develop, and the range of crop plants on which new and existing tools should be applied. While the recommendations encompass far more than the resources of the ICGEB would permit, the participants emphasized the importance of selecting one or a few projects from among those suggested, as permitted by available resources, and warned against the temptation of trying to do too many things and thus not being able to do them well. The recommendations represent narrowing of the general remarks on plant biotechnology, discussed in previous UNIDO papers on the work programme, with a recognition of the fact that it will be the Director and scientific staff that should make the final selection of research projects in plant biotechnology. Recommendations made at this workshop should also be useful to those who formulate work programmes for affiliated centres or other research centres devoted to plant biotechnology in developing countries.

UN and other organizations' news

UN symposium in Hungary

A United Nations symposium on "The Importance of Biotechnology for Future Economic Development", organized by the UN Economic Commission for Europe (ECE) in June 1985 at Szeged, Hungary, brought together delegates from 27 countries including the U.S.A., Canada, Australia, Japan and China during June 1985.

"Europe was said to be vanishing in the tailstreams of the U.S.A. and Japan", according to Barry McSweeney of the Irish Republic, who represented the European Economic Community at the Symposium. The U.S. practice of establishing new, small commercially oriented R&D companies aimed at future markets in genetically engineered products was held up as an example for Europe to follow. Most delegates - Eastern and Western - emphasized the willingness of their countries to support international co-operation both between institutions doing basic research and industrially between companies. R.R. Van der Meer, secretary-co-ordinator of the Netherlands programme committee on biotechnology, stressed that such co-operation would avoid duplication of research and would strengthen the position of the European economy vis-a-vis its competitor countries.

As Klaus A. Sahlgren, the ECE's Executive Secretary, pointed out in his opening statement, the Symposium had to address issues of biotechnology "mainly in the East-West context".

Soviet speakers reported that by 1990, a computerized system of high-capacity fermenters will be on line to produce single-cell protein from natural gas and when a Soviet factory producing fodder yeast using oil paraffins reaches full capacity by the end of this decade,

it will meet the needs for 15 years of the five countries that built it. The plant, at Mozyr in the Byelorussian Soviet Republic, is the joint project of the USSR, German Democratic Republic, Poland, Czechoslovakia and Cuba.

Other Soviet developments reported at the symposium were:

- Streptokinase immobilized by a new approach at the All-Union Research Institute for Antibiotics and Medical Enzymes in Leningrad. The method involves development of open microcapsules from linear water-stable polymers on which hydrolases are fixed. A Swedish spokesman reported that KabiGen AB, Stockholm, has cloned the gene for tissue plasminogen activator, a protein free of the side-effects that limit the use of streptokinase in coronary artery disease.

- Increased antibiotics output by superproducing Streptomyces strains, Moscow's All-Union Antibiotics Scientific Research Institute has developed a technique for amplifying extended fragments of the chromosomal DNA - up to 500 copies per genome.

The Symposium adopted 39 "recommendations" for upgrading biotechnology including national or international case studies to be performed before assessing the long-term impact of the release - deliberate or accidental - of genetically engineered microorganisms into the environment. Legislation in this area would be premature ... However, a system of notification should be established among ECE countries;

- A seminar on the importance of biotechnology for food production and processing to be held in the near future in order to clarify the input that biotechnology can have in this industrial sector;

- Governments should harmonize regulations, particularly with a view to easing the requirement whereby full toxicological protocols and clinical trials are necessary for new products derived from ... biotechnology - especially when the traditional product can be shown to have corresponding chemical structure. (Extracted from McGraw-Hills Biotechnology Newswatch, 1 July 1985)

Nuclear techniques and in-vitro culture for plant improvement
(A symposium report)

Biotechnology currently arouses a great deal of attention in developed as well as developing countries. There are expectations of enormous economic gains, so nobody wants to stay behind. The primary focus of investment and of work is on genetic manipulation of microorganisms which can easily be handled in an industrial way to produce desired chemical compounds. The continuous food shortages in parts of our world, however, lead scientists also to look at the possibilities to use new techniques in the development of better varieties of crop plants. Man successfully followed this aim since he took up crop plant cultivation about 10,000 years ago. However, plant improvement is a never ending task.

The Food and Agriculture Organization (FAO) and the International Atomic Energy Agency (IAEA), through their Plant Breeding and Genetics Section in the Joint FAO/IAEA Division, have paid attention to the need for further improvement of crop cultivars for more than 20 years. The basis for plant breeding is suitable genetic variability and since not all genetic variants desired by man are available in nature or in ancient cultivars, mutation induction was promoted as a means to create additional variation for use by plant breeders. Mutant germ plasm in the meantime has successfully been used in at least 35 countries to develop improved cultivars for agriculture and horticulture. IAEA records list nearly 700 such cultivars in 88 plant species. (Ref. IAEA Bulletin Vo.26 No.2 1984). So it is clear already that natural and traditional germ plasm held in breeder's collections and in so called gene banks can profitably be supplemented by induced mutants.

In recent years, there have been reports that mutation occur also during in-vitro culture of plant material without the application of ionizing radiation or other mutagens and that such mutations could also be used by plant breeders in their never ending task to develop more productive varieties. Therefore it appeared appropriate to discuss this so called "somaclonal variation" and its potential value in relation to the vast experience accumulated already with regard to plant mucants obtained from radiation and chemical mutagen application. This was one of the primary topics of the FAO/IAEA Symposium on Nuclear Techniques and In-Vitro Culture for Plant Improvement, held 19-23 August 1985 at the Vienna International Centre. The symposium was attended by 141 participants from 47 countries and international organizations.

Concerning the so called "somaclonal variation" it was concluded that it derives from different nuclear as well as cytoplasmic disturbances, including chromosomal aberrations and aneuploidy. However, the mechanisms by which these disturbances arise are still obscure.

Provided that strong selection is applied, some of this variation could certainly be useful for plant breeding.

On the other hand, there appeared to be more worries about difficulties in maintaining genetic integrity under in-vitro conditions rather than euphoria about additional variation (which could be obtained anyhow from experimental mutagenesis). Genetic integrity is needed for making use of in-vitro culture, e.g. in virus-free clonal propagation of potatoes, ornaments or fruit trees. It would be also essential for long term preservation in "gene banks" of germ plasm that cannot be maintained in the form of seeds. Although it was confirmed that certain types of plant in-vitro culture are genetically more stable than others (e.g. shoot tip and meristem culture against single cell or callus cultures), the problem is not easy to solve.

In-vitro culture techniques also offer opportunities for acceleration of the plant breeding cycle, thus it seemed appropriate to review at the symposium in which way these techniques could profitably be used in connection with mutation breeding using radiation or chemical mutagens. Mutagens could be applied before or during culture. Mutant selection could be performed during or after culture. Chimeras arising from mutagen treatment of multi-cellular tissue can be dissolved by single-cell derived embryonic cultures. Selected mutants could be quickly propagated by in-vitro micropropagation for the required testing of performance in the field. All these potential advantages were discussed at the symposium. The papers presented indicate, however, that considerable research work is needed in many areas, to derive benefits from the techniques for plant breeding programmes. This applies in particular for in-vitro mutagenesis and for in-vitro mutant selection, where only few traits are amenable and the relationships to field performance is dubious. (Ref. Mutation Breeding for Disease Resistance Using In-Vitro Culture Techniques, IAEA-TECDOC-342, 1985). The most critical bottleneck, however, is the rather limited success in plant regeneration from single cells.

This is also the limiting factor for another very promising technology: the use of haploids (i.e. plants with a single instead of double chromosome set). Haploid plants can be derived from immature pollen grains by in-vitro culture of anthers. The single chromosome set theoretically would allow easy recognition of gene expression and gene manipulation including mutation induction. Subsequently, by chromosome doubling, normal but already homozygous diploid plants could be obtained for the development of cultivars. Unfortunately, for most crop plants the frequency of success in obtaining haploid embryos from anthers is very low, too low for reliable handling of breeding material.

Turning to more fundamental issues, the symposium discussed a number of recent approaches of genetic engineering like protoplast fusion aided by gamma radiation, micromanipulation and transformation of plants using vectors. Particularly relevant from a plant breeding point of view should be the possibility to obtain recombination of extranuclear DNA (located in cytoplasmic organelles) after protoplast fusion. All of these approaches are promising, but likely they will make only little contribution to plant breeding in the near future. The gaps in our knowledge of plant molecular genetics are startling and several speakers pointed out that high investments for research would be required to provide current days mostly empirical plant breeding with new and efficient biotechnological tools.

Social issues

New US bioethics panel proposed

Senator Albert Gore Jr. recently introduced a bill establishing a 15-member National Commission on Bioethics, whose members would be appointed by Congress, specifically a Congressional board on bioethics, and be drawn from a variety of backgrounds, including the general public. As envisioned by Senator Gore, the Commission would be independent, comprised mainly of non-scientists, and would serve no regulatory function. Its sole duty would be to advise Congress, through reports and recommendations, on the ethical implications of advances in technologies. The commission would "provide a forum for the critical examination of the many difficult and complex issues presented by the application of new technologies to human beings", according to the senator. Its first mandated study would be on the ethical ramifications of human genetic engineering. (Source: Chemical and Engineering News, 17 June 1985)

Interest in long-term implications

There is growing interest among public interest groups and regulators in the longer term implications of genetic engineering and biotechnology. The European Parliament is to hold a hearing on 21 and 22 November which will provide a forum for many of those who are concerned about the biofuture. A prime example of the way in which biotechnologists fuel such concern is the work they are now doing on herbicide tolerance genes in crop plants. While

biotechnologists promise genetically engineered crop plants which can thrive without any need for agrochemicals, the work that some companies are doing is likely to produce the reverse result, encouraging farmers to use more herbicides. In the United States groundwater pollution by at least 15 commonly used farm chemicals has persuaded the Environmental Protection Agency that it should launch a major study of the problem next year. Meanwhile, in the UK, the Centre for Economic and Environmental Development (CEED) has published the report of a meeting on biotechnology it convened earlier in the year. The Environmental Implications and Applications of Biotechnology is available from CEED, 10 Belgrave Square, London SW1X 8PH or on 01-245 6440, price £2.00 (incl. p & p). Anyone wanting to know what the environmental agenda for biotechnology will look like should ensure they have a copy. (Source: Biotechnology Bulletin, Vol. 4, No. 8, September 1985)

Regulatory issues

Japan eases r-DNA yeast guidelines

A change in the recombinant-DNA guidelines has made it easier to carry out research. Prime Minister Yasuhiro Nakasone recently approved the Council for Science and Technology's (CST) plan to amend the yeast/virus section of Japan's six-year-old gene-splicing regulations. CST decided to update the rules to bring them in line with the latest safety findings, and because the U.S.A. made the same amendments some two years ago. The original guidelines listed only 105 genotypes of Saccharomyces cerevisiae that could be used as the recombinant hosts at the lowest containment level, P-1. Now CST recognizes that S. cerevisiae poses no safety problems and allows use of all strains without special permit.

The council also reclassified and expanded the list of viruses available for genetic engineering under the stringent P-2 and P-3 containment. They include:

California and Japanese encephalitis viruses
Chinkungunya virus
herpes-viruses alleles and saimiri
hog cholera virus
HTLV-I through III
LCM virus
monkeypox virus.

(Source: McGraw-Hills Biotechnology Newswrtch, 2 September 1985)

Major change in US Biotechnology Sciences Board

A major change in the creation and composition of the Biotechnology Sciences Board (BSB) - the U.S. Government's future "Super-Rac" - was discussed at a Cabinet Council meeting on 1 August. The proposal was set forth in an internal memorandum prepared by the Office of the Assistant Secretary for Health in the Department of Health and Human Services, the agency designated to house the new board.

Besides BSB's originally announced authority to review applications for biotechnology experiments submitted to various federal agencies and "analysis of broad scientific issues involving r-DNA, cell fusion or other techniques," the memorandum establishes the additional mandate that the Board shall "develop guidelines and other documents to provide technical guidance for scientific/commercial endeavours that fall under ... one agency." It stipulates that "current 'technical guidance' documents being prepared by the RAC ... for environmental release and on human gene therapy - should be reviewed and promulgated by the BSB".

This provision would apply "during the transition period" when the Board is being set up, with ten of its 25 members selected from present or former members of RAC - the Recombinant-DNA Advisory Committee to NIH, the National Institutes of Health.

On 22 January this year, NIH had already published a request for public comment on its proposed somatic-cell gene-therapy protocols. Then, on 19 August, the agency published in the Federal Register a revised version of its proposed action, but binding only on its own grant recipients.

Although NIH has never had any legal jurisdiction over anyone else, RAC's expertise and moral authority are widely recognized by medical and industrial researchers, who have voluntarily submitted their protocols to the advisory body for approval. The 1 August memorandum would formally limit RAC's role to NIH-funded experiments. "With the establishment of the BSB", states the document, "... product applications as well as field trials or clinical trials of products that have been submitted to the various federal agencies for administrative review ... will be specifically exempt from jurisdiction of the NIH". (Extracted from McGraw-Hills Biotechnology Newswatch, 2 September 1985)

DNA implants in animals challenged

Jeremy Rifkin, a writer, activist and persistent challenger of genetic engineering, is taking the US Department of Agriculture to court over a research programme that has made dramatic progress in manipulating the genes of animals.

The research in question is a project at the University of Pennsylvania, Philadelphia on the introduction of foreign DNA into the embryos of rabbits, sheep and pigs. It is the first time that anyone has introduced a foreign gene. The gene is a sequence that codes for the human growth hormone in commercially important animals, although the prospect of farmers breeding giant transgenic animals is still some way off. Not the least problem is the question of who would regulate such a practice. The Recombinant-DNA Advisory Committee at the National Institutes of Health (NIH) is responsible for controlling research on genetic manipulation that receives government funds, but the US Department of Agriculture and the Environmental Protection Agency both claim jurisdiction over the release of genetically engineered organisms into the wild.

Rifkin and a coalition of animal-rights groups are testing yet another avenue for controlling this research. They have made a case before the federal court that the Environmental Protection Agency should regulate the work at Pennsylvania, while it is still in the laboratory, because it violates the animals' internal environments.

So far, 1985 has been a mixed year for Rifkin's group, the Foundation on Economic Trends. At the end of May, the foundation won an injunction under the Environmental Protection Act to stop the Department of Defense building a laboratory to investigate biological warfare. The department has since agreed to carry out an Environmental Impact Assessment - a lengthy study required by the act - into the laboratory. Rifkin says the verdict will delay the project by at least six months.

Last month, however, a court in Washington D.C. dismissed another plea by the Foundation which would have placed a new legal hurdle in front of private companies planning to release genetically engineered organisms. The case concerned a firm called Advanced Genetic Sciences, which last year voluntarily submitted a proposal to the Recombinant-DNA Advisory Committee (RAC). At the time, the committee was not able to approve experiments because of a court ruling that arose out of a previous case that Rifkin had fought. (An appeal court overturned that ruling at the end of February.)

On 11 February, meanwhile, Advanced Genetic Sciences withdrew its proposal from the RAC. In what one official called a "somewhat complicated argument", Rifkin claimed that, because the firm had submitted a proposal to the RAC, it was nonetheless bound to accept the committee's findings. At the court hearing, however, the judge said that Rifkin's group had "failed to prove the existence of an enforceable NIH policy of regulating private firms". (Extracted from New Scientist, 25 July 1985)

AIDS test on organs

Health authorities in California have requested that tissues and organs donated for transplant be tested for antibodies to the AIDS virus before they are considered for use. The State Department of Health Services issued guidelines for the new policy which were sent to sperm banks, organ and tissue transplant units and local health departments throughout the state. But the move is purely precautionary at this stage.

No cases of AIDS in California have been linked to transplanted organs or to artificial insemination, but it is known that blood, semen and other body fluids harbour the AIDS virus. In Australia, where some 100,000 women have been artificially inseminated since 1980, all sperm banks were closed last November after four women were found to have contracted AIDS from donated semen. Clinics reopened in April after the government had imposed stringent screening procedures. (Extracted from New Scientist, 1 August 1985)

General

Biomedical Research Center, Vancouver

A new joint undertaking between the Terry Fox Medical Research Foundation, a Canadian charity, and the Wellcome Foundation of the U.K. will be set up on the University of British Columbia campus. Its main focus will be toward "discovery, development, and clinical study of novel means of treating and investigating disease, especially malignant disease like cancer". Emphasis will be on novel agents such as interferons, lymphokines, and monoclonal antibodies. The initial $31 million (Canadian) funding will be spent about equally on building and equipping laboratories and offices, and on running the centre for the first five years. (Source: Chemical and Engineering News, 29 April 1985)

New institute for antiviral, antiaging R&D

Eastman Kodak and ICN Pharmaceuticals have formed a joint research institute to develop compounds against viral infections and to slow the aging process. The firms will invest $45 million over six years to set up and operate the Nucleic Acid Research Institute at ICN's Costa Mesa, California, facility. When fully operational, the institute's research and support staff will number more than 150. Institute president, with special responsibility for pharmacological research, will be Weldon B. Jolley, until now professor of surgery at Loma Linda University Medical Centre. Robert A. Smith, formerly professor of chemistry at the University of California, Los Angeles, will oversee biomedical research, and Roland K. Robins, formerly director of Brigham Young University Medical Center, Cancer Institute, will direct molecular research. (Source: Chemical and Engineering News, 6 May 1985)

Centre to study complex carbohydrates

The University of Georgia is undertaking a new co-operative venture with the U.S. Department of Agriculture under the leadership of Prof. P. Albersheim from the University of Colorado.

Prof. Albersheim will direct a new Complex Carbohydrate Research Center that the university is establishing at its Richard B. Russell Agricultural Center in Athens, where USDA and Georgia scientists will undertake joint studies.

The Complex Carbohydrate Research Center will be the first of its kind in the world, bringing together scientists from different disciplines. Thought uninteresting as little as 10 years ago, complex carbohydrates, Albersheim notes, are now known to play an important role in plant growth and development. But, he says, they are difficult to study and so haven't been studied in detail.

Early in 1984, the university established an integrated Programe in Biological Resources and Biotechnology. It has plans to add 25 new faculty members in molecular biology, to construct a $30 million biotechnology building, and to increase significantly the funding base for biological sciences through a five-year, $5 million investment. The principal biotechnology concentrations are in three areas: plant cellular and molecular biology, of which the new complex carbohydrate center is the latest component; molecular biology-recombinant DNA technology; and microbiology-microbial fermentation. (Extracted from Chemical and Engineering News, 10 June 1985)

New centre of fluorescence research

The Carnegie-Mellon University (Pittsburgh, PA) has opened a $3 million centre for the use of fluorescence spectroscopy (FS) to study the physical and chemical properties of living cells. The Center for Fluorescence Research in Biomedical Sciences, the first of its kind, will be used by researchers in the fields of chemistry, computer technology, the biological sciences, engineering and physics. FS is regarded as a replacement for existing diagnostic tools because it is more sensitive, and because current methods can only analyze dead cells. (Extracted from Chemical Week, 17 April 1985)

MIT plans bioprocess separations centre

A new centre for bioprocess separations research is being established at Massachusetts Institute of Technology. The plan is for it to explore new technologies and approaches to meet future downstream needs of the biotechnology industry.

Co-operating with MIT in setting up the centre is Alfa-Laval, a Swedish manufacturer of process equipment. The programme complements other biotechnology work at MIT - for example, extending the concept of computer control of fermentation.

Among the research areas expected to be initiated at the centre is an investigation of aggregating agents that selectively aggregate cells, proteins, lipids, lipopolysaccharides, carbohydrates, and nucleic acids. The research will consider use of such agents to enhance sedimentation in a centrifuge, filtration efficiency, whole-broth extraction with organic or biphasic acqueous solvents, and cell disruption.

Another expected research area is the study of one of the major problems in the use of membrane filtration - the fouling of ultrafiltration and microporous membranes. The centre will explore the effect of fermentation media components on the fouling process and evaluate the addition of chemical agents that might decrease fouling. (Extracted from Chemical and Engineering News, 9 September 1985)

Gene bank to close

One of the world's best collections of microorganisms has fallen victim to the British Government's cuts in science. A library of over 2,000 strains of microorganisms will be split into two and the centre where it is housed will be closed. Researchers in the field feel that once split, the collection will eventually disappear.

The Culture Centre of Algae and Protozoa in Cambridge will close within two years because of the financial strains that the Government has put upon the Natural Environment Research Council (NERC), which funds the centre. The collection was established in the 1920s. It will be transferred to the Freshwater Biological Association, at Windermere, and the Scottish Marine Biological Association, at Oban. However, not everyone agrees with the splitting of the library. A working party of the Royal Society has told the NERC that it favours the retention of the collection under one roof. (Extracted from New Scientist, 11 July 1985)

DNA bank established at Indiana University

The Department of Medical Genetics at Indiana University School of Medicine has established a DNA storage bank for families with Huntington's disease (HD). The DNA specimens will be used at a later date by family members who want to find out if they possess a marker which would indicate the presence of the gene for the degenerative disorder. The onset of symptoms for Huntington's disease do not appear until the victim is in his late 30's.

The bank, which received its first sample for storage about 14 months ago, is the first of its kind. The Indiana University School of Medicine, the Hereditary Disease Foundation of America, and the Lena Marcus Trust (which gives small grants for research on Huntington's disease) have combined forces to fund and operate the bank.

Dr. M.E. Hodes, professor of medical genetics and medicine at the Indiana University School of Medicine is in charge of the day-to-day functioning of the facility. He described the procedures used to prepare samples for storage as "routine". The DNA is prepared from fresh or frozen blood samples by a process developed by Dr. David Hoar of Canada. To ensure preservation of the DNA for the use of future generations of family members, the sample is divided and stored in two locations - half is refrigerated at 4°C, and the other half is frozen at -70°C.

The bank, which has about 300 samples so far, charges $37 for extracting and storing the DNA. (Extracted from Genetic Engineering News, 22 March 1985)

International Symposium on the Biology Actinomycetes

After nearly half a century of scouring the world's soils for bacteria that make new or better antibiotics, microbiologists are beginning to supplement soil screening with gene cloning, to improve the breed of producer organisms. Some 300 of these scientists, from 29 countries met during August at Debrecen, Hungary for the Sixth International Symposium on the Biology of Actinomycetes.

An Anglo-Soviet cloning system

Since 1969, at Moscow's Institute of Genetics and Selection of Industrial Microorganisms, Dr. Natalia D. Lomovskaya and her associates have been focusing genetic analysis on a Streptomyces-specific bacteriophage -φC31- to serve as an industrial gene-splicing replicon in strains of the bacterium that produce antibiotics. Her cloning vehicle is a counterpart to Escherichia coli's lambda phage vector. Its targets, she says, include veterinary and agricultural applications as well as medical.

Dr. Lomovskaya's Laboratory of Genetics of Actinomycetes and Actinophages has for years carried on a long-distance collaboration with the John Innes Institute at Norwich, U.K. In fact, her paper updating Moscow's φC31 work was read to the Symposium by Dr. Keith F. Chater, a senior molecular geneticist at John Innes.

Dr. Lomovskaya's φC31 actinophage "is a relatively wide-host-range cloning vector for Streptomyces", her paper stated. It acted on 56 strains of 109 species, including six of 15 antibiotic-producers.

Her laboratory intends to introduce the vector into industrial production, but it has not yet applied for a patent, or done any practical cloning with it. But Chater and his associates at John Innes have picked up on Moscow's φC31. Achieving directionally controlled insertion of the phage into S. coelicolor, an antibiotic producer, they found that the DNA cloned into the vector can then recognize its counterpart in the transformed bacterium's genome and integrate it at that precise point.

This enables Chater's group to generate fusion of the host gene determining expression, and thus analyze gene expression for antiobiotic production.

Latest product of the Moscow laboratory, reported at the symposium is a new phage vector, ϕC43, closely related to ϕC31 which has a unique restriction-site sequence usable for introducing DNA into different regions of the phage.

Shuttle vectors made in Hungary ...

Antibiotic production efficiency can be increased by 10 per cent to 20 per cent using bifunctional shuttle vectors, reported Dr. Gyorgy B. Kiss, of the Biological Research Center in Szeged, Hungary. These two-way cloning vehicles were able to replicate in Streptomyces lividans and E. coli, he told the Symposium. The resulting plasmids were transformed into S. lividans, using neomycin selection, and successfully used for cloning foreign DNA in the host.

The cloning system they have developed allows them to isolate independently the genes coded by a given sequence along a multistep chemical pathway, and to reintroduce these DNA sequences into the producing Streptomyces strain. (Extracted from McGraw-Hills Biotechnology Newswatch, 16 September 1985)

Polling results

Most religious, environmental and science policy leaders are confident that biotechnology will increase food production and reduce disease without major risk to society, according to a Northern Illinois University (De Kalb, IL)-Monsanto (St. Louis, MO) joint study. A majority of the 883 leaders polled expected recombinant DNA research or genetic engineering to produce major advances in medicine. More than 70 per cent expect to see major agricultural advances, particularly in the area of crop productivity and control of animal and plant diseases, and 75 per cent believe that the potential benefits of genetic engineering are greater than the likelihood of harm. While the majority of leaders are extremely concerned about the genetic modification of human beings and the production of undesirable or uncontrollable organisms, 64 per cent believe that the present level of regulation is adequate and a majority are supportive of field tests within current guidelines, 19 per cent believe that current regulation is too low and 14 per cent expressed reservations about field tests. (Extracted from Northern Illinois University news release, 8 August 1985)

B. COUNTRY NEWS

Australia

New vegetable based food product

Biotechnology Australia Pty. Ltd., has developed a new vegetable based food product, characterized by its unique cooked minced beef-like texture and appearance and bland flavour. The product, produced using a process developed and patented by the company, contains up to 48 per cent crude protein and 8 per cent total fat.

The process involves an amylolytic fungus being grown on a moist starch-based substrate which includes a nitrogen source assimilable by the fungus, the substrate being provided in the form of small, partially gelatinized particles. During growth, the fungus degrades and utilizes a large proportion of the starch, resulting in a dense matrix of closely interwoven mycelia, randomly dispersed with substances containing the residual starch or starch degradation products. On the denaturation of the fungal mycelium, the product assumes a tough but resilient texture and when diced or minced, has a similar appearance to meat.

The product has been shown to satisfactorily replace 30 to 50 per cent of meat in all preparations such as meat pie, meat loaf, meat balls, sausage roll, pizza topping, hamburger patty etc., and in some cases, with appropriate formulation, up to 100 per cent of meat.

The product can be made in grades with differing protein contents, particle shape and size, texture, flavour and rehydration capacity. (Source: Asia-Pacific Tech Monitor, July-August 1985)

Plan to market moiety-free HGH

Australia intends to market recombinant human growth hormone (HGH) in 1986. The University of New South Wales school of biotechnology has developed a "second-generation" HGH jointly with the Garvan Institute for Medical Research. Its process yields a hormone free of

the add-on methionine moiety attached to early genetically engineered versions of the molecule, according to Prof. Peter Gray, who heads the project.

Clinical trials of the Australian hormone are planned for early in 1986. The Australian Department of Industry, Technology and Commerce is negotiating a manufacturing and marketing agreement with a commercial partner. Prof. Gray foresees that the hormone could be available to physicians in this country before 1987. (Extracted from McGraw-Hill's Biotechnology Newswatch, 2 September 1985)

Money goes to develop malaria vaccine

Australia intends to spend A$15 million over the next three years developing a malaria vaccine aimed at combating the asexual blood stage of the disease. Half of the funds will come from the federal government through the Australian Industry Development Corporation (AIDC) and the remainder from the other four participants in the project.

The federal government has spent over 18 months debating whether to fund the project. Part of the problem is that although a vaccine is of great human benefit to the Third World it has limited commercial value in developed countries. The majority of the product would be purchased by the World Health Organisation, with smaller markets for tourists and defence personnel serving in the tropics. However, after a study into its commercial viability it was decided to go ahead. Development of the vaccine in Australia follows the isolation of antigens from the malaria strain, Plasmodium faliciparum, by researchers from the Walter and Eliza Hall Institute in 1983.

They worked in close collaboration with the Papua New Guinea Institute of Medical Research in Madang, which provided selected blood samples containing antibodies to the malaria parasite from victims of the disease.

The director of the Walter and Eliza Hall Institute, Sir Gustav Nossal, hopes to have a vaccine on the market within three to five years. He believes that in its final stage of development the Australian team will need to link up with American researchers, working on different stages of the malaria parasite's life cycle, and a multinational drug company. (Source: New Scientist, 20 June 1985)

Austria

Genetic engineering patents

Legal tussles over the commercialization of alpha-interferon have taken a new turn with the filing in Vienna by Biogen NV of a complaint against Boehringer Ingelheim Zentrale GmbH for its marketing of a product containing an alpha-interferon produced by recombinant DNA technology. In 1984, Biogen was granted a broad European patent for "recombinant" alpha-interferons. Boehringer Ingelheim is one of several companies that have registered their opposition to the patent with the European Patent Office.

Biogen, of Geneva, Switzerland, and Cambridge, Massachusetts, is suing the West German pharmaceutical company Boehringer Ingelheim over an eyedrop for the treatment of keratitis caused by the herpes simplex virus which has been marketed in Austria since early this year. Acknowledging that the product contains a recombinant alpha-interferon, Boehringer Ingelheim, and its subsidiary Bender, does not believe that Biogen's patent can be enforced. The company has formally objected to the complaint filed by Biogen in Vienna. Boehringer claims it has conducted research with alpha interferons for more than two decades and maintains that the European patent awarded to Biogen a year ago is "invalid" in its current form. The company added that, along with six other firms, it filed an objection to the patent last May. This opposition, lodged with the European Patent Office, is based mainly on evidence that enough information about alpha-interferon and its sequence was known and published before Biogen's patent filing to make Biogen's achievements "non-inventive". Meanwhile Biogen is still expecting to receive patent protection in the United States despite the rival patent granted to Hoffman-LaRoche. (Extracted from Nature, Vol. 316, 25 July 1985)

New biotech test plant

Two Austrian firms have joined together to build a biomass-and-wastes-to-chemicals demonstration facility. The plant will test both enzymatic hydrolysis and waste and refuse gasification processes developed by the two companies.

Engineering and equipment concern, Voest-Alpine, has teamed up with the pulp and paper firm Steyermühl Papierfabriks und Verlag in the demonstration project. The two firms are poised to seal the deal so that construction can start later this year, following planning approval from the Austrian authorities. Start up of the facility is scheduled to occur towards the end of next year. It is hoped that the experience gained from six to eight months' operation will translate into contracts to build full-scale units in other countries.

At the heart of the biological end of the process route is the enzymatic process developed jointly by the two partners and already tested at pilot plant scale for four years by Steyermühl. The raw material is cellulose from biomass and refuse-derived fuel (RDF). It is pretreated and converted to glucose and xylose. The glucose is obtained by enzymatic hydrolysis of cellulose using cellulase enzymes obtained from a strain of the fungus Trichoderma reesei. It can then be used as fermentation feedstock for the production of ethanol, citric acid and a range of other organic chemicals. Xylose can also be used as feedstock or converted to furfural and by-products.

The second leg of the technology package is the waste gasification process developed by Voest-Alpine. A 1 ton/hour gasifier has been operated by the company at its Linz facility using run-of-mine coal. It runs at atmospheric pressure. The technology combines entrained-flow and fluidized-bed set-ups. The demonstration scale gasification unit will test a wide range of feedstocks including coal, waste oils, old tyres and lignin from RDF for the production of synthesis gas and process steam. This unit will operate at 30 bar pressure. (Extracted from European Chemical News, 24 June 1985)

New cancer research institute

A new cancer research institute establishment is to be set up in Vienna, Austria, by Genentech Inc. and Boehringer Ingelheim International GmbH (BII). The Institute will conduct basic research on the molecular bases of cancer, with staffing likely to begin in 1986. Genentech and BII will contribute technical support, and BII has agreed to fund the Institute during its early years. Additional funding will be provided by the Austrian Government and the City of Vienna. Details from: Genentech Inc., 460 Point San Bruno Boulevard, South San Francisco, CA 94080, USA or on (415) 952 1000. (Source: Biotechnology Bulletin, Vol. 4, No. 6, July 1985)

Belgium

New biotechnology joint venture

Petrofina subsidiary, Oleofina, a Brussels-based oleochemicals company, has formed a biotechnology joint-venture with the Belgian dairy co-operative, Sud-Lait, to be called Sodelac. In a first phase, Sodelac's plant at Recogne in the Province of Luxembourg, will employ between 10 and 20 people. Sodelac will exploit a patent on the extraction and purification of lactoferrine and lactoperoxidase, two antimicrobial proteins that are found at very low concentration in milk. (Extracted from Manufacturing Chemist, June 1985)

Brazil

Biotechnology agreements between Latin American countries

In "the first genetic-engineering agreement between Latin American firms", Bioquimica do Brasil (BIOBRAS) will spend $1.5 to $2 million to develop gene-spliced interferon and insulin, in collaboration with two Argentinian companies.

BIOBRAS will combine its fermentation skills with the gene-splicing technology of the Instituto Sidus ICSA, Buenos Aires, to commercialize alpha interferon. BIOBRAS has also signed a second accord with another Buenos Aires company, Polychaco SAI, to develop and commercialize a recombinant human-like insulin. Production will most likely be in Brazil. Brazil's new democratic government has committed $52 million over three years to a technology development programme, one of whose "priorities" is biotechnology. It has created a Federal Secretariat for Biotechnology, but no money has been specifically allocated. (Extracted from McGraw-Hill's Biotechnology Newswatch, 19 August 1985)

Spirulina production

In a corner of a student parking lot at a University in downtown Rio de Janeiro, a Brazilian chemist has built one of her country's first experiments in biotechnology in her spare time. Suspended in the murky water of a 400-square-metre pond at the Pontifical Catholic University are carefully cultivated algae, which Dr. Angela Rebello hopes can help to feed some of Brazil's millions of under-nourished people.

The dark green algae Spirulina platensis is known to health-food fiends as a wonder food, 70 per cent protein that is totally metabolised by the human body. It is also rich in vitamin B12, which is scarce in vegetables and thus valuable to those who practise vegetarianism. Three hundred grams of Spirulina is equivalent in vitamins, protein and minerals to one kilogram of meat, says Dr. Rebello. But it is produced in very few places, primarily at a carbonate plant in Mexico where a large alkaline pond provides ideal growing conditions. Consequently, the prices are also quite high, as much as US$60-70 per kilogram.

Dr. Rebello says she can produce the algae at a cost of about one dollar per kilogram. But the pond needs careful preparation and maintenance with carbonate, sodium, nitrogen and phosphorous. She must harvest when algae growth is at its peak, at about 400-600 milligrams per litre of water, but before any decay sets in spoiling the taste. Not that there is much to write home about taste, she admits.

More than just food, the algae produce dyes of phycocyanin, beta carotene and chlorophyll, which Dr. Rebello extracts at her pond-side laboratory.

Now several companies in Rio have formed a consortium, Rio Part, to test Spirulina's potential for animal feed and for human consumption. Dr. Rebello is also testing strains of native algae that might outgrow Spirulina, native of West Germany. (Source: Asic-Pacific Tech Monitor, July-August 1985)

Bulgaria

Joint-venture company formed

A joint-venture company has been formed in Sofia to open the way for the sale of British biotechnology to Bulgaria.

The company, in which the UK process plant manufacturer APV International has a 51 per cent share, marks a new stage in Bulgaria becoming a leading developer of biotechnology products in Comecon. Negotiations are well advanced with another British company, Celltech, which is a customer of APV and is partly owned by the British Government, for the purchase under licence of cultures for diagnosis and treatment of human diseases. A Bulgarian delegation recently visited Celltech's Swindon headquarters as well as the government chemical research laboratory at Porton Down.

There are no export restrictions on the transfer of such technology or of the equipment needed to mass-produce artificial antibodies, according to the Department of Trade and Industry. (Extracted from Financial Times, 7 May 1985)

Canada

Proteins from wood

Dr. Devinder Sing Chahal, a scientist and teacher specializing in industrial microbiology at Montreal's Armand Frappier Institute, is currently working on a project to develop an improved process for converting forest biomass into protein feed for cattle. The process yields a feed containing nearly 49 per cent proteins, compared with the feed now produced commercially from soya beans that contains approximately 45 per cent proteins.

In the process, wood pulp is first made from particles of poplar trees with nitrogen, phosphorus and sulphur. This compound is then fed to mycelium which, over a 24-hour fermentation period, uses two enzymes (hemicelliolase and cellulase) to convert the cellulose into products that can be assimilated by an organism The fungus that is formed has considerably increased volume. It is dried and then fed to cattle.

In order to produce the raw material on a larger scale so that it can be used as feed for various animal species, Dr. Chahal is building the one now being used. It is expected to take about 16 months for the production. (Source: Asia-Pacific Tech Monitor, July-August 1985)

Protamine genes cloned

ARC, a provincial corporation in Edmonton, Alta., has been working in a joint venture with the firm Bio Logicals Inc. (Toronto) to produce protamine, a protein valued for its clotting capability in human blood. The researchers say they have succeeded in cloning the genes responsible for producing protamine, and have expressed it in yeast cells. More work on controlling the production of the protamine, and in examining its human-health effects, must be done before commercial application can be achieved. (Source: Chemical Engineering, 24 June 1985)

China

Phillips to set up SCP plant in China

China Huanqui Chemical Engineering Co. and Provesta Corp., a subsidiary of Phillips Petroleum of the US, have signed a letter of intent for technical co-operation on a single-cell protein plant. The Chinese government intends to build a 10,000 ton/year demonstration plant, for which the site has yet to be determined. Other plants could

follow. Feedstock for the plant would be derived from either molasses or methanol. Initial engineering will be carried out by Davy McKee in Chicago. Provesta represent Phillips' research and development effort in single cell protein to meet burgeoning demand worldwide for food. The single-cell protein product is based on a proprietary yeast fermentation process and marketed under the tradename Provesteen. Its use of alcohol feedstock makes it suitable for countries with little or no hydrocarbon reserves and which are dependent on biomass-to-alcohol fuel.

Studies carried out by Provesta demonstrate that Provesteen is highly safe and effective when fed at 50 to 75 per cent of the protein requirement. The company claims it lends itself to modular plant construction. Feasibility studies have been carried out for plants ranging from single-module units to as large as 30,000 ton/year. (Extracted from European Chemical News, 29 July 1985)

China building first bio-base

China's first biotechnology "base" is under construction in Ghong Zhou, formerly Canton. Dr. Ray Wu of Cornell University, Ithaca, NY, heads the US Scientific Advisory Committee that is advising China's Center for Biotechnology Development on its nation-wide programme. The planned laboratory is independent of the Chinese Academy of Sciences, which has its own biotechnology facility in Shanghai. It belongs to the broader China State Commission for Science and Technology, which six months ago separated biotechnology as an independent unit within the Commission. A vice-president of the Commission, Yang Juin, heads the biotechnology unit. Its 20 members act as opposite numbers to the eight US advisors. More than 100 scientists of Chinese origin, trained abroad in various fields of biotechnology, have now returned to China. Twice as many are still in the USA, most of them at universities, finishing two or three years of training.

Funding for the base - a subsidiary of the national Biotechnology Center in Beijing - was contributed half by Canton province and city and half by the national budget. Its major research goals, focused on China's problems, include development of a hepatitis B vaccine via gene cloning, and diagnostics for liver and kidney diseases via monoclonal antibodies or DNA probes.

China's Biotechnology Center recently helped set up a joint venture with Promega Biotech Inc., Madison, Wis., to produce restriction enzymes in Luoyang, Henan province. (Extracted from McGraw-Hill's Biotechnology Newswatch, 5 August 1985)

New Chinese patent law demands organism deposit

Inventions related to microorganisms, to be patented in the People's Republic of China (PRC), now require deposit of the organism. A new patent law promulgated 1 April 1985 states that the deposit must be made at a recognized Chinese depository. As the PRC has not signed the Budapest Treaty, deposits in other countries are not accepted. The new patent law describes microorganisms that must be deposited as those that are not "publicly available", but this term is not clearly defined.

When a foreign inventor applies for a Chinese patent, he or she must go to a patent agency designated by the PRC. Although product patents are not recognized under Chinese law, patents may be granted for manufacturing and production processes. Thus, non-patentable products include foodstuffs, beverages, seasonings, drugs, plant and animal varieties, microorganisms per se and substances obtained chemically or using microorganisms.

A Japanese expert observes that even though Chinese patent law contains many ambiguities, an invention is worth filing in that country when it has a high potential for technological export. In such case, the inventor's rights will be protected under a process patent only. (Source: McGraw-Hill's Biotechnology Newswatch, 1 July 1985)

Chinese biotechnology journal

A new journal has begun circulation, called "Chinese Journal of Biotechnology". Its aim is to report on Chinese achievement of their scientists in this field and their wish to promote academic exchange. They appeal for genuine and valuable help for their research.

The journal is in Chinese and English but has all the summaries and titles in English; the graphs and tables are easily understood. Biochemical names are often international scientific language and details of biochemical quantities likewise. An English contents is at the back together with English information for contribution. Further details may be obtained by writing to the Editorial Office of the Chinese Journal of Biotechnology, c/o Institute of Microbiology, The Chinese Academy of Sciences, Zhong-Guan Cun, Beijing, People's Republic of China. (Source: Industrial Biotechnology, June/July 1985)

Czechoslovakia

New biology research centre in Southern Bohemia

The new South Bohemian Biological Centre, under the leadership of academician Vladimir Landa (JCBO) began its operation last May, thus marking the completion of the installation's first stage. Its work enables an assessment of the results of basic research and introduces them into practical use not only in the country but also in response to the needs of the national economies of the other CMEA countries. (Extracted from Bratislava Pravda, 13 June 1985)

Denmark

Plan to market moiety-free HGH

In Copenhagen, Nordisk Gentofte, producers of insulin and pharmaceuticals, announced during August that they aim to start commercial production of HGH sometime next year. Subsequent distribution will depend on approval procedures in various markets, but this should not be difficult as the product will be identical with the 191-amino-acid pituitary-extracted HGH - without the methionine. (Extracted from McGraw-Hill's Biotechnology Newswatch, 2 September 1985)

Denmark moving towards biotech regulation

In a paper presented at Biotech 85, Ole Münster from the Danish Ministry of the Environment cited the cow parsnip as an example of what can happen when foreign or exotic species are introduced into environments ill-fitted to receive them. Cow parsnip was originally used for ornamental purposes but is now out of control as a weed with no natural predators.

Conscious of the need to avoid similar or worse problems with genetically-engineered organisms, the Danish government set up a committee in October 1983 which has been conferring with a wide range of biologists (but none so far with industry) before producing a report suggesting regulatory measures. Münster described his committee's work as a "balancing act" between the promotion of biotechnology and the prevention of adverse consequences. "On the one hand, the government has a responsibility for protecting health, environment, and nature by setting up production conditions under which industry may work with genetically engineered organisms", he said. "On the other hand, governments should stimulate industrial production so that society may benefit from the huge potential for the improved production of goods based on these techniques".

In response to criticisms from the floor that international rather than national regulation was required, Münster insisted that - as with acid rain - individual countries should take the first steps in setting standards. (Souce: Bio/Technology, Vol. 3, July 1985)

New gene splicing plant in Denmark

The technical and environmental committee of the county council for West Zealand has approved the construction of a gene splicing plant in Kalunborg to be set up by Novo Industry Inc. Novo will use the gene splicing technique for producing insulin, the first time this will occur in Denmark.

The new production is due to start in early 1987, but during the interim, the West Zealand county council, in co-operation with the Danish Environmental Commission, will determine more precise requirements for the plant. The Environmental Commission has already stated that basic consent can be given for gene-splicing organisms in industrial production in Denmark. It believes, however, that one must await the views of the committee before final conditions are imposed regarding the spillage of gene-spliced organisms. Several critics have feared that the artificially created micro-organisms could leak out through the plant's discharged water and cause great damage to the environment. However, Novo finds it acceptable that certain artificial micro-organisms escape. The firm asserts that they will sink quickly without causing damage. (Extracted from Berlingske Tidende, 12 July 1985)

Dominican Republic

New sugar-alcohol venture

The Dominican Republic will set up a sugar-based alcohol industry using Brazilian financial and technological aid. Studies by the Dominican State Sugar Council indicate that three of the mills it controls - Santa Fe, Quisqueya and Boca Chica - can jointly produce 28.3 million gal/year of alcohol. The Santa Fe and Quisqueya mills would produce 6.8 million and 8.5 million gal/year, respectively, during the first stage of the project, with Boca

Chica adding capacity for 13 million gal/year in a second stage. (Source: Chemical Week, 21 August 1985)

European Economic Community

European Parliament to hold biotechnology hearing

The European Parliament's Committee on Energy, Research and Technology is to hold a hearing on biotechnology on 21 and 22 November. The hearing will expose parliamentarians to some of the latest developments in biotechnology - and to some of their implications for the structure and health of the European economy, for employment, for the Third World and for international relations generally.

Inevitably, a good deal of time will be devoted to questions about the potential risks to human beings, animals and the environment. There will be questions about adequacy of existing statutory controls in the various Member States - and about the need for harmonisation of the regulatory framework and of patenting procedures. MEPs will want to know what sort of jobs are likely to be created - and where. Will those jobs be of a permanent or temporary nature? Will the computerization of laboratories eventually mean that there are opportunities only for the highly skilled?

Another key set of issues will inevitably revolve around the potential impact of biotechnology on the developing countries. Whereas those MEPs who have thought about biotechnology at all probably think that it will help the food situation in the Third World - unless they recall the recent EEC proposals to convert grain mountains into plastics - there are those who believe that the existing international power structure will mean that the benefits will go mainly to the developed countries.

The negative aspects, meanwhile, may be more rapidly seen in the developing countries - and could include a greater dependence on the Western agrochemical industry and seed companies, fewer opportunities for exporting raw materials to the West, and the use of the Third World as an unprotesting testing-ground for new pharmaceuticals or bio-pesticides. A further possibility might be the ruthless exploitation of the genetic resources of the Third World, further concentrating economic power and leading to severe erosion of the genetic diversity which is one of the most important natural resources potentially available to developing countries. Details from: The European Parliament Committee on Energy, Research and Technology, 97-113 rue Belliard, 1040 Brussels, Belgium. (Source: Biotechnology Bulletin, Vol. 4, No. 8, September 1985)

Economic Community to back biomass

Mindful of the 1989 target date for lead-free petrol in Europe and stricter emission controls starting in 1988, the European Economic Community is to extend its research into the most effective routes for generating ethyl alcohol from biomass. The anticipated need for blended fuel meshes well with the increasingly embarrassing question of how the EEC should deal with its agricultural surpluses. Now gasohol will form a major target of the Community's biomass policy, which has been allocated 20 million ECUs (European Currency Units) over the next four years. Speakers at a conference in Vienna estimated that 32 million tons of ethanol could be produced each year from the 9 million hectares of EEC land that currently generates surpluses.

EEC member countries also agreed recently on a four-year programme of research and training in biotechnology. As well as biomass studies on topics such as lignocellulose conversion, the programme will embrace protein engineering, artificial enzymes, and industrial applications of gene transfer. (Extracted from Bio/technology, Vol. 3, June 1985)

Federal Republic of Germany

Ministry makes focused effort in biotechnology

After years of unfocused support, biotechnological points of emphasis are now being set by the Federal Research Minister. The states - with Baden-Württemberg in the lead - are also moving in the same direction. Against that backdrop, the financial injections, with which the Federal Ministry for Research and Technology (BMFT) supported the new technology in the past 10 years, were rather modest. The objects of support appear however to have been chosen rather haphazardly and without priorities.

However, in 1983 a commission appointed by the federal government closely examined major German research. The committee of scientists came to the conclusion that the development of new technology would have to be accelerated through closer co-operation between industry and productive major research in order to increase efficiency. Biotechnological research is to be carried out primarily in places where industry is not far away. Therefore, research

policy-makers are standing behind the creation of genetic engineering centres in Cologne, Heidelberg, Munich and Berlin. In all four cities, the chemical industry is participating financially in the research. Within this framework, the following co-operation is in progress:

- The University of Cologne jointly with the Max Planck Institute for Breeding Research in Cologne-Vogelsang as well as in co-operation with Bayer in Leverkusen - BMFT annual subsidy: DM 5 million;

- The University of Heidelberg together with the German Cancer Research Centre and the BASF chemical company in Ludwigshafen - BMFT annual funds: DM 6 million;

- The University of Munich jointly with the Max Planck Institute for Biochemistry in Martinsried near Munich and Hoechst AG - BMFT annual support: DM 5 million;

- The University of Berlin in co-operation with Schering AG - BMFT annual subsidy: DM 8 million.

In addition, the German research council is also supporting genetic technology oriented experiments in 14 special research areas, such as, a 3-year project in genome organization or the study of the entire set of hereditary factors of a cell or an organism. However, genetic technology is only one of the points of emphasis. Study teams combining industry and science are also to be created in the areas of cell culture and bioprocessing technology. Seventy-nine of these so-called integrated projects are now in progress in the various areas. Combined cost: DM 82.3 million.

The industrial partners have a special role here. Along with the co-operation, they are given the opportunity to have their employees further trained in methodology and thus receive the essential know-how for industry-specific research. Policy makers and scientists hope that results worked out in this way will be converted more rapidly into marketable products. For, in fact, it is the utilization of basic knowledge in the market which is lacking in the FRG. Experts agree that, because of its favourable market situation, the chemical industry ignored biotechnology for much too long.

Since peak performance can only be expected from highly qualified scientists, the BMFT is also investing in education. The Research Ministry, along with the German Academic Exchange Service (DAAD) and the Association of the Chemical Industry, has granted research stipends: German junior staff members will receive future instruction abroad, in order to link up as quickly as possible with the top accomplishments of others. Also Bonn has granted 2 year stipends in order to force personnel transfer between research and industry at home. If the genetics engineer should find he has a taste for free enterprise, a special state programme continues to help him with a supporting subsidy for founding a high-tech firm. (Extracted from Wirtschaftswoche, 21 June 1985)

New centre approaching inauguration

Despite an attempt to burn it down before it was occupied, and still under makeshift leadership, the Centre for Molecular Biology of the University of Heidelberg (ZMBH) is heading for its official inauguration in November.

Built in the shadow of the German Cancer Research Centre, which has about 60 per cent of its 1,200 staff in permanent posts, ZMBH with 200 staff will give tenure only to eight or so senior scientists.

Research funds will come from three core grants, the biggest one of which has been approved in principle by BMFT and will be worth at least DM 6 million for each of the next four years. The other two grants are from the German Research Society (DFG). One grant, for neuroscience, has been approved. The other, for gene expression, is expected to be approved soon. BASF, best known for cassette tapes, will make a contribution of an annual DM 1 million for ten years. (Extracted from Nature, Vol. 317, 3 October 1985)

German technology yields foam-free fermentation

A fermentation aeration technology developed at Braunschweig avoids foam formation in bioreactors for cultivation of eukaryotic cells. The system, designed by the Gesellschaft für Biotechnologische Forschung (GBF), achieves bubble-free aeration by feeding air or oxygen into the cell culture through an agitated skein of open-pored hydrophobic polypropylene hollow membranes 2.6mm in diameter.

GBF has been using the new gassing technology over several months for continuous production of genetically engineered fibroblast interferon. It scaled up the bioreactor to 20 litres initially, then to 70 litres, in co-operation with Diesel GmbH & Co. in Hildesheim,

which now has a 200-litre unit on the drawing board. (Source: McGraw-Hill's Biotechnology News Watch, 5 August 1985)

France

Biotechnology and champagne

The French government and the agro-food manufacturers, France's second largest industrial community, are worried that their traditional methods of wine making are too unreliable, variable and sensitive to uncontrollable factors such as the weather to secure their place in the world markets against high-technology producers in California, South Africa and Australia. So the French food producers have decided they will use science to help. Champagne will be one beneficiary. One of the most difficult elements of champagne technology, rémuage, is the removal of spent yeast from the wine after the second fermentation that produces the "fizz" and the flavour. This is already being changed by the use of "fixed", pelleted yeast. There is no detectable effect on the flavour, and the advantage will be that rémuage will take only three days, compared with the present laborious three months of slowly turning and raising the bottles until they are cork-down, followed by a swift opening and closing of the bottle by an expert to blow out the unwanted yeast. With fixed yeast, the same blowing-out is necessary, but the yeast pellets sink far more rapidly than individual yeast cells.

The vines themselves are also under study. The small Programme Nationale de la Vigne, established three years ago by the research ministry, held its first scientific conference last spring and raised hopes that gene cloning and transfer techniques together with cell fusion and tissue culture might well produce useful new varieties. In the past, it has taken between 20 years and a century to make a new clone adapted to a particular soil and climate; this time must be shortened if new varieties resistant to disease or less sensitive to spring frosts, for example, are to be developed. (Extracted from Nature, Vol. 316, 18 July 1985)

Ireland

Four new biotechnology centres of excellence

Ireland is setting up a $10 million fund to create four centres of biotechnology excellence. The "National Programme for Biotechnology Research", which is still in draft form and awaiting government approval, reaffirms Ireland's emphasis on attracting biotechnology to the island. Ireland's Industrial Development Authority (IDA), along with other government, association, and private sources, will contribute to the new fund.

The current plan calls for one centre in each of the following fields: immunodiagnostics and mammalian reproduction of cells, food and plant technology, molecular genetics, and microbial fermentation. Existing university structures will be used.

Since 1970, Ireland's aggressive industrial incentive programmes have succeeded in attracting some 350 American companies - including about 50 pharmaceutical makers. Crucially important have been its tax laws, which guarantee a maximum 10 per cent tax on corporate profits through the year 2000 and allow companies to freely depreciate their assets. (Extracted from Bio/Technology, June 1985)

Biotechnology R&D increases

Biotechnology research in universities appears to be booming, judging by this year's National Board for Science and Technology research grants which has risen to £421,000 of the total £1.1m.

Fifteen projects under the Strategic Research Programme are in biotechnology, an encouraging feature of which is that they relate to Irish natural resources.

They include:

- The development of a low salt cheese for people on low salt diets;

- A genetic engineering project to produce cattle whose beef would have more polyunsaturated fats;

- Research on a treatment to produce crops such as peas and beans which will give more nitrogen to the soil.

Many projects are agro-based. One joint project is studying cow fertility; other projects are looking at defending plants from carrot fly pest, applying in vitro technology

to isolating disease-resistant crops, and artificial insemination. Additional projects are concerned with health-care. (Extracted from Technology Ireland, July/August 1985)

Japan

Co-operation with France

Japan and France have recently agreed to exchange their respective plant genetic resources as a first step in their biotechnological co-operation. Government officials said that this is the first time for Japan to undertake full biotechnological co-operation with a foreign country. The government has had some co-operative relationships in biotechnology with Australia, but this has been limited to information exchanges. In elaborating on the Japan-France tie-up, officials said that the plant genetic resources to be exchanged will include various wheats, rapeseeds and pasture. They will all be pure breeds, not mixed, because more than two kinds of good pure breaks are needed to create new breeds in biotechnology. (Source: The Japan Economic Journal, 16 April 1985)

Total of 389 firms and institutions involved in biotechnology

A total of 389 Japanese firms and public institutions are now engaged in biotechnology research according to a Ministry of Agriculture, Forestry and Fisheries council report.

The council, which promotes agricultural technology, based its report on replies from the private sector and public institutions in all of Japan's 47 prefectures. It says the 389 organizations comprised 179 private firms, mainly manufacturers of pharmaceuticals, food and beverages, and 210 public institutions.

The report shows that the 179 private firms have an average of 2,000 genic microbe seeds and other genetic resources, while each prefecture possesses 1,500 such resources. These figures are almost on the same level as other industrial nations.

According to the report, many firms and institutions are gleaning biotechnology information from magazines, seminars and various academic groups as well as data base networks owned by research agencies. Collection of genetic resources is being conducted by individual researchers in many cases.

Both firms and institutions want the government to make efforts to collect genetic information on an official level and be made available to the general public through making use of data bases. (Source: The Japan Times, 13 July 1985)

Anti-cancer agent announced

A promising new anti-cancer agent, a synthetic derivative of an alkaloid extracted from the leaves of camptotheca acuminata, a plant species originating in China, has been developed by the chemotherapy division of the National Cancer Centre Research Institute of Japan. The new agent, called cinocipity-11 (CPT-11), was developed through the joint efforts of researchers at the NCCRI, Yakult Central Institute and Showa University in Tokyo, demonstrated a high inhibitory effect on experimentally produced skin cancer and leukemia in animals. The survival rate was reported to be extremely high in all cases.

The plant has long been known in China for its anti-tumour effect, but its original extract, camptothecin, also shows a strong toxicity. The substance is also not water soluble. These two negative properties have so far prevented its clinical application in Western medicine.

The successful development by the Japanese team of CPT-11, which is water soluble and has a significantly reduced toxicity, was subsequent to a series of experiments on a range of derivatives each with a slightly modified chemical structure. Tests using larger animal models are required before clinical tests on human patients can begin. (Extracted from The Japan Times, 26 June 1985)

Hayashibara to engage in space shuttle experience

Hayashibara Biochemical Laboratories, Inc. (HBL) is to engage in experiments for mass separation and purification of physiological activating substances such as interferon, using the electrophoresis operation in space (EOS) module on board American space shuttle.

Developed by McDonnell Douglas Corp. to separate living cells through electrophoresis, the device will be installed on future NASA flights. Hayashibara will be the first Japanese user of this system in an agreement with its sole agent in Japan, Mitsubishi Corp. The dramatic increase in separation and purification performance of the EOS afforded by the

gravitation-free conditions of space prompted the company's decision. (Extracted from The Japan Economic Journal, 28 May 1985)

Hepatitis vaccine to undergo testing

Meiji Milk, the Japanese dairy concern is to start clinical trials of its hepatitis-B vaccine which was developed jointly with the Tokyo Cancer Institute and Chiba Prefectural Serum Laboratory. It could be on the market in three or four years. While other Japanese companies working on the vaccine have opted to use gene-spliced micro-organisms, the Meiji technique utilizes human liver cancer cell culture to produce the viral surface antigen. Purification is carried out using monoclonal anti-bodies. (Extracted from European Chemical News, 22 July 1985)

Silkworms produce alpha interferon

Silkworms can be genetically altered to produce human alpha interferon, a potential antiviral and anticancer agent. A team from Tottori University, the University of Tokyo and Daiichi Seiyaku Research Institute used a baculovirus as the vector for the transformation. The messenger used to carry a human interferon gene into the silkworm was the Bombyx mori nuclear polyhedrosis virus (BmNPV). This comparatively large virus has a genome of double-stranded DNA which is encapsulated in a geometrically regular protein coat (hence the "polyhedrosis" label). This virus is better than insect pathogens tried in the past because is it "host-specific" and so can not infect wild insects.

The team managed to isolate the gene for the major coat protein of the polyhedrosis virus and treated the gene with enzymes until they were left with only the promoter for the gene. The promoter contains a long, repeated sequence, which is responsible for high levels of gene transcription. The researchers then spliced to this a human gene encoding interferon-alpha, class J, which they obtained from Genentech. The resultant construct contained a long stretch of viral DNA in which the polyhedrin gene is replaced by the interferon gene. The team then dosed silkworm cells in tissue culture with the BmNP virus and an excess of the construct and selected for recombinant viruses.

Silkworms injected with large amounts of the modified virus did indeed make interferon - detected in the haemolymph, or blood of the silkworm at 100 times the concentration attained in other systems. The team then confirmed that the protein produced by the virally infected silkworms was identical to human interferon. They found stable recombinant viruses replicating in the silkworm larvae, each of which synthesizes up to 50 micro-g of interferon. The material can be harvested 4 days after infection by pricking the worm with a pin and collecting the interferon-rich material that seeps out. Silkworms may be the only living systems for economical genetic engineering mass production. (Extracted from Chemical and Engineering News, 24 June 1985 and New Scientist, 11 July 1985)

Seed production project

The Ministry of Agriculture, Forestry and Fisheries (MAFF) will be collaborating with private companies to develop artificial seeds. Companies, including Kirin Brewery Co., have expressed interest in joining such projects. The technique requires tissue culture of cells (embryos) and their protection by synthetic resin capsules and is expected to help realize new plant varieties in laboratories instead of experimental farms. MAFF intends to win the keen worldwide competition for variety development by combining the Ministry's and private firms' effort. The Ministry will set up a unit in its Vegetable and Ornamental Crops Research Station and then form a project team or teams. The major research themes will include techniques for mass propagation of embryos. Initially experiments will be on eggplant, gourd and tobacco families.

MAFF is starting the new project largely because new plant varieties with unique genetic features cannot be expected to be utilized widely - unless their seeds are mass-produced. At present, desirable hybrid crops, such as high-yield rice, are developed by crossing for several generations, but the hybrid rice seeds fail to possess their parent's genetic features. Besides, hybrid seed development requires spacious farms, which contributes to increasing development costs. By comparison, cell propagation and mass-consumption of man-made seeds promise to cut costs. Moreover, a seed quality can be stabilized because cells with the same genes can be extracted from a plant. MAFF wants to develop artificial seeds of such crops as rice and barley in the future. (Extracted from The Japan Economic Journal, 19 March 1985)

Hepatitis-B screening

In future, all pregnant women in Japan will be tested for signs of hepatitis-B virus in their blood. If they are carriers of the virus, their children will be vaccinated soon after birth. This programme alone could eventually prevent half of the cases of liver cancer in Japan.

Hepatitis-B can cause an acute but transient infection when an individual is infected as a healthy adult. But if infection occurs when the immune system is immature (at birth) or impaired, people often become carriers at risk of developing liver cancer. The virus becomes integrated into the DNA of liver cells, where it can induce cirrhosis, chronic hepatitis or cancer, years later. Children who are infected by mothers become positive for a viral antigen three months after birth.

A carrier of the virus always has antigens to the surface proteins of the virus (known as hepatitis-B surface antigen, HBsAg). But the risk of developing cancer is much higher if the blood also contains another antigen - "e" or HBeAg - a protein from the core of the virus. The vaccination scheme will give the highest priority to the children of mothers positive for antigen e. Health authorities plan to administer antibodies for the surface antigen at birth and then a vaccine two or three months later. The vaccine consists of small particles of the virus collected from the blood of carriers; these particles lose, along with their DNA-containing core, the ability to infect cells.

Research is also under way to create a more sophisticated vaccine made of synthetic peptides to surface antigen "a", which is common to the four subtypes of hepatitis-B found throughout the world. Such a vaccine would remove the risk of inadvertently introducing other viruses in the vaccine. (Extracted from New Scientist, 11 July 1985)

Algae make wax from waste

Harima Chemicals, Inc. of Hyogo Prefecture, Japan's leading manufacturer of pine chemicals, has a new method for producing unsaturated wax ester by selective cultivation of Euglena, a single-cell green alga. They first culture Euglena aerobically at 28°C on a glucose-peptone medium for three days, then add oleic and linoleic acids - waste byproducts of pine-resin fractional distillation. They then reculture anaerobically at pH 6.5 for a week. Cell density reaches 20 g/L, and wax yield 10 g/L - about half of cell weight. The conversion rate of added unsaturated fatty acids is some 50%. (Source: McGraw-Hill's Biotechnology Newswatch, 19 August 1985)

Mycotoxin tests near market

Ube Industries, Ltd., Yamaguchi Prefecture, plans to market two monoclonals to detect fungal toxins in food. Developed by pharmacology professor Yoshio Ueno at Science University of Tokyo, the antibodies target mycotoxins ochratoxin A and T-2-toxin. At present, Japan requires testing only of peanuts for aflatoxin B, a mycotoxin implicated as a carcinogen. However, Ube sees a ready market for its easy-to-use kits in monitoring food and feed contamination. (Source: McGraw-Hill's Biotechnology Newswatch, 19 August 1985)

Engineered E. Coli increases H2 output

Japan Synthetic Rubber Co. Ltd., Tokyo, in co-operation with Dr. Isao Karube of the Tokyo Institute of Technology, has engineered bacteria to boost hydrogen production from sugar fermentation. Escherichia coli containing recombinant genes from a facultative anaerobe produces hydrogen from glucose 2.5-times faster than controls - and conversion efficiency increased from 16% to 50%. The goal is to convert cheap organic matter, such as waste molasses, to fuel hydrogen, Karube told a meeting of the Japan Agricultural Society held at Hokkaido University in late July. (Source: McGraw-Hill's Biotechnology Newswatch, 19 August 1985)

Netherlands

Netherlands funds biotechnology research at Delft-Leiden

Biotechnological research in the Netherlands has once again received a boost from the Ministry of Economic Affairs. This time in the form of an annual subsidy of 1.2 million guilders granted to the co-operative alliance Biotechnology Delft-Leiden (BDL), which in part through this subsidy wants to expand into a centre for biotechnological research of international renown. However, the largest part of the research costs will have to be borne by the institutions themselves (Delft University of Technology and University of Leiden) that are co-operating in BDL.

The BDL will receive the subsidy within the framework of the Innovation Oriented Research Program for Biotechnology. This is one of the IOPs (Innovation Oriented Research Program) with which the Ministry of Economic Affairs wants to try to gear research in the Netherlands to the needs of trade and industry in order to promote industrial innovation.

Intensive and well-organized co-operation between the Delft University of Technology and the University of Leiden in the area of biotechnology has been in existence for some time. There are presently approximately 200 people working within the framework of the BDL co-operative agreement. The areas in which research is being done within the BDL are:

- Research on yeast, especially physiological and genetic aspects;

- Research on plant cells, the production of plant by-products and biotransformations;

- Bioprocess and bioreactor technology, whereby attention is being paid in particular to so-called packed bed units (for ion exchange) and fluidized systems;

- The recycling and purification of products of biotechnological processes, with an emphasis on applying column systems.

According to the Program Commission for Biotechnology, it is quite possible that the BDL co-operative alliance will be allowed to grow into a research centre of international renown. The level of the research proposals, the contributions by the institutions themselves, enthusiastic input by the researchers and the intensive co-operation between the two institutions offer good prospects for the emergence of a Centre of Excellence that will be identifiable to trade and industry at well.

The research programme of the co-operative alliance will be evaluated on an annual basis by experts from trade and industry and the universities. In addition to oral progress reports, the BDL will present an annual report and organize a symposium on a yearly basis on the results of the research. (Extracted from PT Aktueel, 2 January 1985)

Norway

Norwegian government funds biotech research for 1985-87

By means of an action plan with a scope of 112 million kroner the development of biotechnology within various fields and industries in Norway will receive a necessary buildup. The Process Engineering Committee of the Norwegian Technical and Natural Sciences Research Council (NTNF) hopes the plan can be carried out from 1985-87 and that 68 million kroner will be public capital, while industry's contribution is estimated at about 44 million. As a result of a survey the committee established a network of interdependent measures which will see that as many of the proposals as possible are carried out. The action plan is based on future co-operation between the four research councils in Norway (NTNF and the agriculture, fishing and general science councils) and the Industry Fund. In addition, the committee is suggesting that a national strategy be developed for biotechnology and that the research councils plan this jointly. (Extracted from Aftenposten, 20 December 1984)

Sweden

New Swedish Centre for Biotechnology

The county council of Stockholm County has formed a new centre - the Huddinge Center for Biotechnology - which is attached to Huddinge Hospital. The chairman of the new institution's board is Professor Bertil Aberg, one of the true pioneers in biotechnology who now works for Skandigen. Other board members include prominent professors from the Karolinska Institute and the undersecretary in the Ministry of Social Affairs, Ingemar Lindberg.

With this move the county council will invest Huddinge Hospital with the research status that has been planned for it from the very beginning. These ambitions on the part of the county council coincide with the interests of researchers at Huddinge Hospital. They have long wanted a research centre for molecular biology in Huddinge or a technical professorship in molecular biology at the Karolinska Institute located at Huddinge. The problem up to now was that there were no funds for this position. Now the county council has promised to provide a total of 60 million kroner over five years for the establishment of the research complex. A separate company has also been set up by the county council, the Huddinge Hospital Development Center, for the purpose of expanding the research complex with other centres. (Extracted from Svenska Dagbladet, 22 March 1985)

Volvo buys Pharmacia AB

According to reports from Sweden, AB Volvo has acquired a majority participation in Pharmacia AB. With 3.2 million shares, it is now the largest shareholder in the pharmaceutical and biotechnology company. This number of shares corresponds to 6.4 per cent of the capital stock and 26.6 per cent of the voting rights. It is said that Volvo paid more than 650 million kroner for this transaction, about 10 per cent over the market price. Volvo supposedly acquired the stock from foundations that are linked with the founders of Pharmacia. Volvo has already indirectly obtained a participation in Pharmacia through the investment company AB Custos, which held 2 per cent of the shares and 4.7 per cent of the voting rights at the end of 1983. With Volvo's commitment, the company is making further

advances into the biotechnology area. It is said that it now owns 22 per cent of AB Cardo, which is involved in the sugar, seed and biotechnology sectors. Its share of KabiGen AB, active in the biotechnology area, is estimated to be at least 15 per cent. Volvo holds about 33 per cent of Sonesson AB, which recently acquired the pharmaceutical companies AB Leo and AB Ferrosan. Sonesson also owns 57 per cent of Gambro AB, which manufactures medical instruments. (Source: Europa Chemie, 15 February 1985)

Human DNA cloned from Egyptian mummy

DNA from the 2,400-year-old mummy of an Egyptian child has been extracted and cloned in a plasmid vector by Svante Pääbo of the University of Uppsala, Sweden. Though only one of 23 mummies investigated contained DNA that could be cloned, that one produced about 5 per cent of the DNA that would be obtainable from fresh human material. "The results establish the feasibility of faithfully cloning substantial pieces of genomic DNA from biological remains of great antiquity", Pääbo says. Among the questions that the cloned DNA may help to answer are the descent of the ancient population of the Nile Valley and the relationships between various dynasties and pharaohs. (Source: Chemical and Engineering News, 6 May 1985)

United Kingdom

SERC reviews biotechnology research

Last June the Science and Engineering Research Council (SERC) began a major review of the role it plays in promoting and funding research into biotechnology. On the agenda was the future of the SERC's Biotechnology Directorate, one of the driving forces behind British research in biotechnology, which faces cuts in its budget and pressure from government to economize. One solution to the funding crisis was suggested as long ago as 1981 by the Spinks committee. The committee suggested the formation of a new directorate to pool the resources of different research councils. Another more remote possibility involves eventually merging the directorate or its successor with the Department of Trade and Industry's Biotechnology Unit, which increasingly is funding applied research in academia. A moratorium on spending imposed last November on the Support for Innovation Scheme, from which the unit draws its money, was lifted in March. The unit recently revealed its intentions to enlist industrial support for a £10 million to £15 million biotechnology programme. (Extracted from New Scientist, 6 June 1985)

Biotech club formed

The UK's Science and Engineering Research Council (SERC) is teaming up with Celltech, Glaxo ICI and RTZ Chemicals to form a protein engineering "club". SERC is to provide three-quarters of a £2 million fund to support a co-ordinated research programme in universities and polytechnics, the rest coming from its industrial partners.

The rights for exploitable products resulting from the collaboration will be signed over to the British Technology Group, but members of the club will receive exclusive licences at a privileged rate for an agreed period of time.

Target areas for research include drugs, hormones and industrial enzymes. The first £1.3 million has already been allocated to universities in London, Bristol, Leeds, Sheffield and York. (Source: Manufacturing Chemist, July 1985)

New biotechnology initiative

A new collaborative biotechnology research initiative aimed at the agricultural and food industries is being launched by the Laboratory of the Government Chemist. Grants of up to 50 per cent will be available to help industrial consortia exploit the biotechnologies developed by academic centres of excellence.

Each collaborative programme may be in plant, animal or food science, with possible priority areas including: genetic applied enzymology; plant and animal tissue culture; applied enzymology; animal and plant physiology; and new assay methods. (Source: Biotechnology Bulletin, Vol. 4, No. 7, August 1985)

Transplant aid licence

An agreement has been made by Wellcome Biotechnology for exclusive licence terms with British Technology Group for the development of a monoclonal antibody for use in bone marrow transplantation.

The monoclonal antibody, called Campath-1 - so-called because it was developed in the Cambridge University Pathology Department - helps prevent graft-versus-host disease (GvHD) which is a serious complication of bone marrow transplantation, leading to rejection of the

grafted tissue. In clinical trials, the antibody has reduced the incidence of severe GvHD from 50 per cent to about 5 per cent. (Source: Manufacturing Chemist, August 1985)

Beecham produces treatment for dissolving blood clots

Beecham, the UK-based pharmaceuticals company has produced a drug to dissolve blood clots. Called Eminase, trials show that the new drug dissolves clots within 30 minutes in 60 per cent of patients tested. It is a chemically-modified combination of a naturally-occurring human clot dissolver and a bacterial enzyme long known to dissolve clots and its mechanism is to activate the body's own clot-dissolving system. Beecham claims that Eminase lasts long enough to be used as a single shot, five-minute injection. In an emergency, a single Eminase injection may be administered by a GP. (Extracted from European Chemical News, 29 July 1985)

US company invests in UK monoclonals unit

Damon Biotech, the fast-growing US biotechnology company, is to build a £30 million monoclonal antibody production facility at Livingston, near Edinburgh, Scotland which will have a manufacturing capacity ten times greater than Damon's existing facility at Needham Heights on the outskirts of Boston and is claimed to be the largest of its kind in the world. The investment package involves UK government grants, as well as venture capital from a European consortium assembled by Advent International of Boston.

The facility will initially focus on the production of monoclonal antibodies on a contract basis to meet demand from European clients, as well as to meet the need for clinical trials of Damon's own biopharmaceutical products. As necessary, Damon Biotech Ltd. will assist with orders from US and Japanese clients that are beyond the capacity of the US facility. (Extracted from European Chemical News, 29 July 1985)

Celltech reagents

Celltech is to launch a range of reagents for the purification of interleukin-2 (IL-2). The latest products in the UK company's immunopurification range, the anti-IL-2 monoclonal antibodies are being produced in hybridoma, developed at its Slough laboratories. The company recently started marketing an antibody product for the purification of beta interferon. This is derived from anti-beta hybridoma licenses from the Japanese firm, Yamasa Shoyu. (Extracted from European Chemical News, 12/19 August 1985)

Anti-AIDS invention sold

A British invention that could protect haemophiliacs from contracting AIDS has been sold to the West German chemicals giant, Bayer. Speywood Laboratories, which specializes in blood products, had a key stake in genetically engineered factor VIII, a blood clotting protein that is essential in the treatment of haemophiliacs, but Porton International, a consortium of biotechnology firms including Speywood, has sold the stake to Bayer. British researchers, supported by Speywood, played a crucial role in developing genetically engineered factor VIII. A group at the Royal Free Hospital in London used biotechnological techniques to isolate the protein. Speywood then passed the valuable protein to Genentech who developed a process for manufacturing genetically engineered factor VIII. Both companies shared world rights to manufacture and sell factor VIII.

Despite its early success with factor VIII, Speywood ran into financial difficulties, forcing it to cut back its genetic engineering programme. After a further injection of several million pounds, Speywood was sold two years ago to Porton International, a consortium of firms run by a British entrepreneur, Wensley Haydon Baillie.

Meanwhile, to raise cash, Speywood's two backers had sold the company's manufacturing rights for factor VIII to Genentech. Now Cutter Biologicals, an American subsidiary of Bayer, has revealed that it has acquired all of Speywood's marketing rights to factor VIII. Porton International, a private firm with a name coincidentally similar to the British government's microbiology establishment at Porton Down, has refused to comment on the deal. (Extracted from New Scientist, 8 August 1985)

United States of America

Exports to potentially hostile nations

When the Co-ordinating Committee for Multilateral Export Controls (COCOM) meets in Paris, its agenda will contain a US recommendation to place key biotechnology substances and methods - possibly including recombinant-DNA techniques, cell-fusion methods, genetic-material sequencers and analyzers, and biochip research - on a strategic watch list to monitor whether they are being diverted to potentially hostile areas of the world.

If the diversion is indeed occurring, COCOM nations, which include Japan and all NATO countries except Iceland and Spain, presumably would then agree on formal export controls on the technologies, to be enforced by each country.

Although the US biotech industry recognizes the need for some regulation, particularly of virulent organisms directly applicable to germ warfare, the prospect of overly broad and strict export controls is of "serious concern" to the Association of Biotechnology Companies. (Extracted from Chemical Engineering, 2 September 1985)

Field-testing of genetically engineered insecticide approved

The US Environmental Protection Agency (EPA) has approved the field-testing of Mycogen Corp's genetically engineered insecticide - giving the San Diego company a head-start on Monsanto. Mycogen, which has transferred a toxin from Bacillus thuringiensis into a strain of Pseudomonas, will be testing the insecticide against some 30 types of caterpillar. This approach is intended to protect the toxin from degradation by micro-organisms or ultraviolet light once applied to crop plants. Mycogen kills its recombinant organisms before applying them to the leaves of the crop plants: Monsanto, instead, has applied for permission to apply live organisms to the roots of the crop plants. (Source: Biotechnology Bulletin, Vol. 4, No. 7, August 1985)

Quarantine rules simplified

The US Department of Agriculture (USDA) has agreed to simplify and streamline its quarantine rules for the import of cell lines. Biotechnology companies have been complaining of delays of as much as a year while tissue cultures and tissue-culture products await testing at USDA's Plum Island quarantine facility.

USDA's quarantine rules apply to imports of any materials that could contain foot-and-mouth disease virus and other livestock diseases not already present in the United States. Thus cell lines prepared with bovine serum or the enzyme trypsin (which is derived from cows and pigs) come under the quarantine. During negotiations between USDA and representatives of the biotechnology industry on speeding up the process, it became clear that most of the delays were bureaucratic. Under the new procedures, companies will be able to establish deposit accounts with USDA so that the tests can be run as soon as products arrive at Plum Island. (Extracted from Nature, Vol. 315, 20 June 1985)

Steady growth predicted for US enzyme market

Two major studies of the US industrial enzyme market are predicting increasingly good prospects for this sector as the products become ever-more popular in the food industry and new uses continue to be found.

According to Frost & Sullivan, enzyme development is at an early and exciting stage: "New uses are found almost daily, and the potential for large volume applications is quite good". Premier among the uses will be food preparations which accounted for three-quarters of the 1983 total of $185 million worth of sales.

The company says enzyme use in food preparations amounted to $140 million in 1983 and should represent some $190 million by 1988. High fructose corn-syrup is replacing sucrose as the prime sweetener in most prepared food uses, and soft drinks, icings and jams use 90 per cent fructose syrup, all of which is enzymatically produced.

Concentrating purely on the food sector, a report from Eldib notes that several European-owned companies have already entered the US enzyme market. The current situation is said to be very competitive. However, Eldib predicts that this competitive situation will cause US domestic producers to switch to other product lines. This should give new suppliers a good opportunity to enter the market with increased sales possibilities.

Second in importance to the food area is pharmaceutical and medical applications, which are expected to retain about 16 per cent of the market throughout the period. Important here are blood-clot dissolution functions (in which urokinase will probably totally replace streptokinase); blood coagulation factors for treating haemophiliacs; alterations to penicillin against some diseases; and diagnostics.

Other applications, such as enzyme uses in detergents, in waste water treatment, leather tanning, textiles, and the paper industry should be doubled by 1988.

"Industrial Enzymes Market in the US" is available from: Frost & Sullivan, 104-112 Marylebone Lane, London, W1M 5FU.

Eldib's study on enzymes in the US food market is available from: Eldib Engineering & Research, P.O. Box 138, Berkeley Heights, NJ 07922, USA. (Extracted from Manufacturing Chemist, May 1985)

Union of Soviet Socialist Republics

Single-cell protein

A unique and quite remarkable food programme involving the production of more than a million tonnes of microbial protein is currently under way in the Soviet Union.

The microbial protein is produced by growing bacteria, algae, fungi or yeasts on various feedstocks. The protein-rich microbial cells which result are called single-cell protein (SCP). The feedstocks used have ranged from petroleum, natural gas, methanol, ethanol, almost every variety of agricultural waste and gases found in mine shafts to peat, timber waste and even sunlight. The SCP produced is then fed to people, either directly, added to traditional foodstuffs, or indirectly and much less effectively via animals, in powdered, granulated or pellet form.

Soviet planners were searching for a new source of protein to offset severe shortages of agricultural livestock. At the same time they had a problem with the recently discovered oil deposits in the Volga-Ural fields, because the oil had a high n-alkane (wax) content. The wax made it harder to pump and handle, decreasing its value. The discovery of a micro-organism that could dewax the oil as well as produce protein offered an attractive and ingenious solution.

By 1964, an experimental plant designed to grow yeasts on petroleum, with an output of 1,500 tonnes a year, had begun in Krasnodar. Toxicological problems arose, however. The SCP was contaminated with carcinogenic polycyclic aromatic compounds derived from the impure gas-oil substrate, making it unsuitable for animal feed. A switch to purified liquid alkanes as substrate in a second experimental plant at Ufa (with a capacity of 12,000 tonnes) removed this obstacle, and many biological tests were carried out to check the safety of the product - called protein-vitamin concentrate - as an animal foodstuff.

Large-scale plants which used n-paraffins as feedstocks followed - at Ufa (100,000 tonnes per annum) in 1968, Gorki (100,000 tonnes per annum and later expanded to 200,000 tonnes per annum) in 1970 and Kirishi (100,000 tonnes per annum) in 1972. Other n-paraffin plants have also been built at Angarsk, Krasnodar, Kstovo, Novocherkassk, Polotsk and Svetloyarsk. Three further plants at Kremenchug, Novopolotsk and Mozyr are nearing completion and may even have started production: they have capacities of 120,000 tonnes, 120,000 tonnes and 300,000 tonnes a year respectively.

Apart from protein, the Soviet Union also plans to use the lipid (fat) fraction of yeasts grown on liquid paraffins. A pilot plant is already under construction. Extracting the lipids will increase the protein content of the remaining yeast, and the lipids will then be used to produce high-quality soaps (triglycerides) and lubricating oil, or products for the medical industry (phospholipids) or the paint industry (oleic, linoleic acids and so on). Biologically active substances such as ergosterol (from which vitamin D is made) may also be isolated from the lipid fraction.

The Soviets also hope to increase existing capacities by introducing automated production lines and more powerful fermenters. Over the past decade, fermenters have increased in size, and current models can produce up to 35 tonnes of protein a day.

Inevitably in such a large-scale development, there have been serious difficulties to overcome. For example, the SCP produced on n-alkanes was deficient in the amino acid methonine, and a plant for its manufacture had to be imported from France. The level of carcinogenic polycylic aromatic compounds in the final product has also given cause for concern, and may explain why the authorities are reluctant to use SCP directly in human foodstuffs. There is still a risk that livestock may be adversely affected by residues with carry-over into their meat.

The Soviet microbiological industry is also a major source of environmental pollution. Large discharges of protein dust into the atmosphere created a need for dust-catching devices now being installed, with capacities of 1,150,000 cubic metres an hour. Nor have some Soviet experts dismissed the possibility of industrial micro-organisms being released from factories and causing major epidemics. A further problem is that contact with the raw materials of production - yeast and paraffin - is undoubtedly affecting the health of workers in the industry.

But the most pressing problem now facing Soviet planners is probably to find a suitable feedstock to replace n-paraffin, as supplies of paraffin are too small to meet future needs

of the microbiological industry. Soviet experts are increasingly turning their attention to natural gas as a substrate, especially as its output is now growing far faster than that of crude petroleum.

The time and cost involved in developing the technology to use natural gas may, however, persuade the Soviet authorities instead to import an already proven Western process. The Soviet Union has already started negotiating with Imperial Chemical Industries (ICI) about the purchase of its "Pruteen" technology, which converts methanol synthesized from natural gas into protein.

Using ethanol as feedstock is another possibility for the Soviets. One factory at Ufa has been reconstructed and now produces ethanol-derived SCP for large-scale testing in agriculture. So far, results suggest that the yeast may be of a high quality, suitable for human consumption. The Soviet Union plans to build a pilot plant that is based on ethanol feedstock and will produce 100,000 tonnes a year.

As well as possessing huge reserves of petroleum and natural gas, the Soviet Union also has the largest forested area of any country in the world. This prompted planners to look at ways of producing SCP from a whole range of timber and agricultural by-products - from wood chips, sawdust, corncob cores, rice husks, sunflower husks, cotton hulls, bagasse and molasses waste to wood pulp and sulphite liquor.

Such an advantage was also obvious to Nazi Germany, which revived its interest in SCP production as a result of the war economy in 1936. A target was set of 100,000 tonnes a year for yeast production to supplement human and animal diets, but the disruption of the economy brought about by the war resulted in production of only 15,000 tonnes a year.

The Germans used sulphite waste liquor as feedstock (a by-product of the sulphite process in paper manufacture). There were eight manufacturing centres, the most important being I. G. Farben's based at Wolfen near Leipzig, and most historians believe that food yeast made an important contribution to the German diet during the war.

Non-hydrocarbon feedstocks now account for more than half the total SCP production in the Soviet Union, using methods similar to those developed by the US Department of Agriculture during the Second World War. Apart from the substrate (the wood chips, sawdust or whatever), typical raw materials for the production of SCP are sulphuric acid, superphosphate, aqueous ammonia, potassium chloride, lime, urea, lysine, soda, and fish oil or soapstock.

The micro-organisms are mostly yeasts of the genus Candida, though during production the fermenter often becomes contaminated with low-yielding (25-30 per cent) strains which pass in with the water and nutrient salts. Conversion to sterile conditions would allow better control of the microbial synthesis process, but this has yet to be achieved.

Soviet researchers are selecting better strains which give good results in the laboratory. One example is "Tul-6", which yields a biomass of 56-80 per cent, has a growth rate of 0.25 per hour and a crude protein content of 54 per cent. However, factories where these strains do not become properly established still have problems: ideally, each enterprise ought to develop its own strains or modify those it is given, because a factory in Siberia operates under a different temperature regime than one, say, in Kazakhstan. But a lack of qualified people or equipment seems to be preventing such refinements and may be a major obstacle to the achievement of efficiency within the industry.

Agricultural wastes are not just used as a substrate for SCP production, many are enriched with protein to make them suitable as fodder. The raw material is partially hydrolysed with a weak acid, then inoculated with yeast or fungi. The mycelium fungus Spicaria has, for example, raised the protein content of fodder by 5.8 per cent in trials.

The Soviet microbiological industry will also soon make extensive use of the country's huge peat reserves: some 210 million tonnes are extracted annually. Following the success of a pilot plant in Lithuania, a full-scale factory is now being constructed and another 98 plants are planned, with a target of some 1,965,000 tonnes of protein a year from peat.

Considering the impact that Soviet microbial protein production could have on Soviet grain purchases from North America, it is surprising that the scale of the operation has not attracted more attention from Western specialists.

The domestic livestock industry is making greater demands than ever before. In 1983, the Soviets needed protein for 123 million sheep and goats, 93.7 million cattle and 61.5 million pigs: an awesome task by any standards. Protein deficits are thought to be enormous; in the Ukraine alone, for example, the deficit was about 1.8 million tonnes

(equivalent to 11 million tonnes of oats). At the moment, huge amounts of home-grown and imported grain are helping to make good the shortfalls. Microbial protein could have an enormous impact in this area: the addition of one tonne of SCP to feed creates an extra 0.4-0.6 tonnes of pork or about 25,000-30,000 eggs, and releases 5-7 tonnes of grain. (Extracted from New Scientist, 27 June 1985)

C. RESEARCH

Research on human genes

Switching off protein production

A discovery by Israeli scientists could help establish how higher organisms regulate production of proteins, a phenomenon which, until now, has been one of nature's best-kept secrets.

Professor Yosef Aloni and his colleagues at the Weizmann Institute, Israel, were studying simian virus (SV40), an organism that replicates in monkey cells and whose genetics is well understood. The team focused its investigations on viral protein 1 (VP1), a protein that coats and protects the virus as it moves from one monkey cell to another. As two other proteins, VP2 and VP3, are used for the same purpose, production of all three must be carefully controlled to ensure correct outfitting for the virus. A particular viral gene is triggered into making VP1 by an enzyme called polymerase II. The gene for VP1 is transcribed to make numerous messenger copies (mRNA) which act as templates from which the protein is built.

When examining DNA complexes formed in this way, Aloni's team found that only a limited number of complete gene copies were generated. Production ceased, after just a fragment of a gene copy had been generated instead of a complete copy. They concluded that transcription was being aborted.

Further investigation revealed that the mRNA migrated from the cell's nucleus to its cytoplasmic lining where it manufactured not VP1, but a much smaller peptide called agnoprotein, which it also encodes. It is this peptide that holds the key to regulating the production of VP1. When the concentration of the peptide reaches a certain point, it binds to its own mRNA, causing it to change shape. This slight alteration initiates production of VP1 in the cytoplasm. However, agnoprotein also leaches back into the nucleus where, again, it binds to newly produced mRNA. Here, though, it causes a different alteration in shape which results in production of an incomplete copy. Thus the nucleus is directed via the agnoprotein to enter the abortive phase and to cease production of mRNA for VP1.

The team intends to study the other two coating proteins, VP2 and VP3, to see whether the same type of regulation mechanism exists. Also, they hope to examine in greater detail how the agnoprotein binds to and distorts the RNA. (Extracted from New Scientist, 12 September 1985)

Synergy between gamma interferon and TNF

Biogen scientists told the Third European Conference on Clinical Oncology in Stockholm that tests with the company's Immuneron gamma interferon and tumour necrosis factor (TNF) indicated that the two proteins, when used together in in vitro studies, had greater killing effect on malignant cells than either used alone. It was reported that this synergistic effect had been observed in a large number of cell lines - including cells derived from breast, cervix and colon tumours. The tests indicated that most of the cell lines sensitive to TNF become much more sensitive in the presence of gamma interferon. Similar synergy was seen between TNF and gamma interferon in mouse cancer cell lines but not normally sensitive to TNF, but highly sensitive when gamma interferon is added. Immuneron has been tested in over 500 patients and is expected to enter the third phase of human clinical trials later this year. TNF, which is also being developed by Cetus and Genentech, is in an earlier stage of development and is expected to begin the first phase of clinical trials shortly. Neither product will be available for general use until the tests required for regulatory approval are completed. (Extracted from Biotechnology Bulletin, Vol. 4, No. 6, July 1985)

Mapping the complex code of human genetics

Nothing in the history of conventional cartography comes close to matching the stupendous challenge of mapping the human genetic code. Determining the structure of Homo sapiens' 300,000 genes is a task akin to cross-indexing every work in an encyclopedia. But the payoff would be spectacular. Deciphering the DNA that determines heredity could pinpoint the causes of inherited diseases - and lead to cures.

One biotech company believes it has a way to simplify the job. Scientists at Collaborative Research Inc., of Lexington, Mass., are using special enzymes to chop the DNA into large sections, called Restriction Fragment Length Polymorphisms. By charting just 1,000 of these, they hope to be able to pinpoint genetic abnormalities in a developing fetus.

The project, which is years from completion, has already yielded a test to determine if a patient is rejecting transplanted bone marrow. Another test under development will be able to identify an infant's father with 99.9 per cent accuracy. (Source: Business Week, 23 September 1985)

Human leukocyte antigens

Genetic clues have been found in some baffling diseases, including juvenile diabetes, multiple sclerosis, lupus erthematosus, Grave's disease, Addison's disease, myasthenia gravis and narcolepsy. Human leukocyte antigens (HLAs) are the focus of studies in all the diseases, which are believed to be caused by immune system abnormalities. HLAs were first studied in relation to tissue typing for organ transplants. Blood typing is much simpler, based on only four antigens while tissue typing involves 80 or more HLAs. Patients with some of the autoimmune diseases mentioned above are far more likely than the general population to have certain characteristic HLA markers. This information may eventually enable more effective treatment, but even now, knowing about the markers may allow persons at risk to take precautionary measures. HLA substance B27 is present in 90 per cent of people who develop ankylosing spondylitis, an unusual form of arthritis. (Extracted from New York Times, 20 August 1985)

Antibody switches

Biological factors that function as switches to activate antibody producing genes have been discovered by researchers at Kyushu University (Japan). Each of the two factors isolated have a molecular weight of less than 200,000. One has a promotive effect on antibody producing genes and the other a suppressive effect. To function inside a cell, a gene must contain a special 'enhancer' sequence or be adjacent to one. The 'expressor' and 'repressor' factors are believed to function by binding to the enhancer. (Extracted from Japan Economic Journal, 16 July 1985)

Oncogene linked to cancer therapy resistance

Further clues to the role of the oncogene N-myc are emerging from studies at the Memorial Sloan-Kettering Cancer Center, New York City, the National Cancer Institute, and at the Naval Medical Research Institute. A year ago, researchers found an increased number of copies of the oncogene in about half of untreated cases of a childhoood nerve cell cancer called neuroblastoma. Now large increases in the product of this gene in neuroblastoma cells that have developed resistance to cancer therapy have been found. This is the first evidence of a connection between a cell's resistance to therapy and increased activity of oncogenes.

The investigators derived four cell lines from two patients with neuroblastoma. For each patient, they derived a pretreatment cell line and another one from cells that survived initial therapy and were beginning to redevelop the tumour. Cells from these treatment-resistant cell lines had up to seven times the level of the product of the N-myc on oncogene than did cells from the pretreatment cell lines. Although the product of the N-myc oncogene was increased in both treatment-resistant cell lines, the number of copies of the gene present was elevated in only one of these lines. Thus, there appear to be at least two biochemical pathways that neuroblastoma cells may use to increase production of the oncogene product.

Neuroblastoma is a cancer of undifferentiated cells - called stem cells - of the nervous system, and the N-myc gene seems to be involved in regulating that differentiation, the researchers find. They treated their laboratory-grown cells with several agents that induce cell differentiation and found that these agents reduced production of N-myc gene products 90 per cent. The cells then began to differentiate and their growth stopped. Retinoic acid was particularly effective in reducing production of N-myc product, causing a 50 per cent decrease within six hours and an 85 per cent decrease within 40 hours. Those cells in which N-myc product was not decreased remained undifferentiated, the researchers find. Retinoic acid at the levels used in this study already has been shown to be safe for clinical use, so a therapy using this agent might be devised. Since the N-myc oncogene seems particularly active in cells that resist other kinds of therapy, treatment of these cells with agents that reduce the oncogene's activity might be especially useful. (Extracted from Chemical Week, 27 June 1985)

Prourokinase developed to replace urokinase

An artificial prourokinase has been developed by Sagami Chemical Research Center [SCRC], an institute owned by 25 companies. The new prourokinase's dissolving capacity roughly equals that of human tissue plasminogen activator. SCRC utilized a genetic engineering technique so that Escherichia coli can produce the thrombi-dissolving substance. Natural prourokinase made by extraction from animal cells is thought to be highly effective, but its production is difficult. Once inside the human body, the natural type is believed to become unstable. By comparison, the artificial prourokinase - made by replacement of one section in the amino acid arrangement with a different amino acid - combines the natural type's effectiveness with high productivity as well as stability. SCRC and its five research partners now intend to upgrade their efforts to acquire the know-how necessary for commercial production. (Extracted from The Japan Economic Journal, 21 May 1985)

Mass production of 'chimeric antibody' possible

Mass production of monoclonal antibodies with persistent effect in fighting human cancers has become possible with a recombinant DNA technique developed by a Kyoto University team, linking human and mice genes to form a 'chimeric antibody'. Previously, antibodies created by murine lymphocyte sources to neutralize human cancer cells have not been altogether effective when administered to patients, since the body recognizes these as foreign matter and produces antibodies directed against them in an immunological response. To bypass this problem, Prof. Tasuku Honjyo of Kyoto University's Medical College and his assistants have devised an ingenious method whereby the antibody genes from both human and murine sources hae been joined together to form a potent agent capable of escaping immunological attack. Linking the variable region antibody gene of a mouse to the constant region antibody gene of a human being and utilizing a retrovirus as the DNA-replicating machine, they have succeeded in producing a gene possessing the necessary information to turn out chimeric antibodies. Compared to conventional monoclonal antibodies, compatibility is thought to be much higher, while mass production should be possible through incorporation of the chimeric gene in microbial hosts. Plans for commercialization in joint venture with private industry are being hastened. (Extracted from The Japan Economic Journal, 21 May 1985)

Virogenes may cause scrapie, GSS and CJS

Virogenes, genes that can generate viruses, may be responsible for the diseases kuru and scrapie, according to researchers at the Clinical Research Centre, Northwick Park Hospital (London). They have been studying Gerstmann-Straussler syndrome (GSS), a rare form of progressive dementia. The disease is inherited according to a clear pattern of autosomal dominant inheritance. When tissue from the brain of a patient who had died of GSS was transplanted into brains of eight marmosets, all the monkeys developed GSS, so a transmissible agent must also be involved. GSS is similar to another degenerative brain disease, Creutzfeldt-Jakob syndrome (CJS), which can also be transmitted experimentally to monkeys. CJS is similar to scrapie, a brain disease of sheep, and kuru, a human brain disease spread by eating enemies' brains in New Guinea. The same antigens are present in tissue from brains affected by all these conditions. The agent responsible could be an infectious protein, although it has never been isolated. The virogene theory could explain why no DNA has been found in prions. The virogene theory could also explain Parkinson's disease, Alzheimer's disease and motor neurone syndrome. (Extracted from New Scientist, 4 April 1985)

Revealing the secrets of arthritis

Research teams in Britain and Japan believe that they have uncovered the first clues to the fundamental cause of arthritis. They have discovered significant differences between antibodies known as immunoglobulin type G (IgG) in patients with rheumatoid arthritis or osteoarthritis. The changes that have been detected have the effect of bending the antibody molecule. This could expose previously hidden parts of the proteins, so that the body's immune system attacks them as foreign proteins. This attack then triggers the disease.

For many years, researchers have been looking for new antigens in the blood and joint fluid of arthritis patients to explain what seems to be the body's attack on its own joint linings. They have not found them. Instead, they found the antibodies binding to themselves. This suggested that, in this case, they must be both antibody and antigen. Researchers in the Oxford Oligosaccharide Group and the Institute of Medical Studies in Tokyo wondered if the various short oligosaccharide units (sugars) on the IgG protein molecule could be involved. They evaluated 1,400 different oligosaccharide sequences from 46 different IgG samples and reported their findings in Nature.

They found no novel oligosaccharides in serum from patients suffering from rheumatoid arthritis and osteoarthritis. However, they did find variations in the proportions of different oligosaccharides. Those with either disease had far fewer oligosaccharides containing the sugar galactose than in healthy people. Normally, about 10 per cent of the molecules lack galactose. In osteoarthritis 19 per cent were without and in rheumatoid arthritis the figure was 40 per cent.

The simple increase in numbers of such molecules could make the difference between no symptoms and full arthritis.

The researchers suggest that these variations in oligosaccharide sequences could upset the process called glycosylation, when the oligosaccharides are attached to the protein. This is the final stage in the genetically controlled assembly of proteins, which could explain a possible inherited predisposition to arthritis.

The researchers are not sure yet whether the unusual glycosylation pattern is inherited directly or whether it is triggered by an external factor such as a virus. One possibility is that it could result from the activation of a normally silent gene, perhaps by a virus, in the same sort of way as so-called oncogenes can be turned on in the development of cancer. (Extracted from New Scientist, 1 August 1985)

New technique to cut DNA

A new method to cut single-stranded DNA at any point has been developed by two separate teams of researchers. Normally, restriction enzymes are used to cut DNA at particular sites of defined nucleotide sequence. The new technique takes a short stretch of DNA to bind to the DNA sequence to be cut. The short stretch of DNA is then linked to a reactive chemical group that can cut the DNA. The activated probe can then be added to target DNA to cut it where desired. The technique could also be used to cut RNA and may make it easier to investigate and exploit genetic information of large genomes. (Extracted from New Scientist, 16 May 1985)

DNA molecules photographed

A team of Japanese researchers has used a supercooled electron microscope to take what it claims are the first photographs of molecules of DNA in suspended animation. They did it by improving the resolution of their microscope by cooling it with liquid helium.

The photographs were shown for the first time at a meeting of the Japan Society for Electron Microscopy. Researchers from the Department of Biophysics and the Institute for Chemical Research at Kyoto University collaborated with researchers from Japan Electronic Optic Laboratory, one of the world's biggest manufacturers of electron microscopes.

The molecules were photographed in a "frozen-hydrated" state, on a stage that was supercooled to nearly absolute zero (-273°C). The company's microscope has a maximum resolution of 0.6 nanometres, which is about 0.3 nanometres better than similar instruments that are cooled by liquid nitrogen.

Supercooling protects the specimen from damage by electrons. To increase the magnification of a specimen, it is necessary to increase the intensity of the electron beam focused on the sample. But the beam can become too intense, and can destroy complex molecular structures like those of DNA or proteins. The colder the specimen, the more these destructive reactions are slowed down. The Japanese team says that their supercooling reduces the destructive power of the electron beam to a twentieth of what it is at room temperature.

Supercooling a specimen fast enough to minimise the formation of ice crystals also helps "fix" it for viewing while it still contains natural amounts of water. Most electron microscope specimens have to be dehydrated first, which can distort their normal appearance.

One problem, however, is that the liquid helium boils off, causing the specimen to vibrate. This makes it impossible to take good pictures. The Kyoto team's solution is to separate the tank containing the liquid helium and the stage of the microscope that holds the specimen by a thin metal grid made of a material based on silver and platinum. This material passes heat quickly at low temperatures, from the specimen to the liquid helium.

Seen through the microscope, the DNA looks like a straight line of dots. By photographing the molecule repeatedly at intervals of 1.7 nanometres, equivalent to one-half the pitch of the DNA helix, the team produced a compcsite image showing the distinctive double-helix structure of DNA at a final resolution of 2 nanometres. (Extracted from New Scientist, 25 July 1985)

The race for synthetic human growth hormone

Creutzfeldt-Jakob syndrome, a rare disease of the central nervous system, does not usually affect people under 40 years of age. When doctors linked the slow-incubating virus earlier this year with the deaths of four younger men - three in the U.S. and one in Britain - health officials became suspicious. When the Food and Drug Administration learned that all of these men had received naturally derived human growth hormone (HGH) as children, the agency decided to act.

On 2 April, FDA asked U.S. distributors to withdraw the product that is extracted from the pituitary glands of cadavers. The agency fears the hormone preparation could have been contaminated by the rare virus. Soon afterward, officials in Britain, the Netherlands, Belgium, Sweden and Greece followed FDA's lead and banned the use of the product.

FDA's move has seemingly paved the way for companies that are poised to provide genetically engineered synthetic HGH. Developers say that recombinant-DNA HGH is safer because it can be produced under controlled conditions where there is no risk of the product being contaminated by a virus. Once its use is approved, the availability of a synthetic product could vastly increase the therapeutic uses of HGH, which, because of the scarce supply of cadaver glands, is now virtually restricted to the treatment of dwarfism.

FDA's concern is that natural HGH may have acted as the vehicle for Creutzfeldt-Jakob syndrome. All three U.S. victims of the virus had been treated during the 1960s and 1970s with HGH prepared by the National Institute of Health's (NIH) National Hormone and Pituitary Program. (Extracted from Chemical Weekly, 10 July 1985)

Human growth hormone technology developed

Toyo Soda Mfg. (Japan) has developed technology to produce a human growth hormone. It used a basic technique developed by the Science & Technology Agency and Osaka University whereby fragments of DNA are made to adhere by a chemical process and incorporated into a new vector. The vector carries the fragments inside E. coli where the hormone is made. Toyo Soda determined the optimum conditions under which the E. coli can produce the hormone and developed an efficient way to extract the high-purity product. The hormone will be produced commercially in 7-8 years. (Extracted from Japan Economic Journal, 4 June 1985)

Recombinant lipocortin made

Using recombinant DNA techniques, scientists at Biogen have succeeded in making the rare human protein lipocortin which is produced naturally by the body to fight inflammation in amounts large enough to demonstrate activity and effectiveness in animal trials. Only trace amounts of animal protein have been available for study until now. Biogen thinks it has the potential of treating inflammatory diseases such as arthritis and asthma without the undesirable side effects that often limit use of conventional anti-inflammatory agents in treating chronic diseases. (Extracted from Chemical and Engineering News, 10 June 1985)

Bombesin as a growth factor

One hypothesis of how a cancer cell grows indefinitely proposes that the cell produces growth factors which then bind to its surface and induce proliferation. Researchers at the National Cancer Institute in Bethesda, Maryland, have confirmed that the brain peptide bombesin can induce proliferation of small cell lung carcinoma (SCLC) cells. More interestingly, a monoclonal antibody directed against bombesin inhibits proliferation of cells in vitro and in vivo. Previous work had already shown that bombesin and bombesin-like peptides can stimulate mouse fibroblasts to replicate in vitro, and that SCLC cells secrete bombesin-like peptides. (Extracted from New Scientist, 5 September 1985)

Cal Biotech clones gene for human lung surfactant protein

Researchers at California Biotechnology, Inc. (Mountain View, Calif.), announced that they have successfully cloned the gene that codes for human lung surfactant protein. The lack of natural lung surfactant - a complex mixture of protein and lipids which aids the O_2/CO_2 exchange between the blood and lungs and prevents the lungs from collapsing - results in respiratory distress syndrome (RDS), the leading cause of infant mortality and morbidity in the U.S. and other developed countries.

Now that the lung surfactant protein gene has been cloned, sufficient quantities of the protein should become available for testing as a treatment for RDS, as well as for adult lung disorders such as adult RDS, bronchitis and pneumonia.

"We are purifying the protein and developing a process for re-constituting it with synthetic lipids to produce an artificial lung surfactant", said Dr. James Schilling, project leader at CBI.

A major reason for lack of progress in lung surfactant therapy has been the unavailability of adequate quantities of human surfactant protein. Until CBI's announcement, the only sources of this protein have been normal adult human lung and amniotic fluid.

In addition to the development of lung surfactant protein, CBI scientists have developed a specific diagnostic assay for identifying surfactant levels in amniotic fluid. CBI anticipates that such an assay, based on monoclonal antibodies specific to the protein

component of surfactant, will overcome many of the problems associated with present assays. (Extracted from Genetic Engineering News, March 1985)

Leprosy vaccine

The British Leprosy Relief Association (LEPRA) has announced the launching of a full-scale trial of a newly developed leprosy vaccine in northern Malawi in 1986 in conjunction with the government of Malawi, the London School of Hygiene and Tropical Medicine (LSHTM) and the World Health Organization (WHO).

About 15 million people suffer from leprosy, and although drug treatment is available, it can be very slow and often too late to prevent irreversible neural damage. Excitement is understandable at the development of a potential vaccine, which has been made possible largely by the collaborative efforts of a group of scientists within the WHO Special Programme for Research and Training in Tropical Diseases (TDR) co-ordinated by Dr. Barry Bloom of Albert Einstein College of Medicine, New York.

The vaccine consists of heat-killed Mycobacterium leprae, the causative agent of the disease, purified from the tissues of the nine-banded armadillo, four colonies of which are maintained by TDR for this purpose. Safety trials have been completed in Norway, where leprosy was eradicated as recently as 1950, and a large-scale non-random trial of 60,000 leprosy contacts is under way in Venezuela which will be completed later this year.

The Karonga district of Malawi has been chosen for the first population-wide trial largely because prevalence of the disease is rather high (1-2 per cent) and because of the groundwork laid by LEPRA's comprehensive evaluation programme in this region directed by Dr. J. H. Ponninghaus and co-ordinated by Dr. P. Fine of LSHTM.

There is evidence from earlier trials that vaccination with Bacille Calmette-Guérin (BCG) against tuberculosis can provide some protection against leprosy and, indeed, animal experiments and therapeutic work in Venezuela suggest a vaccine containing both killed M. leprae and BCG is most promising. The aim therefore is essentially to compare this mixed vaccine with BCG alone in a randomized control trial of the whole population, except those who do not wish to be involved and those who will be excluded on the grounds of age, ill-health or already diagnosed as leprosy cases. (Extracted from Nature, Vol. 316, 18 July 1985)

Leprosy antigens cloned

Antigens of the leprosy bacillus could become available in large amounts for use in research on the disease as a result of a recombinant DNA method worked out by researchers at the Whitehead Institute for Biomedical Research at Massachusetts Institute of Technology and University of Washington, Seattle; Washington University; Stanford University; and Albert Einstein College of Medicine. The researchers cloned genes that specify five highly antigenic proteins of the leprosy bacillus and produced in Escherichia coli fragments of the proteins recognized by all 13 bacillus-specific monoclonal antibodies tested. The researchers note that availability of antigens may make it possible to develop simple and specific assays to screen populations for individuals producing antibodies to bacillus antigens. This, in turn, might make early diagnosis and treatment feasible. (Extracted from Chemical and Engineering News, 19 August 1985)

Blood pressure hormone genes expressed

Researchers at California Biotechnology Inc. (CBI), Mountain View, have cloned and expressed two human genes which regulate increases and decreases in blood pressure. The expression of the gene for renin, a hormone which produces increased blood pressure, was announced in mid-January.

The hormone, produced in minute amounts in the renal tissue, initiates the production of a peptide known as angiotensin I, which is transformed by a separate enzymatic reaction into angiotensin II, which directly elevates blood pressure. Drugs already on the market block the transformation of Angiotensin I to Angiotensin II, but can cause severe side effects. Renin inhibitors may block the same pathway at an earlier step and with fewer side effects.

Although the existence and role of renin have been known for some time, precise structural and functional analysis has been impossible because of the minute amounts available for study. The only natural source of renin has been patients with a rare kidney tumour which produces an excess of the hormone. CBI is already discussing development of therapeutic renal inhibitors with "several" major pharmaceutical companies. CBI's success with renin follows the announcement of the isolation of the gene for auriculin (atrial natriuretic factor) by CBI and a team at Cornell University. CBI also reported expression of the gene. Auriculin, produced in the upper chambers of the heart, lowers blood pressure

in test animals by relaxing t... smooth muscles of blood vessel walls and stimulating the excretion of sodium and excess fluids.

Both renin inhibitors and auriculin are expected to find wide use in treating hypertension and congestive heart failure. (Extracted from Genetic Engineering News, March 1985)

Cetus clones gene for blood cell protein

Cetus has cloned and expressed the human gene that codes for colony-stimulation factor-1 (CFS-1), a glycoprotein that may be a promising treatment for cancer and viral, parasitic, bacterial, fungal and yeast infections. CSF-1 also could restore the white cell populations of those whose immune systems are impaired by immunosuppressive drugs, cancer chemotherapy or genetic defects. Cetus will file an investigative new drug application for human testing with FDA in 1986.

Cetus isolated CSF-1 from human urine, sequenced the first 12 N-terminal amino acids and made oligonucleotides corresponding to this sequence for use as probes. Scientists found nine samples that shared a 3,800-nucleotide sequence for portions of the CSF-1 from mouse and human sources. They made a second 32-nucleotide probe corresponding to the sequence and used it to isolate CSF-1 messenger RNA (mRNA) from pancreatic tumour cells that had been stimulated to produce the protein. CSF-1 mRNA was used to make a DNA blank that could infect monkey kidney cells, which produced CSF-1 protein. (Extracted from Chemical and Engineering News, 12 August 1985)

Yeast-made hepatitis B vaccine

The first human vaccine made by genetic engineering is expected to be a product of yeast. Initial human trials of a hepatitis B vaccine made by yeast have been encouraging and Food and Drug Administration approval is expected in 1986.

Pearl Toy of San Francisco General Hospital is studying the yeast-made vaccine in infants born to hepatitis B carriers. The vaccine has worked well in the first 30 infants, but it is still too early to tell if it is effective. After University of California at San Francisco researchers were able to get yeast saddled with hepatitis B virus DNA to synthesize a hepatitis B protein, some of them started Chiron Corp., an Emeryville, Calif., genetic engineering firm whose first project was to produce a yeast-derived hepatitis B vaccine. They licensed the technology to Merck Sharp & Dohme of West Point, Pa., a drug company that already produces a hepatitis B vaccine purified from the blood of chronic carriers. There is no treatment for hepatitis B infection, which attacks the liver and can lead to death from cancer or cirrhosis. The blood-derived vaccine takes a year to manufacture and costs about $100 for the three-shot regimen - a price that puts it beyond the means of Third World countries, where in some areas as much as 20 per cent of the population carries the virus.

The recipe for yeast-engineered products is similar to the bacterial process. Enzymes are used to snip out the DNA that produces the product in question. "Cut-and-paste" enzymes insert the DNA into circular pieces of yeast chromosomes that are then put into yeast. There they float about and produce the desired product, which is harvested by breaking open the yeast. The advantages of yeast are that unlike bacteria it does not produce toxins; the technology for growing it is well developed; and the species being used - bakers' yeast and brewers' yeast - do not infect humans.

Chiron is now testing yeast-made products for osteoarthritis and feline leukemia, and doing toxicology studies on several other yeast-produced agents. (Extracted from Science News, 27 July 1985)

Hepatitus virus possible AIDS cofactor

Hepatitis B virus (HBV) DNA sequences have been found in fresh and cultured lymphocytes from several patients with acquired immune deficiency syndrome (AIDS) even in the absence of conventional HBV serological markers, according to a team of researchers at Pierre and Marie Curie University, Paris; the National Cancer Insitute, Bethesda, Md.; and the Pasteur Institute, Paris. Analysis of the cellular DNA before and after digestion with restriction enzymes suggests integration of the HBV genome. Although the retrovirus now being called HTLV-III/LAV has been casually related to AIDS, infection with the virus induces different responses depending on the individual. The present findings prompt the researchers to suggest that HBV could play a role in the pathogenic mechanism that leads to the severe immune depression characteristic of AIDS or could enhance the likelihood that HTLV-III/LAV infection will result in AIDS. (Source: Chemical and Engineering News, 5 August 1985 and 19 August 1985)

Diversity in the genomes of the AIDS virus - human T-lymphotropic virus type III (HTLV-III) - is a characteristic and prominent feature; variation between isolates of the virus ranges from slight to extensive; and most patients appear to be infected with only one or two predominant forms of the virus at any one time. The studies undertaken compared the genomes of virus isolated from 18 individuals with AIDS or who were at risk for AIDS. Each showed a different restriction enzyme pattern, which other studies have shown correlates with nucleotide sequence divergence. What the findings mean for diagnosis, therapy, or prevention is not clear. One possibility is that HTLV-III could be similar to certain other viruses in avoiding elimination by host immune defence mechanisms by undergoing changes in envelope proteins during the course of infection. (Source: Chemical and Engineering News, 19 August 1985)

Possible malaria vaccine synthesized

It is less than a year since groups headed by J. B. Dame and V. Enea independently announced they had cloned and sequenced the gene for the circumsporozoite (CS) antigen of the malaria parasite Plasmodium falciparum. In that short time a collaborative effort among scientists at Smith Kline & French Laboratories (Philadelphia, Pa.), the Walter Reed Army Hospital (Washington, D.C.), and the National Institutes of Health (Bethesda, MD) has turned the sequence into a promising candidate vaccine.

This unique team have described the high level expression of an immunodominant epitope of the CS antigen. The CS protein is the key antigen associated with the protective immunity induced by sporozoites.

The group first attempted to express the complete CS protein in Escherichia coli. Although the genetic manipulations were straightforward, the protein was unstable when synthesized in the bacterial host. The strategy which eventually led to the successful synthesis of the candidate vaccine molecules may prove of general use in designing parasite vaccines.

Protection to malaria induced by sporozoites is correlated with circumsporozoite precipitin (CSP) antibodies. Even when administered without adjuvant, the constructs with two or three copies of the repeat region induce antibodies with strong CSP reactivity. Another correlate of sporozoite induced immunity is the ability of sera to block sporozoite invasion of cultured hepatoma cells. The two and three copy repeat proteins elicit antibodies with strong blocking power, and again adjuvant is not required. Further animal and clinical studies are in progress. (Extracted from Bio/Technology, Vol. 3, June 1985)

Recombinant vaccine holds promise for widescale use against rabies

A new recombinant technique may sharply reduce the costs of producing a rabies vaccine, paving the way to a massive vaccination programme for both animals and humans. Medical authorities are confident that worldwide immunization could score a total victory over rabies, thus writing the final chapter in the annals of this dreaded and perhaps oldest recorded human disease.

Dr. Jacques-Pierre Lecocq, scientist director of Transgène (a research group in Strasbourg, France), described the new technique, which integrates rabies virus genes into the DNA of a non-virulent strain of the vaccinia virus. Vaccinia is renowned for its use in the worldwide vaccinations that achieved the present eradication of smallpox, another ancient viral infection. The use of the engineered virus as a live vaccine circumvents the need for expensive tissue culturing procedures currently used in manufacturing the rabies antigen itself on an industrial scale.

"The existing rabies vaccine is very effective but very costly," Dr. Lecocq said. A logical move to sidestep expensive tissue culture procedures was to turn to recombinant DNA methods. In the early 1980s, classic genetic engineering experiments rapidly yielded tangible, but ultimately unsatisfactory results. For example, isolated genes for the rabies virus coat protein worked comfortably in a bacterial setting, but the antigen proved to be temperature sensitive and it performed feebly as a mobilizer of antibody. Work with yeast seemed promising, since the critical glycoprotein antigen was assembled in the cells and it stimulated high levels of antibody. Unfortunately, the yeast produced only meagre levels of the antigen.

The disappointment with earlier attempts explains some of the excitement surrounding the new rabies-vaccinia combination. It is readily produced and it stimulates high antibody production in rabbits, the only animal with reported results to date. The new development stemmed from the joint efforts of an international research team, including Drs. Lecocq, M.P. Kieny, R. Lathe, and S. Skory of Transgène; Drs. R. Drillen and D. Spehner of the Laboratoire de Virologie of the Institut National de la Santé et de la Recherche Médicale

(better known as INSERM); and Drs. Tadeusz Wiktor and Hilary Koprowski of the Wistar Institute in Philadelphia.

Although not yet approved by regulatory authorities, the new vaccine is destined to undergo preliminary animal trials in the near future, eventually leading to human clinical trials.

While a vaccinia-based vaccine appears to hold great promise for the future, for the present, the disease is a significant human and animal health problem. Tens of thousands of people die each year - horrifying deaths of slow, convulsive strangulation. In South America alone, 300,000 undergo emergency treatment every year for rabid dog bites. Unfortunately, the nerve tissue vaccines used in Third World countries cause neuroparalytic reactions in one out of every two to eight thousand individuals vaccinated, depending on the preparation.

Worldwide eradication depends on the availability of a cheap, stable, effective vaccine. The new recombinant rabies vaccine is generating excitement as having the potential to meet these criteria. History has already credited the vaccinia virus - with its cheap mass production and long storage characteristics - with the annihilation of smallpox. (Extracted from Genetic Engineering News, March 1985)

Progress on a recombinant hookworm vaccine

Using a combination of protein purification and recombinant DNA techniques, scientists at The Rockefeller University in New York have made significant progress towards the development of a cheap and reliable vaccine for hookworm disease. This parasitic disease currently afflicts many mammals, including dogs, cats, and over a fifth of the world's human population.

Hookworms are gastrointestinal parasites which suck blood from the lining of their host's small intestine, thereby causing chronic gastrointestinal blood loss, iron-anemia deficiency, hypoalbuminemia, and mental and physical retardation. With a large enough worm burden, death ensues. Symptoms of the disease include extreme weakness, pallor, respiratory tract infections, skin irritations, heart palpitations, and gastrointestinal distress.

Human hookworm disease causes an estimated worldwid ood loss equivalent to the total exsanguination of a million and a half people per day. The disease, which was rampant in the American rural south only a few generations ago, is endemic to tropical and semi-tropical regions, and has reached catastrophic proportions in the third world.

The vaccine being developed at the Rockefeller University is known as histolytic proteolytic enzyme (HP). The research project is under the direction of Dr. Peter J. Hotez, a biomedical fellow in Rockefeller's Laboratory of Medical Biochemistry. Collaborators for the project include Drs. Nguyen Le Trang and Anthony S. Cerami from the Rockefeller University, Dr. Gerhard Schad from the School of Veterinary Medicine at the University of Pennsylvania, and Drs. Nina Agabian and George Newport from the Naval Biosciences Lab at the University of California at Berkeley.

The potential vaccine functions by interfering with the worm's feeding process. "Hookworms feed by attaching themselves to their host by biting and holding on to a small piece of the mucos lining on the inside of the host's small intestine" explains Dr. Hotez.

Then the hookworm secretes a few micrograms of enzyme from glands located within its mouth. This enzyme, which degrades host proteins such as those found in tissues and capillary walls, keeps the host's blood from clotting at the site of the bite. This permits the hookworm to feed for an indefinite period of time. The two types of hookworm that afflict humans, Necator americanus and Ancyclostoma duodenale, can live and suck blood for up to 14 years in a single host.

The HP vaccine would introduce a small amount of synthetically produced enzyme directly to the host, who would then produce antibodies to the HP enzyme. These antibodies would thus be available to neutralize the enzyme secreted by worms during a subsequent infection. As a result, host proteins would not be degraded and the worm would be unable to feed.

"We have found that this method appears to compromise the feeding capacity of the hookworm, and ultimately limits the extent of the disease," Dr. Hotez said.

Studies on the histolytic proteolytic enzyme have suggested other avenues of commercial and basic science research. For example, the enzyme is structurally similar to certain enzymes isolated from snake venoms and from leeches. Scientists believe that this similarity suggests that either an evolutionary link or an interesting parallel is involved between the development of microscopic parasitic worms, and the larger leeches and snakes. The

HP vaccine also may have useful application in the field of blood research and heart disease, due to its anti-coagulant properties.

Open to question is whether or not the approximately 900 million human beings in the developing world and elsewhere who suffer from hookworm disease will receive vaccinations. Such wide-scale preventive measures depend on the cost of the vaccine and the logistics of getting it to where it is needed, Dr. Cerami pointed out. "A polio vaccine exists but people are still dying of polio - there are many economic and political factors involved," he said. "That is why there are so few drugs for parasites around today."

Although is is possible to cure hookworm infection by known anti-helminthic drugs such as mebendazole, pyrantel pomoute, and tetrachloroethylene, these measures have been found largely ineffective. The drugs are expensive and the need for repeated administration with each new infestation of hookworm make them impractical, especially in impoverished and remote areas. A vaccine, which would be administered only once, has long been hoped for, and if produced through recombinant DNA technology, would be relatively inexpensive.

It is also possible to apply certain preventive measures towards hookworm disease. Hookworm larvae live in the soil in moist humid areas. Eggs are generally deposited in areas used for defecation, and hookworm disease is usually contracted whenever the hatched larvae come in contact with an exposed skin surface, such as when people walk barefoot over the area. By wearing shoes or changing sanitation habits, much hookworm disease can be avoided.

There are, however, many other ways to contract hookworm, such as through fertilizing fields with nightsoil - the practice of fertilizing with human excrement. Thus, a vaccine would have inestimable and immediate value.

According to some estimates, hookworm disease is exceeded only by malnutrition and malaria in the production of human misery and economic loss. (Extracted from Genetic Engineering News, May 1985)

Research on animal genes

Three sets of chromosomes for IHN virus resistance

Tripling, rather than doubling, the number of chromosome sets in a trout-salmon hybrid makes the offspring resistant to a viral epizootic infection now threatening the U.S. trout hatcheries. But so far, the induced triploidy yields smaller fish.

Dr. James Parsons, a research geneticist for Clear Springs Trout Hatchery, Buhl, Idaho, reported these results in late June to the Second International Symposium on Genetics in Aquaculture. Initial outbreaks of the disease - infectious hematopoietic necrosis (IHN) - have caused losses to fish growers of 40 to 60 per cent.

To breed an IHN-resistant fish, Parsons and his co-workers took sperm from the coho, or silver, salmon which does not catch the disease, and crossed them with rainbow trout eggs. Twenty minutes after fertilization, the cells were heat-shocked at 27°C for 20 minutes, which caused their polar bodies - cells normally shed in the earliest stages of embryonic development - to persist, and add their 30 chromosomes to the 60-chromosome diploid complement of the hybrid, resulting in triploidy.

Almost 90 per cent of the trout-salmon triploid hybrids survived a challenge with IHN virus, as did all-coho diploid controls, but only 20 per cent of all-rainbow diploids - and triploids as well - survived the viral attack. Ordinary diploid hybrids produced by interspecies salmonid fish crosses apparently do not live or grow, Dr. James' triploid hybrids weighed only 13 grammes on average, against 20 to 25 for controls.

There is no vaccine yet against IHN, but Oregon State University virologists have already cloned the entire viral genome and identified its immunogenic proteins. The researchers hope to obtain expression in Escherichia coli this year. (Extracted from McGraw-Hill's Biotechnology Newswatch, 5 August 1985)

Livestock gene expression

Gene expression in livestock can be controlled by adding certain drugs to animal feed, according to T. Wagner of the Edison Animal Biotechnology Center of Ohio University. The gene for bovine growth hormone can be inserted into the cattle embryos but farmers want the gene to be active only during lactation. By combining the growth hormone gene with a segment of DNA that seems to be the recognition site for glucocorticosteroid hormones, researchers can switch on the gene by adding the hormones to feed. Ideally, only the cells concerned with lactation would have the bovine growth hormone gene switched on. (Extracted from New Scientist, 6 June 1985)

Possible coccidiosis vaccine

A characteristic protein of one species of the parasite that causes coccidiosis has been produced, making production of a vaccine possible, according to R. McCandliss of U.S. Department of Agriculture and researchers at Genex. The parasitic disease causes considerable losses to the poultry industry. When the newly synthesized protein is injected into chickens, the antigen stimulates the production of antibodies. The protozoa prevent efficient digestion in birds. Some coccidia strains produce an immune response in birds that prevents the pathogen from penetrating intestinal cells, while other strains provoke an immune response after the protozoa are already inside the cells. It is not clear which method of immunity is stimulated by the new antigen, which only gives partial protection against the disease. Researchers hope to modify the antigen to afford more complete protection. (Extracted from Science News, 25 May 1985)

Research on plant genes

DNA plant technology in oil palm venture

DNA Plant Technology (DNAP) has agreed in principle to form a venture with United Fruit Co. to develop and commercialize applications of techniques for large-scale cloning of enhanced varieties of oil palm trees. The venture, owned two thirds by United Fruit - which would fund initial research by DNAP - and one third by DNAP, would focus first on developing trees with higher yields of palm oil. The venture would own the technology and market cloned plantlets of enhanced varieties to growers. (Source: Chemical and Engineering News, 17 June 1985)

Good in the weed

Tobacco causes cancer, so it is ironic that tobacco leaves contain the chemical alpha-cembratriene-4.6 diol to protect them from mildew. It is also thought this chemical might also slow the growth of cancer tumours. Researchers at the Yokohama laboratory of the Japan Tobacco Corporation applied cancer-inducing chemicals to the backs of mice, waited for tumours to begin and then administered a cancer-promoting agent to the mice for 20 weeks. All the mice developed papillocarcinomas, but a group of them that had received a milligram of alpha-CBT immediately after receiving the cancer-inducer grew half as many papillocarcinomas and the tumours grew at half the rate.

Perhaps alpha-CBT could be easily extracted and used as a cancer prophylactic. Mass extraction could be accomplished with common organic solvents. Alpha-CBT's anti-tumour action is not all that potent; it is weaker, in fact, than that of vitamin A. Japan Tobacco hopes to improve the chemical's performance by tinkering with its molecular structure. (Extracted from The Economist, 28 September 1985)

New plant reproduction method

A method of reproducing plant cells in solution will be pilot-tested under an agreement between Fluor Corp. (Irvine, Calif.) and Bio-Foods, Inc. (Santa Ana, Calif.). The process has been lab-tested on a variety of vegetables and on coffee by Bio-Foods; one of the advantages of the technique is that growth is simpler and faster than cultivation of the whole plant. A means has been devised to remove live tissue from mature plants, sterilize it, and then grow it in a solution of nutrients and hormones. The solution is fed through conventional dialysis tubing (cellulose acetate membrane), while another nutrient solution is pumped along the outside, eventually permeating the tube. Growth occurs around the clock; and it is reported that cell volumes have been doubled in as little as 5 hours. When the cells emerge, they are recovered by centrifuge. Bio-Foods and Fluor plan to pilot the process. (Source: Chemical Engineering, 24 June 1985)

Electrical current may permit DNA to enter cells

High voltage electrical current may create pores in plant cell membranes to allow foreign DNA to enter the cells, according to researchers at the Boyce Thompson Institute for Plant Research (Ithaca, NY). Electrotransformation or electroporation could make it unnecessary to use plasmids to introduce foreign genes into plant cells. Currently, bacteria are used to deliver the plasmid to the plant cells, but then the bacteria must be destroyed. The procedure is also limited to plants that the bacteria can infect, which are mostly dicotyledons. Electroporation could allow any gene to be directly introduced into plant cells. Experiments conducted so far used wild carrot cells treated with enzymes to remove the cell wall. Short pulses of 40-V direct current were then applied to a mixture of plasmid molecules and the treated carrot cells. About 2 per cent of the carrot cells took up and expressed the foreign DNA, but without electroporation, only 0.0001 per cent takes up foreign DNA molecules. Cells containing the plasmid regenerated into plant embryos, but then grew

aberrantly because of the extra hormone encoded by the foreign genes. Electroporation could also be used to introduce RNA into plant protoplasts. (Extracted from Science News, 13 July 1985)

Herbicides the natural way

Two scientists in the US have developed a new type of herbicide that kills weeds but leaves crops such as barley, oats and wheat intact. The herbicide is based on an amino acid found in plants and hence is thought to be safe.

Mr. Constantin Rebeiz and Mr. Herbert Hopen worked out the details of the biosynthesis of chlorophyll in plants, and developed a herbicide which when sprayed onto plants overloads the synthetic pathway in such a way that the plant dies.

The herbicide is delta-aminolevulinic acid (ALA) plus a chemical activator. ALA forms compounds called tetrapyrroles. In the presence of sunlight these are processed into chlorophyll. Normally, a plant will make only enough tetrapyrroles it needs. If too many are made, the excess tetrapyrroles participate in a reaction where oxygen in one particular chemical state is converted to a highly reactive free radical. This free radical irreparably damages the plant cell wall, thus killing the plant eventually.

The scientists have taken advantage of this known plant bio-chemistry when they designed the herbicide. The ALA manufactures a large reservoir of tetrapyrroles in the plant which produces free radicals that kill the plant.

However, this effect is seen only in certain plants as different plants produce different tetrapyrroles, some of which do not take part in the reaction that produces free radicals. The scientists found out that wheat, oats and barley are not affected by the herbicide whereas several weeds are. The scientists are now looking for chemicals which will stimulate plants to produce excess amounts of ALA. (Source: Asia-Pacific Tech Monitor, May-June 1985)

Spicy flavours via cell culture

Botanists in Edinburgh are growing chilli pepper and saffron in the hope of producing their valuable flavours on a commercial scale. Professor Mike Yeoman and his colleagues are perfecting means for producing the flavours in cultured cell plants using natural plant cells and, for a change, without the aid of genetic engineering.

The first product they are developing is capsaicin, the hot component of chilli pepper. Capsaicin flavours snack foods such as crisps and is a multi-million dollar business. Capsaicin is produced only in mature fruit. The problem is to get cells that are normally undifferentiated to ripen in the right way and then to sustain production. Professor Yeoman has overcome it by first immobilizing the cells. He is at present working with chemical engineers at the University of Manchester Institute of Science and Technology to scale up the technique for commercial production.

Saffron is made from the stigma in the centre of the flower of a special crocus. It is used for colouring and flavouring food, especially rice. Each plant makes only one flower a year. Saffron has three ingredients: the bright yellow colouring (crocin), a bitter taste (picrocrocin) and a spicy taste (saffronal). Professor Yoeman is developing crocus cells that will make all three. The project has been backed by the venture capital company Prutech. (Source: Asia-Pacific Tech Monitor, May-June 1985)

Vaccine against cucumber mosaic virus

A method to protect vegetables from cucumber mosaic virus (CMV) by genetic manipulation of the virus to create a vaccine has been developed by the Hokkaido National Agriculture Experiment Station. The virus, which causes necrosis and mosaic disease in tomatoes, melons, pimentos and other crops, has five RNA components. A CMV strain of low virulence was obtained by replacing the fifth RNA component with a component showing very weak symptoms. Plants were then inoculated with the weak strain, and subsequent infection with highly virulent CMV had little effect on their growth. (Extracted from Japan Economic Journal, 2 April 1985)

New plant chromosome transfer technique

A new technique to transfer all or part of a chromosome into plant cells using a glass needle has been developed by R. J. Griesbach of the U.S. Department of Agriculture. Many important traits such as drought- or salt-tolerance require co-ordinated activity of large sets of genes that may be spread out throughout the plant's genetic material, although the

genes are often clustered on a chromosome. The rigid cell wall must first be removed and the central vacuole left intact. The new technique involves removing the vacuole by centrifuging the protoplast. (Extracted from Science News, 25 May 1985)

Pesticides from plant chemicals

Researchers are investigating plant chemicals to develop new pesticides. Traditional synthetic insecticides need to be replaced because of harmful side effects to higher organisms and insect resistance. Pesticide chemistry consultant M. B. Green, however, points out that most plants are resistant to most pests and diseases. Some plant chemicals repel insects or make the plant unappetizing, while other chemicals interfere with insect reproductive cycles. Some plant compounds can kill harmful bacteria or prevent fungal spores from germinating. Secondary plant metabolites used as defensive weapons include alkaloids, cyanogenic and triterpenoid glycosides, nonprotein amino acids, phenols and flavonoids. These natural chemicals are far superior to synthetic pesticides. Researchers at the Royal Botanic Gardens (Kew, England) have isolated polyhydroxyalkaloids from legumes that are potent inhibitors of specific sugar enzymes and toxic to insects. The compounds are actually sugar analogs in which the oxygen has been replaced by a nitrogen. One of these nitrogen sugars inhibits trehalase, a sugar enzyme important in insect physiology but not in mammalian physiology. Cotton plants that produce gossypol inhibit the growth of cotton bollworm and tobacco budworm. A mixture of gossypol and another volatile terpene produced by cotton plants may act synergistically. Scientists may also try to breed plant defence mechanisms into related species, rather than trying to produce synthetic pesticides. (Extracted from Chemical and Engineering News, 27 May 1985)

Why only some plants can fix nitrogen

Fundamental genetic research into the intimate biochemical relationship between leguminous plants and the bacteria that fix atmospheric nitrogen into the soil is revealing why attempts to establish similar links to benefit other crops have failed. It is also showing how genetic engineering might help such crops succeed in the future.

All living things need nitrogen, but few can make use of the molecular form of nitrogen that makes up nearly 80 per cent of our atmosphere. Fixing nitrogen is an ancient ability that may predate the first plants. Oxygen produced by photosynthesis poisons the nitrogen-fixing enzymes and so cannot be done by the plant itself. That rules out genetically engineering nitrogen fixation into plants. Instead, nitrates have to come from the soil, from fertiliser or from bacteria such as Rhizobium which form nodules on the plant's roots. In return the bacteria take the energy from the plant that they need to power the fixation process.

Only leguminous plants, such as peas and beans can support Rhizobium nodules and, until now, no one has understood why. All attempts to innoculate other plants with the bacteria failed. Now, geneticists at several centres, including the John Innes Institute in Norwich and Stanford University in California, have found the answer.

The John Innes researchers established a way of mutating genes at random, marking them in the process. They used jumping genes, transposable elements of DNA, which can interrupt the sequence of a gene so it can no longer function. This made it possible to prepare lots of different Rhizobium mutations and, on the ones that could no longer fix nitrogen, locate the disabled genes responsible.

Professor Sharon Long and colleagues at Stanford University made 6,000 such mutants of Rhizobium. Just two could no longer nodulate plants. The genes involved turned out to be not in the main strands of DNA but in a large circular plasmid. It contains over a million DNA base pairs. The function of much of it remains a mystery. The genes involved in the invasion and nodulation of plants are very close to those for the enzymes of nitrogen fixation itself. By making more mutations of specific bases in the DNA, Sharon Long could narrow the genes down still further and clone them in other bacteria. In fact, four genes are involved in nodulation, the nod genes.

The bacteria spend much of their time living free in the soil where the nod genes are not active. Somehow, they then invade leguminous plants, the nod genes are activated and nitrogen fixation begins. It is now clear that the genes are turned on not by something in the bacterium, but by a substance, secreted by the plant. Only legumes give out that signal. The bacterium responds to the signal by sending a signal back to the plant, switching on plant cell division and causing the plant to grow the nodules where the bacteria reside.

The relationship is far more complex and subtle than anyone expected and immediately explains why only a few plants can form the symbiosis. (Extracted from New Scientist, 22 August 1985)

Improving the nutritional value of seeds

In the early days of genetic engineering, there was much talk of using the new technology to improve the nutritional value of seeds. Now a molecular biologist has transferred, from one plant to another, a gene for a protein normally produced in quantity only in the seed - and most significantly make it behave as it should.

Many of the proteins in the seeds of cereal crops are deficient in the eight amino acids that people must take in their diet. But the genetic engineers came up against two major stumbling blocks to tinkering with all the genes. First, the genes that encode the storage proteins, especially in cereals, turned out to be numerous and packaged into complex families. None the less, researchers isolated a few genes and successfully introduced them into other plants (using the well-established T-DNA/Ti plasmid vector, which exploits the ability of a virus to carry genes into plant cells). Yet the results were disappointing: the genes were expressed - their proteins produced - at very low levels and in the leaves and stems as well as the seed.

A breakthrough by Timothy Hall of Texas A & M University gives new life to the campaign for perfect seeds. He has introduced a gene for one particular seed protein - phaseolin from the bean Phaseolus vulgaris - into tobacco cells growing in culture. This gene was expressed at very low levels in the tissues of the regenerated plants. But the seeds produced amazingly high levels of the protein, comparable to the amount produced from a gene for a typical storage protein in a normal plant. Hall is not yet sure how this feat was accomplished, but the answer will tell us much about how plants regulate the expression of their genes. (Extracted from New Scientist, 1 August 1985)

Harvest from bioplants

Genetic engineering of crop plants presents enormous difficulties and, in some cases, will lead to serious economic disadvantages. According to a recent study called "The potential impact of molecular biology and genetic engineering in agriculture 1982-2000", prepared by the biotechnology consulting firm Bernard Wolnak and Associates (Chicago). However, Zolt Harsanyi, director of Porton International (London), says that a "more cautious view" has been held by some in the industry for five years. Indeed, he observes that payoffs are "not around the corner".

Specifically, the Wolnak report concludes that:

- Plant tissue culture in conjunction with classic plant breeding has the most immediate promise to promote the genetic diversity that could lead to improvements in plants.

- Significant basic knowledge necessary to produce new varieties of crop plants effectively using recombinant-DNA techniques does not now exist.

- Even if a substantially improved, genetically engineered variety were currently available at the greenhouse level, years of field testing would be required before a seed could be sold. Published forecasts of annual growth rates of 57 per cent for the genetically engineered seed market from 1985 to 2000 are unfounded.

- Biological nitrogen fixation consumes enormous amounts of energy and would have to be fueled, for the most part, by metabolism of plant carbohydrates. The resulting yield loss is frequently of greater economic value than the reduced expense for nitrogen fertilizer.

- Historically, improving the nutritional quality of cereals has resulted in significant yield loss and, thus, economic loss has been greater than economic benefit. Genetic engineering is not likely to reverse this trend.

- Development of highly profitable crop agriculture programmes based on genetic engineering will be limited to the few companies that make the difficult transition from impressive research feats to successful marketing.

- Significant results from genetic engineering are not likely to be felt before the end of the century, if that soon. (Extracted from Chemical Week, 10 July 1985)

Research on yeast and fungus genes

Phillips Petroleum announces a new gene-splicing mechanism for yeasts

The technique for transferring and expressing genetic material is said to result in greater control over what types of proteins can be produced, and a higher yield per cell. Phillips Petroleum (Okla.) says it is "marrying" this new technology with its existing expertise in high-cell-density fermentation, which has been used experimentally to produce

single-cell protein. The result could be high-volume production of various animal- and human-healthcare products. The company also says that the use of yeasts differentiates the process from most other gene-splicing (which involves bacteria cells), and thus could have advantages in many applications. The technique was worked out on Pichia pastoris, an industrial yeast, using several genes that regulate the consumption of methanol feed. Researchers were able to locate specific genes in the yeast, define the mechanisms for transferring them, and confirm the expression of one of them, which produces an alcohol oxidase enzyme. (Extracted from Chemical Engineering, 24 June 1985)

By yeast, to yeast

Dr. D. P. Henry of the University of Queensland has developed the Bio-Wastech Process, a process for the conversion of organic wastes utilizing the yeast Candida ingens, on a pilot plant scale. Laboratory tests and the surface culture pilot plants operated to date have indicated that the Bio-Wastech process converts organic wastes into high protein yeast (comparable with soybean meal and meatmeal), ammonia, nitrogen and a stable sludge suitable for use as a low grade fertilizer. In the process, it destroys pathogenic bacteria such as Salmonella, Escherichia coli and the vibrio of cholera.

These indications are yet to be verified fully as further research and development goes on. The possible applications of the process are also to be investigated with the treatment of a wider variety of wastes. A successful adaptation of the process would treat each waste to remove its pollutional qualities and at the same time produce a high protein yeast concentrate suitable for feeding to animals such as pigs, poultry, fish or carnivorous pets, when mixed with cereal grain. Tests conducted so far using Candida ingens grown on pig wastes showed it to have useful potential as a fodder protein for monogastric animals when mixed with cereal grain. No defects were detected during these tests which could have been attributed to any toxicity from the yeast. Candida ingens has been found to be the specific nutrient for a Drosophilia (fruit fly). (Source: Asia-Pacific Tech Monitor, May-June 1985)

Cellulose, Repligen lignin deal

Cellulose Du Pin, the French pulp and paper firm, has engaged Repligen to develop an enzyme system for the degradation of lignin.

Based on enzymes produced in nature by the white-rot fungus, Phanerochaete chrysosporium, the lignin-degrading and modifying (LDM) system is to be integrated into the pulp processing operation with the aim of increasing yields and product quality and reducing energy consumption, corrosion and production costs.

Scientists at Repligen, the Cambridge, Massachusetts-based company, have isolated the family of LDM enzymes from the fungus and are cloning the genes prior to insertion into workhorse microbes.

The enzymes will help displace chlorine-based bleaches and may also have applications in the speciality chemical, adhesive, pharmaceutical and petrochemical areas, he predicts. (Extracted from European Chemical News, 3 June 1985)

Fungus degrades long-lived pollutants

A common white-rot fungus, Phanerochaete chrysosporium, which normally degrades lignin molecules in the environment, can also degrade man-made pollutants such as DDT, dioxins, and lindane. Biochemists at Michigan State University have shown in radiolabeling experiments that the fungus can degrade halogenated aromatic rings and dechlorinate alkyl chlorides to produce carbon dioxide. In cultures containing 1,250 picomoles of substrate, the fungus converts as much as 117 picomoles of benzo[a]pyrene and 191 picomoles of lindane (a polychlorinated pesticide, 1, 2, 3, 4, 5, 6-hexachlorocyclohexane) during a 30-day incubation period. The researchers propose adding P. chrysosporium cultures to biotreatment systems as an effective and ecological means of biological detoxification and disposal of long-lived halogenated chemical wastes. (Source: Chemical and Engineering News, 17 June 1985)

Ligninase utilization

A better way of making and utilizing the enzyme ligninase has been developed by researchers at the Institut National de la Recherche Agronomique (INRA), Paris using the micro-organism. Ligninase is valuable because at atmospheric pressure and ambient temperature it breaks down lignin in biomass, freeing cellulose for feedstock in fermentation reactions. Other routes, which employ caustic soda or ammonia, are claimed to be more expensive because the cellulose must be purified before it can be used. INRA researchers' patented strain of P. chrysosporium is claimed to produce 30 times more ligninase than results published by the USDA team. Moreover, INRA's enzyme is said to degrade lignin more

than 100 times faster than the USDA material. Enzyme efficiency has been improved, INRA claims, by adding equal weights of hydrogen peroxide and substrate during the degradation process. The enzyme itself generates H_2O_2 when it attacks the lignin. INRA is now scaling up enzyme production from the laboratory to a 30-litre fermentation unit. (Extracted from Chemical Engineering, 19 August 1985)

Research on viral genes

Triple-valent vaccine

By inserting antigenic foreign genes from three viral pathogens into the genome of a fourth virus, New York State Department of Health researchers are closer to creating a multiple-threat prophylactic in a single vaccine. Such a 'one shot' pharmaceutical is well suited to vaccination programmes in developing countries and in veterinary protocols where multiple innoculations are not always feasible or economical. Two years ago, Dr. E. Paoletti and co-workers at the Laboratory of Immunobiotechnology, Wadsworth Center for Laboratories and Research, Albany, engineered the vaccinia virus, which was the basis of the smallpox vaccine, to individually express antigens to strains of herpes, hepatitis and influenza virus. Now the group has spliced DNA segments from all three into a single vaccinia host.

Specifically, the group cloned DNA for the hepatitis B surface antigen, herpes simplex virus glycoprotein D and influenza virus hemagglutinin. As much as 20kb to 25kb of DNA can be inserted into vaccinia, they note. Rabbits innoculated with the live, polyvalent virus produced antibodies to all three cloned proteins, which were expressed in vivo under control of the vaccinia virus. So far, none of these triple-protected test animals has been challenged with any of the pathogens. The multiple, vaccinia-virus vaccine has many commercial advantages, Paoletti explains. "It's safe, stable, easy to freeze-dry and reconstitute"; now it can be made polyvalent. "But the real advantage may be in cattle and swine", he adds. There it could markedly bring down immunization costs. He envisions 'cassettes' of antigens cloned into vaccinia that are tailored to a particular geographic location. (Extracted from McGraw-Hill's Biotechnology Newswatch, 16 September 1985)

Research instrumentation

Extracellular matrix/serum-free method for superior tissue culture results

A method combining the use of extracellular matrix (ECM)-coated tissue culture dishes and serum-free medium which result in improved epithelial cell culturing are now available from International Bio-Technologies (IBT) Ltd., of Jerusalem, Israel. The serum-free medium serves to suppress overgrowth of the culture by stromal fibroblasts. ECM, a naturally produced substrate which closely resembles the basal lamina of the body, is an improved growing surface for a wide range of cells. Cells plated on ECM attach, flatten and migrate rapidly; exhibit higher plating and cloning efficiencies; proliferate faster and reach a higher saturation density. Epithelial cell culture is a key to cancer research and biopsy examination. This ECM/serum-free method has application in other fields such as endocrinology, for the growth and maintenance of hormone secreting cells; neurobiology, where the method supports attachment of glial and neuronal cells; and for biotechnology, for the production and secretion of biologically active materials. ECM coated tissue culture plastics are available from International Bio-Technologies Ltd., which supplies a range of tissue culture dishes, flasks, multiwell plates and coverslips, as well as a coating service for disposables. (Source: Company News Release, 7 July 1985)

General

Tokyo Institute test 'first working biochip'

A light-sensitive bacterial pigment coupled to a transistor is the "first working model" of a biochip, says its inventor, Prof. Isao Karube of the Tokyo Institute of Technology. Working with a team from Ajinomoto Co. Ltd., he used a bacterially secreted pigment, rhodopsin, to create a membrane-bound electrical switching device in a beaker.

When fully developed, computers based on ultra-small biochips - using rhodopsin as a storage element - would be theoretically capable of perhaps a billion-fold greater integration than the conventional semiconductor models. Karube chose an ion-sensitive field-effective transistor (FET) as the electrode, and vapour-deposited an insulation membrane of silicon nitride around it. Next, he laminated on a porous, acetyl-cellulose membrane as a matrix for the rhodopsin and a phospholipid, which he applied ultrasonically. Bound to the membrane, the 27,000-dalton rhodopsin pigment from a halophilic bacterium was connected to an amplifier and placed in a buffer solution along with a reference electrode. Each time during the next 12 hours that Karube turned on a nearby 300-watt light bulb, the proton-pumping pigment generated a membrane potential of 100 millivolts. (Extracted from McGraw-Hill's Biotechnology Newswatch, 2 September 1985)

D. APPLICATIONS

Pharmaceutical and medical applications

Monoclonal antibodies trials for lung cancer

The first clinical trials using monoclonal antibody and monoclonal antibody-drug conjugates against lung cancer are expected to begin soon at the Scripps Clinic & Research Foundation, La Jolla, California. The trial using monoclonal antibody alone has already been approved by the USFDA, and the antibody-drug conjugate trial is in the final stages of evaluation. Both trials will attempt to take advantage of the specificity of certain monoclonal antibodies for antigens produced by nonoat-cell cancer of the lung, the most common form of human lung cancer. The conjugate test will bind the monoclonal antibody to the anticancer drug methotrexate. (Extracted from Chemical & Engineering News, 3 June 1985)

Vaccine against venereal disease

A research programme at Stanford University in California has developed promising new vaccines against gonorrhoea and cystitis. They may, eventually, be administered to patients as inoculations of live, genetically engineered bacteria. Two separate projects used a common approach to find effective antigens for the bacteria that cause both afflictions. The best immunity might come from applying them directly to the vaginal surface in the patients. If they were carried by live genetically engineered bacteria, long-term immunity would result.

The bacteria that cause both diseases have in the past evaded the attack from the immune system. By the time antibodies have been made, the bacteria have altered the proteins on their surface. The antibodies fail to recognise the new antigens and so are useless. The only means of fighting the bacteria is with the help of antibiotics, but there are many strains of pathogenic bacteria and some of them are already resistant to antibodies. The research team looked on the surfaces of bacterial cells for proteins that do not change from generation to generation, and must therefore have important functions. They concentrated on the so-called pili, tiny hair-like structures which the bacteria use to hang onto the mucosa, the cells lining the genital tract in the case of gonorrhoea and the urinary tract in the case of cystitis.

Purified pili were injected into rabbits and the resulting antibodies used to screen for pili proteins that were common to all strains. In gonorrhoea they found a short peptide that was indeed conserved. They tested an antibody made against this peptide on human mucosal cells in tissue culture. It prevented gonococcal bacteria from binding to the cells.

Dr. G. Schoolnik, who runs both projects, describes the peptide, in situ, as cryptic, hidden from the immune system. Somehow the peptide, while still on the cell surface, is not recognised by the immune system. If the peptide is isolated from its bacterial camouflage, however, antibodies can be made against it, which can bind to the peptide even in situ.

Fortunately, the peptide is short; the "business" end being only about 15 amino acids. The peptide can therefore be synthesised cheaply in large quantities. That is good news for people in West Africa and parts of Southeast Asia where gonorrhoea is becoming an epidemic. In parts of Africa, a quarter of all women are infertile by the age of 25 because of the disease. In the West, too, a vaccine is needed, especially for adolescent girls in whom the most serious complications, such as pelvic inflammation, can arise.

The new vaccine, administered as an injection, is about to be tested. Since there are no animal models for gonorrhoea, testing will have to move straight from cell culture to humans. Once toxicity has been ruled out, healthy male volunteers will be vaccinated and then exposed to infection.

Schoolnik's work on cystitis has been supported by the Cetus Corporation. In that, the binding protein in the pili is larger and is manufactured in genetically engineered bacteria. That is not difficult because the disease is itself caused by a pathogenic strain of the bacterium beloved by genetic engineers, Escherichia coli. The protein is made in large amounts on its new host's cell surface.

By raising antibodies to the protein with which the bacteria bind to urinary tract cells, it should prevent invasion of both kidneys and bladder. In tests, it protected 90 per cent of a strain of mice (BALB/c) particularly sensitive to the disease.

Two groups might be shortlisted for vaccination: women of reproductive age who have had a history of infections; and young girls at greatest risk.

The question is, how to make immunity last, because infections can recur in nature. This is what has led Schoolnik to contemplate using the live, genetically engineered bacteria that produce the vaccine to guard the entrance to the urinary tract.

Trials with live bacteria could begin by the end of the decade. They are certain to arouse controversy, however. Equipped with the binding protein, the new bacteria themselves might be pathogenic. Bacteria are known to swap genes between strains, so others might become able to bind to the urinary tract cells. To solve this, the gene might be coupled with a sort of genetic time bomb that would destroy it after a number of generations. (Source: New Scientist, 19 September 1985)

Whooping cough vaccine developed

A safer whooping cough vaccine is due to undergo clinical trials in the UK next year. The vaccine, developed by scientists at the Centre for Applied Microbiology and Research at Porton Down, Wiltshire, consists of a number of purified antigens extracted from the bacterium Bordetella pertussis. Several antigens have been incorporated into the vaccine as researchers believe more than one is involved in conferring immunity to susceptible individuals. Bacterial toxins have been removed.

The new vaccine is similar to a Japanese whooping cough vaccine which has been on the market in Japan since 1981. However, the Japanese vaccine is apparently less well defined chemically than the UK version. (Extracted from Manufacturing Chemist, May 1985)

Biotech pregnancy test

Unilever's newly-created diagnostics company, Unipath, has launched a monoclonal antibody-based pregnancy testing kit which is claimed to be 99 per cent reliable. The kit, called Clearblue, claims to give an unequivocal result on the first day of the woman's expected period, and the whole test takes 30 minutes to complete.

The test can be sold over the counter and comprises a dipstick, the tip of which contains a monoclonal antibody for human chorionic gonadotrophin (HCG), and a plastic tray containing three wells of reagents. A blue colour is produced if levels of HCG are above 50m iu/ml, indicating that the result is positive. Each test kit contains two tests so that the test can be repeated. (Extracted from Manufacturing Chemist, July 1985)

Boots-Celltech fertility test

A human female fertility test created by Boots-Celltech is to receive financial backing from LRC International to see it through development and into marketing. Based on technology involving monoclonal antibodies, the test will be used to assist couples who are having trouble in conceiving, and eventually, it is hoped, as a method of contraception.

Two versions are likely to appear. The first, for hospital use, should be available next year, but the real breakthrough is not expected for two or three years when a model will be launched for direct sale to consumers. The tests work by assaying urine samples, detecting the preovulation rise in oestrogen and the postovulation rise in progesterone levels, thus indicating a woman's fertile days. (Extracted from Manufacturing Chemist, July 1985)

Human protein

A British brewery, Bass, is investing considerable sums of money into a process for converting yeast to produce human proteins, using genetic engineering. The priority is human albumin, a staple standby of every emergency ward for treating shock and severe burns. In addition other more valuable blood factors, such as factor VIII, the treatment for haemophilia, will soon be produced through genetic engineering. The Bass process, described in a patent issued last July, aims to turn a waste problem into a valuable asset by using the yeast to manufacture pharmaceuticals. If the process proves economic, Bass hopes other breweries will use the technology under licence. The company has set up a subsidiary, Delta Biotechnology with another company, Cavendish Technology Partnerships, to further exploit its process.

The Bass scientists inserted a gene coding for human albumin into ordinary brewer's yeast, Saccharomyces cerevisae, used in their wort. The yeast cells were thus primed to do two jobs: make beer, and produce human proteins. A method was found to keep the albumin gene "silent" during brewing so that the yeast would not begin making proteins until separation from the wort.

Many technical hurdles remain before what is essentially a laboratory process becomes commercially viable. For example, the company is developing normal ways for separating the small quantities of albumin from the vast amount of yeast cells debris, and nutrient liquor. Then tests will have to be run to ensure the albumin is a functional molecule. Clearance as a pharmaceutical could take some years. (Extracted from Financial Times, 11 July 1985)

Cambridge consultants offer engineering skills for biotechnologists

A new biophysics group has been set up by Cambridge Consultants Ltd. (CCL) to service the biotechnology sector. Led by Dr. Brian Moon, a colloid scientist, the multi-disciplinary team has expertise in microbiology and biochemistry, biophysics and bioanalysis, colloid science, optical monitoring, filtration technology, transducer design, sterile engineering and cell immobilisation. Other technologies available within CCL include fibre optic and microelectronic sensing, signal processing, data storage and handling, systems engineering and process control.

Among the other senior staff in the new group are Dr. Andrew McKay, a biochemical engineer who has specialised in the design of equipment for biological processing, and Rosemary Albinson, a biophysicist who has expertise in molecular biology and forensic analysis. Services offered range from market research through to the development of pre-production prototype equipment. Details from: Dr. Brian Moon or Dr. Andrew McKay, Cambridge Consultants Ltd., Science Park, Milton Road, Cambridge CB4 4DW or on (0223) 358855. Telex: 81481 (CCL G). (Source: Biotechnology Bulletin, Vol. 4, No. 7, August 1985)

Prostate cancer tests

Cetus Corp. now has available two diagnostic tests it has developed for prostate cancer, both based on monoclonal antibody technology. The Cetus EPICHROME PAP (prostatic acid phosphatase) test has received marketing clearance from the US Food and Drug Administration (FDA), while the company's EPICHROME PA (prostate-specific antigen) test is available for sale for research use.

Cetus has also introduced its PRO/GROUP system, an automated liquid handling instrument for research use in clinical reference laboratories and hospital laboratories. The system is under development for a FDA submission covering automated clinical applications such as blood grouping and diagnostic tests for diseases such as AIDS and hepatitis. The system automates a broad range of manual pipetting tasks required in ELISA and other immunoassay procedures. Details from: Cetus Corp., 1400 Fifty-Third Street, Emeryville, CA 94608, USA or on (415) 420 3300. (Extracted from Biotechnology Bulletin, Vol. 4, No. 7, August 1985)

Water-in-oil preservation process for living cells

The process of 'undercooling', now being offered by Pafra Ltd., permits the long-term storage - without freezing - of a variety of plant and animal tissues, from eggs and sperm used in test-tube baby operations through to tissues from endangered tropical plants. It is also seen as appropriate for biotechnology companies wishing to store bacteria, yeast and other micro-organisms.

Developed in the 1970s by Dr. Felix Franks, a senior research fellow at Cambridge University and special professor of biophysics at Nottingham University, the invention grew out of research on the freezing behaviour of water in living cells. Existing freeze-storage methods often damage stored cells and tissues, even when cryoprotectants are added to minimise such damage. Conventional freezing can result in high losses of material, up to 99 per cent in the case of some yeast cultures.

Standard cryopreservation involves storing biological material in liquid nitrogen, thereby slowing biochemical activity, but the materials which cannot be stored in this way include human liver cells. In addition, the chemical protectants used to cut freezing damage, including dimethyl sulphoxide, can also be toxic to cells. Besides liquid nitrogen storage facilities may be beyond the reach of potential Third World users.

The Franks method, on the other hand, requires only a domestic freezer, a little paraffin oil, water, and a common piece of laboratory equipment, similar to a household blender - in which cells are kept in a supercooled state in a water-in-oil suspension. The process results from the discovery, some fifteen years ago, that if small droplets are dispersed in water it is possible to supercool the resulting emulsion to well below its usual freezing temperature of 0°C. In fact samples can be undercooled to as low as -40°C before they freeze spontaneously.

The Franks' patented technique starts with the dispersal of cultured cells in a small amount of inert oil, together with a small amount of their growth medium to maintain viability, and placing the mixture in a laboratory blender for a few minutes. The resulting glutinous mixture is then simply transferred to plastic tubes for storage in a freezer, where the oil sets into a jelly. With this method, yeast cells can easily be undercooled to below -20°C for at least 16 weeks, with no detectable loss of viability. Details from: Max Kochmann, managing director, Pafra Ltd, Bentalls, Basildon, Essex SS14 3BU or on

0268 280606. Telex 995241 PAFRA G. Or Dr. Felix Franks, now a director of Pafra Ltd, on 0223 862921. (Extracted from Biotechnology Bulletin, Vol. 4, No. 7, August 1985)

FDA approval for digoxin and T4 tests

A cloned enzyme donor immunoassay (CEDIA) for heart-drug monitoring and thyroid function became the first recombinant-DNA clinical tests to gain US Food and Drug Administration approval. Later this year, the Microgenics Corp. (Calif.) will begin selling the genetically engineered tests for monitoring digoxin, a congestive-heart-failure drug, and for total T4, an indicator of thyroid dysfunction, particularly in newborns.

In the proprietary CEDIA technology, beta-galactosidase DNA is cut in two and each half cloned into separate Escherichia coli cultures. In the digoxin test, the drug is covalently attached to one half of the enzyme. When the two halves are mixed they spontaneously recombine. A digoxin antibody and a sample of the patient's blood complete the cocktail. The antibody complexes with serum digoxin, but it also attaches to the digoxin linked to the enzyme half, and thereby renders it incapable of recombining with its cloned peptide partner. Therefore, drug concentration is directly proportional to the amount of beta-galactosidase created, as monitored by hydrolysis of the substrate, O-nitrophenyl-beta-D-galactopyranoside. (Extracted from McGraw-Hill's Biotechnology Newswatch, 19 August 1985)

Du Pont may market tests for AIDS and hepatitis

A joint agreement to develop and market new diagnostic blood tests for several forms of hepatitis and acquired immune deficiency syndrome (AIDS) has been signed by Centocor (Malvern, Pa.) and Du Pont. Under the agreement, the companies will jointly engage in product research and development, and Du Pont will market any products that emerge from the effort. Food and Drug Administration (FDA) approval already has been received for marketing Centocor's hepatitis B immunoassays, which are said to be the only blood tests based on monoclonal antibody technology. Centocor's AIDS virus antibody-detection test is said to be the nation's first assay based on recombinant-DNA technology. FDA approval of the product is expected later this year. (Source: Chemical Week, 10 July 1985)

Joint venture to detect dental disease

BioTechnica International has set up a subsidiary to develop and sell diagnostics to detect dental disease. The venture, BioTechnica Diagnostics (BTD), is based upon a collaborative research agreement with Forsyth Dental Center in Boston, Massachusetts.

The two parties will jointly develop ther initial tests for infectious diseases of the mouth. (Extracted from European Chemical News, 3 June 1985)

Livestock applications

New method makes vaccines without disease organism

A new vaccine method has been perfected that permits effective vaccines to be mass produced without using the disease organism itself, or even knowing the specific antigen. Heinz Kohler, MD, a research professor of microbiology at the State University of New York at Buffalo and director of Roswell Park Memorial Institute's Department of Molecular Immunology, has produced an effective streptococcus vaccine for animals by using monoclonal antibodies.

Certain requirements have limited the application of the traditional vaccine method, which uses the disease organism itself and requires the isolation, purification and extraction of the disease organism or its antigen. Difficulties with the normal process for vaccines include the question of technology, since viruses, for example, require very specific conditions such as live cells, and the question of price, because purifying a virus becomes very expensive and impractical for mass production.

The new vaccine method will not replace vaccine already produced economically and safely, but will apply in certain situations where vaccines are not currently possible or feasible. The vaccines produced by this new method will be much safer than inactivated or attenuated viruses that carry risk factors, says Dr. Kohler.

The most promising application for the new vaccine method is for various types of cancer, while another valuable application will be for infant disease . With Dr. Kohler's experiment, the antigen used was a virulent strain of streptococcus pneumonia, and the result was a vaccine that proved effective against the bacteria in mice. The next step is to develop an experimental cancer vaccine for mice and then for humans. (Source: Canadian Research, March 1985)

Mutant blowfly maggots dropped on Australian island

A small island off the South Australian coast will be bombarded with more than 60 million genetically engineered blowfly maggots over the next seven months. The experiment is part of an ambitious project by Australian scientists to eradicate sheep blowflies.

The experiment involves the entomologists flying up to six tonnes of mutant male maggots to Flinders Island, 35 kilometres off the South Australian coast. The maggots have all been genetically altered so that females mating with the adult flies will produce abnormal offspring, many of which will be sterile or blind. These traits will be handed down, conferring genetic death on subsequent offspring.

Blowflies have a breeding cycle of between three and seven weeks and the team should know within three to four months if the experiment at Flinders Island has been a success. The original mutant flies were produced by radiation with gamma rays. These were then bred to select particular characteristics. Repeated crossing with field flies then obtained the desired mutations and ensured that the flies can compete in the wild. (Extracted from New Scientist, 12 September 1985)

Progesterone tests for cattle

The oestral cycle in cattle, as in all mammals, is controlled by hormones, one of which, progesterone, is secreted in the milk of the cow. If its presence and concentration can be detected swiftly and accurately, it can notify the farmer, as well as the uterus, of imminent ovulation. The thing to look for is the exceptionally low level of progesterone that occurs just before the onset of oestrus, when a cow becomes fertile. In Britain, the Milk Marketing Board provides results of a progesterone test in about four days. It is designed to tell if the cow is pregnant. If it is not, the news may be too late, because the crucial time may have passed.

Three tests are now on the British and Irish markets to change this. The three now available are all varieties of immuno-assay, and are made possible by the development of monoclonal antibodies. They involve a plastic tray of wells lined with antibodies which are designed to attract progesterone molecules. The milk is put into them, and so is a mixture of artificial progesterone bound to an enzyme. The natural and artificial progesterones compete for the attention of the antibodies, a competition decided entirely by force of numbers. After the wells are rinsed, the degree of enzyme activity is seen as a colour change. A strong colour change reveals that the artificial progesterone has won the competition, meaning there is little progesterone in the milk. (Extracted from The Economist, 28 September 1985)

Agricultural applications

Plants that provide a protein-rich diet

Kawal, a protein-rich food made from a wild African plant could replace expensive food imports from industrialized countries as it contains all the essential amino acids needed by people. It is already eaten by many people in the Sudan.

This conclusion is the result of a joint project set up by Khartoum University and Queens University in Belfast. Hamid Dirar, David Harper and Martin Collins investigated the food value of kawal, and found that its amino acid content was enhanced by the traditional way in which it is made. Kawal is made by fermenting the leaves of a wild legume, Cassia obtusifolia. The leaves are pounded to a paste, placed in an earthenware jar, covered with sorghum leaves and buried in a cool, shaded place. Every three days, the jar is dug up and the contents mixed by hand. After about two weeks, the contents are removed, moulded into small balls and dried in the sun. The finished product is usually cooked in spicy stews with onion and okra.

It is during the fermentation and sun drying that the concentrations of some of the amino acids increases. A particular value of kawal is that it contains sulphurous amino acids, which are normally obtained from either fish or meat.

The traditional, cheap way of making kawal is well suited to tropical Africa. (Source: New Scientist, 8 August 1985)

Large-scale automated plant cloning systems

Arthur D. Little and DNA Plant Technology will jointly develop commercial applications for large-scale, automated plant cloning systems that could provide commercial quantities of identical copies of economically important crop plants. A prototype bioreactor system using

spin-filter technology has been developed. The firms are now negotiating with major corporations on development of customized systems for specific crops. (Extracted from Chemical Week, 10 April 1985)

Ethiopian wheat genes and famine

Many of the high-yielding strains of wheat and barley depend on genes which came originally from wild grasses of the Ethiopian highlands. The world depends on them for food. Plant breeders have turned wheat, barley, rice and maize into super-producers which have made famine a thing of the past for most people. But for the peasant people of Ethiopia itself, who grow and eat different kinds of grain, the crop-breeding revolution has passed by.

Ethiopians eat a grain called t'ef, which is admirably suited to their land and climate. If the advantages of t'ef were exploited by modern agricultural science, some botanists think it could boost food production not only in Ethiopia, but throughout the drought-prone semi-arid world. Up till now, however, t'ef has been virtually ignored by Western scientists. They even classified it into the wrong genus when they discovered it late in the last century. Even now, t'ef's agricultural potential is known largely through the work of one British scientist, Glyn Jones of the University of London.

T'ef needs less rain than maize or sorghum, and can be grown in higher and colder regions than either. It also needs less rain than the usual high-altitude crops, wheat and barley. At the same time, t'ef withstands the occasional floods that characterize the feast-or-famine pattern of Ethiopian rainfall. It can germinate and grow on black soils that lack oxygen, the sort that would result from waterlogging. T'ef straw is soft, and good for animal fodder. Its pinhead-sized grains are nutritious for humans, too. Ethiopians grind them and make a paste, which they ferment to make a flat bread called injera. This Jones says, "is delicious". The unusual technique of bread-making, he says, is one reason Westerners never investigated the grain. T'ef evolved in the widely varying conditions of the Ethiopians highlands, and for that reason the hills are full of t'ef varieties. "There are over 1,000 lines at the Plant Genetic Resources Centre in Addis Ababa," says Jones. "Its genetic diversity makes it a strong candidate for improvement by breeding."

There are technical difficulties with breeding. One difficulty discovered by Tareke Berehe, an Ethiopian scientist who worked with Jones, is that t'ef blooms only for 15 minutes in the early morning, immediately after sunrise. "A good worker can cross-pollinate about 10 plants before they all close up again", says Jones. This slows breeding work.

On the other hand, each crossed plant produces 5,000 grains, each with different combinations of the parent genes, which can speed selection. Wheat, by comparison, produces only about 100 different grains.

What has chiefly slowed breeding has been a near-total lack of funding and interest. Berehe and an Iranian student were paid by the UN's Food and Agricultural Organisation (FAO). Jones has been unable to get any other funding.

T'ef would fit the requirements of most relief agencies that say they want to fund long-term agricultural development in Ethiopia. It has always been used by upland farmers as an insurance crop. "Subsistence farmers put a bit of t'ef in on the most marginal land in case the rains, and all the other crops, fail," says Jones. "There are varieties that will mature in two months, on very little moisture."

The trouble in developing the crop's full potential is that what little selection of t'ef strains has been done by Ethiopian agronomists has been done largely on state farms. These are in the lowlands, and generally on the best land. The strains they have selected tend to be high producers, but slower to ripen, and unsuited to severe highland conditions.

This could turn into tragedy for upland farmers. "T'ef is the only domestic grain that free-threshes, that is, drops its own seeds on the ground," says Jones. "Some always springs up after a harvest." But with two years of drought now ending as the summer rains fall, farmers are being given different seed. Agencies are sending in wheat and barley seed, while Ethiopian state farms favour high-yielding t'ef varieties.

Seyfu Ketema at Addis Ababa University's experimental station at Debre Zeit, has started breeding t'ef. So far this has produced high-yielding strains whose heads are so heavy that the plants fall over in the field. This was a problem with early improved wheat, too, until short-stemmed varieties were fou[illegible]. Even without improvement, t'ef yields almost as much grain per hectare as improved wh[illegible]s in Ethiopia. At Debre Zeit, some yields have been increased tenfold.

Areas of extremely high genetic diversity were named Vavilov areas after the Russian scientist who discovered them. Ethiopia is a Vavilov area for as many as 32 cultivated species, according to the Plant Genetic Resources Centre in Addis Ababa. Among them are wheat and barley.

The centre also says that Ethiopia's plant diversity is threatened by the introduction of high-yielding strains of crops produced by plant breeders, by deforestation, drought, and by "the expansion of state farms". The centre works to preserve irreplaceable plant genes by collecting them, storing them in Addis, and sending them abroad.

Ethiopia is a Vavilov centre, one of a dozen spots in the world where plants are unusually diverse. This means two things. The first is that virtually the entire genetic repertoire available to crops that evolved in Ethiopia is still to be found there. These genes are necessary for plant breeders to meet the ever-changing threat of pests and disease. The second is that lots of other strange plants grow there too, whose usefulness may be known to the locals, but whose potential value for people elsewhere in the world has never been investigated.

Crops whose genes still lurk in Ethiopia include:

Peas: There are subspecies of peas in Ethiopia that are found nowhere else, and literally hundreds of strange varieties. Peas are an important legume, whose range could be extended, especially to arid zones, by cross-breeding with Ethiopian varieties.

The Lablab bean is another important legume, grown widely in India. Its centre of genetic diversity, too, is Ethiopia.

Guizotia: This relative of the daisy yields a highly prized drying oil of the sort used in paint. It is grown largely in India, where its value as a cash crop depends on Ethiopian genes.

Ethiopian cabbage and castor beans are other commercial oil seeds with their centres of diversity in Ethiopia.

Coffee evolved in Ethiopia's Kefa province. Mohammed is said to have brought it back from his sojourn there in exile, and in return to have prohibited his followers from attacking the country, which remained a Christian enclave. This was a rather better return for its gift than Ethiopia gets now from the world's coffee industry.

Crops whose potential is still unknown include:

Ensete, or the false banana, which yields the "banana seeds" sold as indoor plants in Britain. In Ethiopia it produces a tuber which peasants use as a survival food. Its yield per hectare is very high.

Yheb nuts grow in the disputed Ogaden region near Somalia. They tolerate semi-desert conditions and can be grazed by goats, but still yield a highly nutritious nut. Some experimental work on yheb is starting in Kenya. (Extracted from New Scientist, 8 August 1985.)

Natural pesticides

The US government is about to approve the use of a pesticide extracted from a tree native to India whose farmers have been exploiting the properties of the neem tree (Azadirachta indica) for thousands of years.

In India, about 14 million trees, often planted along roadsides, produce fruit, wood and leaves - all of which have special uses to villages.

Parts of the tree have strong insecticidal properties. Farmers have been using these properties for centuries against the insects and nematodes that thrive in India's climate. Some simply mix neem leaves with grain in storage. Others make an extract by crushing the fruit in water, to spray on crops in the fields. The cake left behind after crushing also has uses; it can be ploughed as mulch into land, where it acts as a fertiliser as well as controlling nematodes in the soil.

An ideal natural pesticide must have a number of special properties. It must come from a perennial plant, which should be easy to grow, not be destroyed by harvesting and should preferably have other uses, too. Most important, it should be safe and economic, which means that the plant must not consume pesticides, fertiliser or water from irrigation schemes, and the neem tree seems to meet all these criteria. It seems to grow anywhere except in waterlogged soils. The Government of the Philippines has planted 40,000 neem trees in one project.

In the US, researchers at the government's Agricultural Research Service have been studying neem and its properties for the past five years. Industry is already interested. According to Martin Jacobson, chief of the department's Biologically Active Natural Products Laboratory, the Environmental Protection Agency is about to approve one product for protecting non-food crops such as flowers.

The research that leads to approval should provide the best data yet on neem's toxicity to humans.

At least 2,000 plants are known to have pesticidal properties, yet only two, pyrethrum and tobacco, are so far exploited commercially on a large scale. (Extracted from New Scientist, 6 June 1985)

Morels via genetic engineering

The possible genetic engineering of morels is another topic of interest. Because fruiting bodies of these ascomycetes had not been produced in the laboratory until very recently, they have never been manufactured commercially or subjected to any kind of breeding. After the discovery by K. Esser and his colleagues of extrachromosomal genetic elements in fungi, F. Meinhart of the Ruhr-Universität Bochum, F.R.G., decided to search for similar DNA fragments in edible mushrooms.

One species of morel, Morchella esculeuta, yielded no such elements, but Meinhart has found linear extrachromosomal DNA in 8 out of 13 different strains of Morchella conica. Restriction analysis and electron microscopy of the two plasmids discovered in one strain have revealed that their sizes are six and eight kilo-base pairs. The 6 kbp element carries inverted repeats of about 0.7 kbp at both ends. As the plasmids appear to be autoreplicative, they might represent a valuable tool for the genetic manipulation of these economically important fungi. (Extracted from Bio/Technology, November 1984)

Food production and processing

Cellulose enzyme

Genencor has introduced a cellulase enzyme that it claims is the most cost effective currently available. It is said to be characterised by its ability to hydrolyse or degrade cellulosic materials from a wide variety of sources. Depending on enzyme dosage and reaction conditions, the extent of hydrolysis can be tailored as necessary. Developed for applications requiring complete breakdown of cellulose to fermentable sugars, the Cellulase is said to contain much higher levels of the critical enzyme activities said to be normally in short supply in conventional products. It is also claimed to be extremely effective if only partial cellulase breakdown is required and can result in major process or yield improvements. (Extracted from Manufacturing Chemist, August 1985)

Aflatoxins detection kit

Biotech Research Laboratories will soon begin field trials of the first enzyme immunoassay kit for detecting aflatoxins in food and individuals. Aflatoxins are potent carcinogens, and their contamination of milk, grains and peanuts is a potentially serious public health hazard. Current testing methods using thin-layer chromatography are subjective and tedious. Biotech's kit features a competitive inhibition enzyme immunoassay with an aflatoxin-specific monoclonal antibody. (Extracted from Chemical Week, 17 April 1985)

Mycoprotein scale-up

Britain's Imperial Chemical Industries and Rank Hovis are to scale up the production of their mycoprotein following its first commercial success. Production is to be increased from the 50 ton/year pilot scale to 1,000 ton/year at ICI's Billingham facility.

The product, obtained from the fungus Fusarium graminearum, was originally developed by the food group RHM in the 1970s, and following the formation of the company's joint venture with ICI, is being sold in savoury pies by a major UK supermarket chain. It is expected to be in other snack products later this year. A major selling point is the absence of animal fats.

The fermentation process is being scaled up by ICI engineers, using the lessons learned during the costly development of ICI's single cell protein, Pruteen. The 1,000 ton/year unit will provide technical information necessary for further scale-up to 20 times this capacity. (Extracted from European Chemican News, 3 June 1985)

Low-calorie synthetic sweetener

Another low-calorie synthetic sweetner has been developed that its creators say not only tastes like sugar - with no bitterness or aftertaste - but also does not promote tooth decay. Chemically similar to the widely used synthetic sweetner aspartame, this new compound appears to overcome a major drawback associated with aspartame - its short shelf life in liquids such as soft drinks.

The result of a National Institute of Dental Research programme to identify promising new non-cavity-producing sweetners, it must still undergo years of further toxicity and development testing before any decision on its commercial potential is resolved.

For convenience, the new sweetner, DL-amino malonyl-D-alanine isopropylester, has been designated RTI-001.

So far 001 has gotten a clean bill of health from the Ames bacterial test (to gauge mutagenicity, and hence carcinogenicity), and several mouse toxicity assays. Moreover, it does not contain phenylalanine. 001's major advantage over aspartame is likely to be its stability in liquids. Tests showed that within 36 days at 77°F, half of the aspartame that had been dissolved in water with an acidity characteristic of soft drinks had broken down. (Extracted from Science News, Vol. 127, 27 April 1985)

Chemical applications

Biology moves into the photographic world

Engineers working for Canon in Japan have come up with a new idea for recording photographic images. British patent application 2 153 544 reveals that Canon can now take pictures on a film which is coated with enzymes, rather than with photo-sensitive silver salts.

A base film of plastics is coated with amylase in a collagen carrier. The enzyme covers a layer of starch and organic copper phthalocyanine.

The film is exposed to light in the usual way. This leads to the creation of an image because light lowers the enzyme's activity. Activity remains high in the regions not exposed to light. To develop the image, the film is dipped in water. This initiates the decomposition of starch by the enzyme in those areas where it is still active.

As the starch decomposes, it produces glucose, which carries off the copper phthalocyanine. The copper remains in the irradiated regions where the enzyme was rendered inactive. The film is dried for 15 minutes to stop the enzyme decomposing the starch further. The result is a black-and-white image, which is similar to that on conventional silver film. (Extracted from New Scientist, 26 September 1985)

Energy and environmental applications

Potential ecological risk by modified organisms

Many ecologists believe that scientists involved in genetic manipulation of crops and microorganisms are not adequately considering potential ecological risks posed by the modified organisms, and even if they did, the ecologists are unable to predict the fate of a given organism in the environment. Ecologist F.E. Sharples of Oak Ridge National Laboratory says that the introduction of exotic species into new environments could eventually serve as a model for predicting what will happen to genetically modified organisms, but much more research needs to be done. Many of the traits to be altered, such as frost or salt tolerance or the production of an insecticide, are ecologically very significant. The altered organisms are also likely to be released in disturbed ecosystems, where natural controls may be lacking. S.J. Risch of the University of California (Berkeley) points out that some arguments favouring environmental release are inconsistent. For example, researchers say the altered genes are of limited significance, but that the alterations will make the organisms unable to survive in the wild. He also points to the potential for genetic exchange between crop plants and weeds, which may be closely related. Transfer of herbicide resistance (for example) from the crop to the weed could have far-reaching consequences. B. Healy of the US Office of Science & Technology Policy says appropriate regulation must be decided on a case-by-case basis, but warns that overregulation could hurt the US in the world biotechnology race. A. Robbins of the US House Committee on Energy & Commerce Staff, however, says that new regulations are needed to make sure that the lure of big profits does not obscure safety considerations. Nonetheless, biotechnology is thought to hold the key to solving many of the world's problems in medicine, agriculture and energy, and should not be hindered by overregulation. (Extracted from Chemical & Engineering News, 17 June 1985)

Method uses enzyme to detect pesticides

A method for detecting the presence of organophosphate and carbamate pesticides has been developed at Midwest Research Institute, Kansas City, Mo. The method makes use of the enzyme cholinesterase to produce a colour change on filter pads in a detector called an enzyme ticket. The ticket consists of a polyethylene support with a filter pad attached at each end, one pad containing the immobilized enzyme and the second a chromophoric substrate. Dipping the enzyme pad into water suspected of containing a pesticide activates the system. The support is folded to bring the pads into contact, the uninhibited enzyme reacting with the chromophoric substrate to produce a blue colour. A white disk means the water is contaminated. The enzyme ticket is specific for cholinesterase inhibitors and is the only quick and inexpensive test available that can be used in the field without instrumentation. Sensitivity of the ticket is in the 0.1 to 10 ppm range for the most widely used organophosphates and carbamates. (Source: Chemical & Engineering News, 8 July 1985)

Unnamed peptide used by plants to bind with metals

A peptide that could be used to recover toxic metals from soil and effluent has been discovered by scientists at Los Alamos National Laboratory (Los Alamos, N.M.). Produced naturally by the monkey flower and jimson weed, commonly found in the US, the unnamed peptide is used by those plants to bind with metals, thus avoiding other biochemical reactions that might harm the plants.

The compound, which has affinity for zinc, cadmium, mercury and copper, is apparently manufactured when a dormant gene is activated by the presence of a toxic metal. This boosts production of an existing enzyme that stimulates peptide output. In tests with cultures of jimson weed, the peptide was found to combine with more that 80 per cent of the cadmium that entered the cells. Tests with whole monkey flower plants showed that it could tolerate ten times as much copper (in a hydroponic solution) as other plants of the same species. Scientists are now trying to discover the compound's binding mechanism and how the gene is regulated. (Extracted from Chemical Engineering, 22 July 1985)

New microbial decontamination process

A microbial process for removing pentachlorophenol (PCP) from soil has been developed by Bio-Clean, Inc. (Bloomington, Minn.). The three-day, batch method is said to reduce the level of PCP and related polyaromatic hydrocarbons in soil from about 500 ppm to less than 1 ppm. Costs run about $140 to $180 per ton, depending on the level of contamination.

Used primarily as a preservative for exterior wood products, PCPs have been difficult to remove bacterially from contaminated soil because crude oil used in the application of the compound clings to soil particles, and so prevents bacteria from reaching the PCP. To solve the problem, Bio-Clean excavates the contaminated soil and places it in a digester with caustic and water. The slurry, which has a pH of 12, is then heated to 180°F and agitated for 24 hours. This effectively strips the oil-laden PCP from the soil. After the slurry has cooled to ambient temperature, it is inoculated with a form of Arthrobacter bacteria, allowed to rest for 48 hours, and dewatered. (Source: Chemical Engineering, 30 September 1985)

Bacterial coal desulphurization

The West German mining research institute Bergbau-Forschung at Essen has reduced anorganic sulphur content of coal by more than 90 per cent through the application of micro-organisms.

At present, the results of laboratory work will be transferred to a pilot plant for continuous operation to get planning data for a demonstration plant. Parallel studies concentrate on the application of special bacteria to reduce organic harmful substances in process water of coal treatment plants. It is expected that biotechnological research will lead to methods for processing coal to added-value products. Bergbau-Forschung closely co-operates with a number of research institutes. (Source: Bio-Journal, No. 3, 1 June 1985)

Pesticides degrading bacteria

Two new examples of bacteria that degrade pesticides have been discovered by J. Karns of USDA. Enzymes produced by Flavobacterium degrade coumaphos, a pesticide used to control insect pests of livestock. Enzymes produced by Achromobacter degrade carbofuran used to control corn rootworm and other crop insects. Coumaphos is long-lived in soil, and remains toxic for long periods. Previous attempts to degrade it with ultra-violet light have been unsuccessful. Achromobacter can degrade several N-methyl carbamate insecticides, such as carbofuran, using them as a nitrogen source. (Extracted from Science News, 25 May 1985)

Extraction industry applications

Scleroglucan used in enhanced oil recovery

Within about two years, scleroglucan made in submerged aerobic culture by a Sclerotium species should be on the market as a thickening agent for enhanced oil recovery (EOR). A linear chain of D-glucopyranose units crosslinked into a structure of average molecular weight under 1.5 million, scleroglucan will compete with - and in some ways be superior to - the xanthan biopolymer currently employed for EOR.

The non-ionic "Actigum CS" is stable in the presence of salts; 500-day trials at 90°C in sea water show that it is relatively insensitive to high temperature. Like xanthan, it has high shear resistance, remaining viscous after the extremely strong mechanical shearing employed to remove it from fungal mycelium. Long-term core flooding tests also indicate that Actigum circulates freely, with good non-plugging characteristics.

Additionally, scleroglucan has the advantage that the pH of the culture falls to about 2.5 during the first few hours of fermentation. Together with the reduced oxygen flow attributable to rapidly increasing viscosity, this means that sterility is not a major problem. Because contamination is unlikely, it is even possible to consider establishing the fermentation on-site in an environment less strictly controlled than would otherwise be necessary. The product is being produced at Elf Aquitaine (France). (Extracted from Bio/Technology, Vol. 3, July 1985)

Process to unlock precious metals

A biological method initially developed for recovery of copper and uranium from ores, is currently being adapted by P.M. Mineral Leaching Technologies, a subsidiary of Giant Bay Resources of Vancouver, British Columbia, for use as an alternative to smelting or roasting minerals that contain precious metals.

The company began operations this May in Burnaby, British Columbia, on the Biotankleach process to see whether biological recovery of gold can work on a large scale. The process uses specially adapted strains of the common bacterium T. ferrooxidans to treat refactory gold ores, in which precious metals are bound within the crystal structure of sulphides.

The Biotankleach process begins by agitating precious metal concentrates in tanks containing the bacteria, for one to five days. The bacteria attach themselves to the sulphide crystals and they drill their way into the 'weak' spots where the gold is found in the crystal structure.

The sulphides are oxidized to sulphuric acid and the liquid containing the bacteria is then drawn off and can be recycled and reused. The solid material left behind is treated with conventional cyanide solutions to remove the gold.

This process is similar to that used for copper ores and for treating pyritic uranium ores but it is less complex because the metals remain as solids and do not have to be recovered from solution after treatment.

The advantages of biological recovery are economic and environmental. The standard cyanide recovery will not work with refactory ores until they are either broken down by roasting or smelting or by biological action.

Currently, roasting, which produces problems with removal of acidic pollution, can be done at only two plants in Canada. Transportation of ores to the plants can cost more than $100 a tonne. The Biotankleach process, however, can be done in small tanks at the mine site.

In small-scale experiments using samples of seven different levels of concentration they achieve up to a 45 per cent better recovery of gold and a 128 per cent better recovery of silver than from cyanide treatment of unbioleached concentrates. In bench-scale experiments, an average of 98 per cent recovery of gold was achieved from concentrates over a 30-day period of continuous operation. Concentrates of up to six ounces gold a tonne were used in the test period.

Treatment costs are estimated at $83 a tonne, including capital costs for a plant with a 50-tonne-a-day capacity, to $55 a tonne for a plant with a 150-tonne-a-day capacity.

In addition, there is no pollution associated with the process and promises a way to handle arsenopyrite ores that could create arsenic hazards if handled by smelting or roasting. Any arsenic or antimony in the biologically treated concentrate is oxidized during the leaching process and is left in an environmentaly safe, insoluble form.

The bacterial process can also be used for heap leach operations and is not greatly affected by temperature. The reaction releases heat which keeps a heap from freezing, even at minus 40 degrees. The surface crust may freeze but the interior temperature remains fairly constant.

When the pilot plant study is completed next year, P.M. Mineral Leaching hopes to apply the process to larger scale applications.

The modular Biotankleach process could be used by an individual operator to handle as little as a quarter tonne of ore a day. (Source: Canada Weekly, Vol. 13, No. 23, 5 June 1985)

Industrial microbiology

Rennin gene put into bakers' yeast

Researchers at Collaborative Research Inc., a Lexington, Mass.-based biotechnology firm, have developed a strain of bakers' yeast that produces and secretes the enzyme rennin. Rennin, normally produced in calves' stomachs, is used in cheese making to cause milk to clot into curds. The gene for calf rennin has been previously inserted successfully into Escherichia coli and other yeast strains, but its insertion into bakers' yeast is an advantage, according to company spokesmen, because this yeast secretes rennin in fully active form. Rennin produced recombinantly by bacteria and other yeast strains requires further treatment before it can be used in cheese production. (Source: Chemical & Engineering News, 22 April 1985)

Bacterium that makes cellulose fibre

A bacterium that makes large amounts of cellulose fibre is being developed by the University of Texas (Austin). The bacterium, Acetobacter xylinum, synthesizes cellulose ribbons that float to the surface of the fermenter. Sterilized cellulose can then be processed into products such as parchment, paper, cotton swabs and surgical sutures. The fibres will be less costly and more energy-efficient to produce than wood pulp and could be used to coat the surface of synthetic fibres, permitting them to 'breath' like cotton. (Extracted from Chemical Week, 7 August 1985)

Industrial equipment

Foam-block blanket cozy for bacteria

Georgia-Pacific Corp. (Atlanta) has developed a unique method to ensure wintertime efficiency of biological-treatment ponds: a blanket of expanded polystyrene (EPS) blocks.

The system has been tested since November 1984 at the firm's Columbus, Ohio, resins facility, and company officials are quite pleased with the results. Plant manager Andy Norman attests that the biological treatment unit kept operating at peak efficiency last winter, with no shutdown needed because of bugs' dying from cold, and he maintains that the technique looks good for any aerobic biological treatment facility that experiences cold weather.

Georgia-Pacific Resins Inc.'s Columbus plant makes 2 million lb/wk of urea-formaldehyde concentrates, 1 million lb/wk of formaldehyde, and another 2 million lb/wk of urea-formaldehyde and phenol-formaldehyde thermosetting resins. Effluent from the processes contains some formaldehyde and phenol, and the plant treats all effluent (to bring phenol levels down to zero discharge) prior to releasing wastewater to Columbus's municipal treatment network.

The plant collects all effluent (including rainwater) in a holding tank that is tested daily. If pH is between 6.5 and 8.5, and the phenol loading is below 500 lb, the waste (typically 20,000 gal) is charged to the treatment pond. There, phenol-specific bacteria operate on the wastes during a 72-h residence time.

The temperature span over which the bacteria remain viable, says plant manager Norman, is about 18-38°C. But the optimum temperature for operation of the biopond is about 32-34°C. Because of the severity of Ohio winters, the bugs died. The company had to store all wastewater (including atmospheric precipitation) for around three months, until the bacterial colony could be re-established and brought to equilibrium. Needless to say, this taxed the plant's storage capacity.

Alternatives were considered and plant officials eventually decided to try to fashion a floating blanket from EPS blocks fabricated for quality-control purposes at the company's

Painesville, Ohio, plant. The 4 x 2 x 1-ft blocks have an insulation value of R48, and a density of 1 lb/ft^3. They were coated with latex paint to minimize damage (wear from surface agitation due to the lagoon's aeration). Polypropylene lines keep the blocks tethered in place, and prevent strong winds from blowing them out of the lagoon.

The low temperature in the biopond over the winter of 1984-85 was 26°C, the average effluent exit temperature from the lagoon was 30°C, versus 8°C for the previous two winters, and phenol and formaldehyde levels were maintained below pretreatment standards in effect for the plant.

During summer, the plant had to pull off about 2,000 of the 5,000 blocks to prevent overheating, a job done by two men over a weekend. The installation of a heat exchanger in the aeration-line header may cool the air enough to eliminate the need for removing blocks during the summer. (Extracted from Chemical Engineering, 16 September 1985)

Two new bio techniques

APV, the UK equipment firm, has unveiled two developments which it claims could revolutionize large-scale production of biological materials. The first is a ceramic membrane and the second, a new cell culture technique.

The ceramic membrane, which was originally developed for isotopic separation in the French nuclear energy sector, has "enormous potential", the company believes. Although more expensive than conventional plastic membranes used in ultrafiltration, the APV membrane is claimed to have a working life of several times longer.

APV says that the system is already in use at a hygienic processing company in France. Made from aluminium oxide, the multichannel system is capable of separating particles between 40,000 molecular weight to 5 microns.

Meanwhile, the company is also touting the use of its heat exchanger as a cell culture system. APV maintains that such a device has several advantages for the large-scale cultivation of anchorage-dependent cells.

The system has been tested for production of interferon from fibroblast cells by Beecham and of vaccines and enzymes at the Centre for Applied Microbiological Research at Porton. (Source: European Chemical News, 3 June 1985)

Biohazards

OSHA issues guidelines for biotech workers

As biotechnology companies move their products from the laboratory into commercial production, concern for the safety of workers who will produce these materials has increased. The US Occupational Safety & Health Administration, charged with protecting workers from hazards, has published guidelines for this area. The main point in the guidelines is that current regulations appear to cover all known hazards and that no additional regulations are needed at this time.

The notice in the 12 April Federal Register points out that biotechnology normally uses conventional chemicals and processes, already subject to health and safety rules. OSHA health protection standards likely to apply to this industry include, in part, limits on airborne toxins, rules giving workers and their representatives access to exposure and medical records, the hazard communication standard scheduled to go into effect on 25 May 1986, and regulations on respiratory protection. A new regulation also is being drafted to regulate exposure to toxic chemicals in laboratories. Some of the current safety standards would cover normal operations such as fire protection, electrical safety, and handling of compressed gases. (Extracted from Chemical & Engineering News, 22 April 1985)

E. PATENTS AND INTELLECTUAL PROPERTY ISSUES

Patent for microbes against Agent Orange

Microbes that eat Agent Orange and PCBs in the environment have been patented (No. 4,535,061) by Drs. A. M. Chakrabarty and S. T. Kellogg of the University of Illinois. The 1980 US Supreme Court ruling that life forms can be patented was based on a patent application Chakrabarty filed in 1972 for the invention of a bacterium of the genus Pseudomonas. The Environmental Protection Agency is now negotiating with Chakrabarty and Kellogg to develop the new bacteria. (Extracted from New York Times, 17 August 1985)

Biogen wins US patent for interferon production

Biogen, the Swiss-US genetic-engineering company, has obtained a US patent covering the production of genetically engineered Alpha interferons. This follows the granting of a similar European patent last year.

Worldwide rights to Biogen's Alpha-interferon patents are licensed to the Schering-Plough group of the US, whose branded production "Intron A" is under review by national agencies for use against cancer and viral infections. Although Biogen says the US patent gives it the right to exclude others from the manufacture, use or sale of recombinant Alpha interferons in the US, this will not affect a recent agreement between Schering-Plough and the Swiss Hoffman-La Roche concern. The agreement enables each company to market Alpha interferons without infringement of patent rights. Hoffman-La Roche, in part together with the US genetic engineering group Genentech, already holds such patents in a number of individual European countries. Earlier this year it obtained a product patent from the US authorities for "homogenous Alpha interferon, regardless of the method of production". (Extracted from Financial Times, 26 July 1985)

Cetus gets new US patent

Cetus Corporation says it has been granted a broad US patent covering a number of human therapeutic proteins. The Californian concern has also just launched two monoclonal antibody-based kits for the detection of prostate cancer.

The latest patent follows a product patent granted to Cetus by the US patent office earlier this year for its interleukin-2 "mutein". It is a broad composition of matter patent for a pure and oxidized form of microbially-produced proteins containing disulphide bonds, including interleukin-2 and beta interferon - both potential anticancer treatments. It also covers a process to make them at the purity levels required for clinical trials.

The company expects to receive patent protection for its beta interferon mutein shortly. Cetus says its muteins are genetically modified proteins with increased stability, activity or purity compared with the natural compound.

Cetus is developing beta interferon, under the tradename Betaseron, jointly with the Shell Oil subsidiary, Triton Biosciences. The company is commercializing IL-2 via an R&D limited partnership. Both products are in phase II clinical trials against various cancers and infectious diseases. (Extracted from European Chemical News, 12/19 August 1985)

List of recent patents

Purpose, use or process	US Patent No. Date issued Date filed	Assignee Inventors
PLASMID: CORYNEFORM VECTOR Product: Cloning vehicle composed of "drive-unit region from a plasmid ... capable of propagating in Coryneform glutamic acid-producing bacterium, and ... gene fragment or fragments (and optionally, a 'drive-unit' region) derived from a plasmid ... capable of propagating in Escherichia coli or Bacillus subtilis". Benefit: Improving Coryneform bacteria, which produce glutamic acid, lysine, and other amino acids.	4,514,502 30 April 1985 10 June 1982	Ajinimoto Co., Inc., Tokyo, Japan. Kiyoshi Miwa, et al.
PRODUCT RECOVERY: BACTERIOLYTIC PROTEIN FROM INSECTS Product: Two non-lyzozyme proteins, each with a molecular weight of about 3,500 daltons, cause "efficient lysis of the bacterial cell wall" of Escherichia coli and other species, even if enzyme is boiled for 30 minutes. Process: Hyalophora cecropia (giant silk moth) pupae are innoculated with Enterobacter cloacae, and proteins purified from hemolymph.	4,520,016 28 May 1985 2 August 1982	KabiGen AB, Stockholm, Sweden. Dan Hultmark, Hakan Steiner, Torgny Rasmuson Hans G. Boman

Purpose, use or process	US Patent No. Date issued Date filed	Assignee Inventors
Benefits: "... significantly increase the yields from genetically engineered bacteria", and "control certain bacterial infections".		
AIDS: HTLV-III ANTIGEN AND TEST KIT Product: 41,000-dalton HTLV-III envelope proteins recognized by antibodies from AIDS and pre-AIDS patients and used in ELISA and Western blot test kits. (See Newswatch, 1 April, p. 7.)	4,520,113 28 May 1985 23 April 1984	US Dept. of Health and Human Services, Washington, D.C., USA. Robert C. Gallo, et al.
Process: HTLV-III is grown in a cell line that is resistant to the virus' cytotoxic effect. Benefits: Serum assay for detection of human AIDS and pre-AIDS		

Purposes, use or process	Japanese Pub. No. Priority	Applicant Country
LEUKEMIA: DNA coding for antigenic human T-cell leukemia virus peptide and its bacterial production.	60-61534	Kyowa Hakko Kogyo Co. Ltd. and Foundation for Cancer Research, both of Tokyo, Japan.
HORMONES: Recombinant-DNA production of human insulin-like growth factor and epidermal growth factor.	60-69029 US 501353 US 506078	Genentech, Inc., S. San Franciso, Calif., USA.
HEPATITIS: Vaccine and compound reacting to hepatitis-B infection	60-69030 GB 8321789	Biogen NV, Curaçao, Netherlands Antilles.
HORMONE: Preparation of secretin, a duodenal polypeptide that affects pancreatic secretion.	60-69098 DE P3328793.7	Hoechst AG, Frankfurt, German Federal Republic.

Purpose, use or process	Application System/No. Pub. data Date filed; Priority	Applicant Country Inventors
INDUSTRIAL		
YEASTS: TRANSFORMING YARROWIA TO USE MORE CARBON SOURCES Product: Vectors comprised of genes from Yarrowia lipolytica - a yeast used industrially to produce citric acid and single-cell protein. Inserted into E. coli plasmid PBR322, vectors can be amplified and used to transform Y. lipolytica. Benefits: Vectors containing genes coding for utilization of various carbon sources "afford means for improving fermentation characteristics ... (by) broadening the spectrum of utilizable carbon sources of Y. lipolytica" transformed with these cloning vehicles.	EPO 138 508 24 April 1985 3 Oct. 1984 US 539591 6 Oct. 1983	Pfizer Inc., New York, NY, USA. Lance S. Davidow, John R. Dezeeuw

Purpose, use or process	Application System/No. Pub. data Date filed; Priority	Applicant Country Inventors
PLANTS: ALTERED BACTERIA REDUCE FROST DAMAGE Product: Bacteria promoting nucleation and formation of ice crystals on plants - such as Pseudomonas, Xanthamonas, and Erwinia - with all or part of the gene coding for ice nucleation deleted or to prevent nucleation. (Newswatch, modified 4 February, p.3.) Benefits: Modified bacteria are applied to plants in aqueous or dry formulations "at an early stage of growth, so that they become established prior to the colonization of the plant" by natural ice-nucleation-capable bacteria, thereby competing with the natural bacteria and reducing frost damage stimulated by them.	EPO 138 426 24 April 1985 21 Sept. 1984 US 534851 22 Sept. 1983	University of California Berkeley, Calif., USA. Cindy S. Orser Steven Lindow Nickolas J. Panapoulos
FOOD PRODUCTS: INACTIVATION OF SOYBEAN TRYPSIN INHIBITOR Product: Starfish trypsin-1 (DIT_1) from Dermasterias imbricata used with a proteolytic enzyme such as carboxypeptidase B to inactivate soybean trypsin inhibitor (STI). Process: DIT_1 binds to STI and complex is inactivated by proteolytic enzyme; DIT_1-enzyme combination can be used to treat soybean foodstuffs or fed directly to livestock. Benefits: "... more economical and efficient than heat deactivation" to overcome trypsin inhibition in animals or human babies fed soybean-based products.	EPO 138 544 24 April 1985 8 Oct. 1984 US 541208 12 Oct. 1983	Genentech, Inc., S. San Francisco, Calif., USA. Mark S. Dennis, et al.
ANTIBIOTICS: AMINOGLYCOSIDE PRODUCTION INCREASED BY FUSING STREPTOMYCETES Product: Aminoglycoside antibiotics such as nebramycin and kanamycin produced by fused protoplasts of Streptomyces tenebrarius and/or S. kanamyceticus. Process: After fusing protoplasts from cells of Streptomyces, strains with modified genetic material are isolated and those with increased antibiotic-producing abilities selected. Benefits: "... significantly increased" production of aminoglycosides - antibiotics "of major therapeutic and commercial importance".	GB 2 146 015 11 April 1985 15 May 1984 16 May 1983	Biogal Gyogyszergyar, Debrecen, Hungary. HU 1678 Lajos Ferenczy, et al.
PHARMACEUTICAL		
CANCER DETECTION: ANTIBODY SPECIFIC TO SMALL-CELL LUNG CARCINOMA Product: Monoclonal antibody that binds with high specificity to small-cell carcinoma cells (SCC) of human lung. Benefits: Antibody can be used in diagnosis, quantification, and therapy of pulmonary small-cell carcinoma and "to cleanse a clinical sample, e.g., bone marrow, of metastic SCC cells". Its ability to	EPO 147 118 3 July 1985 7 Dec. 1984 US 561196 14 Dec. 1983	Dana-Farber Cancer Institute, Boston, Mass., USA. Samuel D. Bernal

Purpose, use or process	Application System/No. Pub. data Date filed; Priority	Applicant Country Inventors

distinguish between SCC and other carcinoid lung tumors can prevent the "grave consequences (of) misdiagnosis".

(Extracted from patents listed in McGraw-Hill's Biotechnology Newswatch, 1 and 15 July, 5 and 19 August 1985)

F. BIO-INFORMATICS

Just published by the OECD: "Biotechnology and Patent Protection"

The report, by a group of experts, sets out recommendations for legal protection of the inventor in biotechnology and for better international harmonisation of patent law.

The report shows that the need to protect living matter, as against inanimate matter in the past, creates new problems, particularly at a time of rapid scientific and technological change. It emerges that there is no other field of technology where patent laws vary so widely and on so many points as in biotechnology. On the whole, United States law and Japanese law appear to give biotechnology better protection than the law of other OECD countries.

The report says the impact of the new biotechnologies on the economy might arrive earlier and be more far-reaching than expected. Governments are increasing budgets to support biotechnology particularly where their responsibilities are large - in public health, nutrition, energy and the environment.

("Biotechnology and Patent Protection - An International Review" by F.K. Beier, R.S. Crespi, J. Straus, 134 pages, OECD, Paris 1985, ISBN 92-64-12757-7.)

New journal, Biotechnology Progress

Engineering aspects of biotechnology provide the unifying theme for a new journal to be published by the American Institute of Chemical Engineers. The quarterly publication, called Biotechnology Progress, will cover diverse topics. Artificial organs, blood rheology, pharmacology and pharmacokinetics, food production and processing, and uses of recombinant organisms, tissue cultures, and enzymes are examples. The journal will include research papers, topical and review papers, and some news coverage. Annual subscriptions cost $16 for members of AIChE and $50 for nonmembers. Information is available from AIChE Subscription Department, 345 East 47th St., New York, N.Y. 10017; phone (212) 705-7663. (Chemical and Engineering News, 22 April 1985.)

Reference books

A Dictionary of Genetic Engineering (by Stephen Oliver and John Ward, Cambridge University Press, pp. 153, £12.50)

The technical vocabulary of genetic engineers is proliferating nearly as rapidly as their publications. So A Dictionary of Genetic Engineering is a welcome aid to the weary reader.

The authors of this dictionary go to admirable lengths to define the state of the rapidly evolving newspeak, informing us, for instance, that "cut" is "slang meaning to make a double-stranded break in a DNA duplex". All the same, the complete beginner may spend a lot of time looking up words in the definition and still be none the wiser and the dictionary does not indicate which words appearing in definitions have their own entries. The book is certainly an invaluable guide for the biologically literate venturing into the molecular jungle for the first time. (New Scientist, 5 September 1985)

A selection of recent textbooks on genetic engineering:

Enzyme Structure and Mechanism, 2nd edition by A. Fersht, W.H. Freeman, pp. 475, £14.95 pbk.

Proteins: Structures and Molecular Properties by T.E. Creighton, W.H. Freeman, pp. 515, £28.95.

Genes II by Benjamin Lewin, Wiley, pp. 768, £16.75 pbk.

A Dictionary of Genetic Engineering edited by S.G. Oliver and J.M. Ward, Cambridge UP, pp. 153, £12.50.

Understanding DNA and Gene Cloning: A Guide for the Curious by Karl Drlica, Wiley, pp. 205, £11.45.

Principles of Gene Manipulation, 3rd edition by R.W. Old and S.B. Primrose, Blackwell, pp. 288, £11.80.

Gene Cloning: The Mechanics of DNA Manipulation by D.M. Glover, Chapman and Hall, pp. 222, £15 hbk, £7.95 pbk.

An Introduction to Recombinant DNA Techniques: Basic Experiments in Gene Manipulation by P. Hackett, J.A. Fuchs and J.W. Messing, Addison-Wesley, pp. 200, £21.50 pbk.

.eshaping Life: Key Issues in Genetic Engineering by G.J.V. Nossal, Cambridge UP, pp. 158, £6.96 pbk.

Setting Genes to Work: The Industrial Era of Biotechnology by S. Yanchinski, Viking, pp. 157, £10.95.

Plant Molecular Biology by D. Grierson and S.N. Covey, Blackie, pp. 184, £17.95 hbk, £8.95 pbk.

Principles of Plant Biotechnology: An Introduction to Genetic Engineering in Plants by S.H. Mantell, J.A. Matthews and R.A. McKee, Blackwell, pp. 200, £10.80 pbk.

Science Writing for Beginners by A.D. Farr, Blackwell Scientific, pp. 96, £5.80.

Proceedings of VII International Biotechnology Symposium, New Delhi, February 1984

The Proceedings of VII International Biotechnology Symposium sponsored by the Commission on Biotechnology, the International Union of Pure and Applied Chemistry and the Indian National Science Academy held at Delhi in February 1984 will soon be available for distribution. In this volume all invited lectures, comprising four key lectures, twenty plenary lectures, twenty two position papers and four panel papers will appear. These contributions cover the entire gamut of biotechnology from the concepts of "new biology" to many of the questions related to engineering applications that need adequate solutions. In this respect this volume will be a unique treatise dealing with the use of biotechnology for society, no matter how it is defined. All contributors to this volume are very eminent in their own right and most of them are known to the decision makers in both developed and developing countries.

Topics covered are:

Algae and photosynthetic bacteria;
Bioinsecticides;
Biometallurgy;
Bioprocess engineering and control;
Biotechnology of food and feed;
Biotechnology - resource base and priorities;
Downstream processing;
Fuels and feed stocks;
Immobilized biocatalysts;
Industrial effluents;
Metabolic regulation;
Microbial growth kinetics;
Microbial transformations;
Monoclonal antibodies;
Novel bioreactors;
Plant cell cultures;
Recombinant DNA technology;
Transport processes.

Copies of the Proceedings VII International Biotechnology Symposium, New Delhi, may be ordered from:

Prof. T.K. Ghose
Editor

Proceedings VII International
Biotechnology Symposium
Biochemical Engineering Research Centre
Indian Institute of Technology, Delhi
Hauz Khas, New Delhi - 110016
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In addition, the report of an advisory group meeting held in Vienna in October 1984 on mutation breeding for disease resistance using in-vitro culture techniques organised by the Joint FAO/IAEA Division of Isotope and Radiation Applications of Atomic Energy for Food and Agricultural Development, is available from the International Atomic Energy Agency, Vienna, Austria or from the IAEA sales agents.

The Gene Factory by John Elkington

In The Gene Factory, the author John Elkington takes the reader into the world of the adolescent biotechnologies relatively painlessly, in an essentially anecdotal account of the ups and downs of dozens of the new companies and some of their more cautious elders. Above all, it is highly readable and avoids the mistake of over-stressing the science of genetic manipulation. Rather, Elkington's aim is to show what the industry has done with all the money poured into the new biotechnologies, put at $2,500 million by 1984; who has waxed fat and who has been swallowed.

Anyone thinking of investing in the new biotechnologies should read Elkington's book. From all over the world, bio-entrepreneurs have contributed insights. From Japan, we learn that fermentation is rooted to the extent that, on average, each Japanese drinks 10 litres of soy sauce a year. From Dr. Charles Reece, ICI's canny director of research, we learn that biotechnology has "taken the first few steps up a very long staircase". (Price: £12.95) (Extracted from New Scientist, 13 June 1985)

Biotechnology and Genetic Engineering Reviews

Biotechnology and Genetic Engineering Reviews, which will be published as hardback volumes annually, will provide and accelerate communication between all people concerned with biotechnology in the widest sense of the word, with particular emphasis on the interface between genetic manipulation of organisms and industrial, agricultural, veterinary and medical processes. Volume 3 covers agriculture, energy production, food industry, genetic manipulation, pharmaceuticals, medicine, microbiology, veterinary science and waste disposal. The price for this volume is £80.00, volumes 1 and 2 cost £60.00 each. Copies may be obtained from the publishers: Intercept Ltd., P.O. Box 2, Ponteland, Newcastle-upon-Tyne, NE20 9EB, United Kingdom.

The biotech business - Open University course

The UK Department of Trade and Industry and the Open University, with support from the Science and Engineering Research Council, have put together an OU course to educate British business people and others on the likely impact on their businesses.

The course, simply entitled Biotechnology, will include video tapes of the television programmes, an annotated bibliography, and complete glossary and will cost £100.

The Open University says that the Biotechnology study pack is designed for people who need to learn about the subject quickly. Judging by the first few programmes, the course, for the most part, hits the right sober note while being entertaining and informative.

The series quite rightly avoids trying to cover all of biotechnology, and focuses instead, on near-term, practical goals. Using four case histories, the course examines some of the biological advances and process technologies that underpin biotechnology, and investigates whether it may be worthwhile to incorporate the new biotechnology in some specific areas of industry.

For further information, kindly apply to: The Open University, Walton Hall, Milton Keynes, MK7 6AA, Buckinghamshire, United Kingdom

(Extracted from New Scientist, 6 June 1985)

'Sing-along-a-syllabus' - educational audio visual package

Biorhythms 1 & 2: basic biology set to words and music

Words by H. Baum, music by P. Shade, sung by the Metabolites, Learn through Music Ltd. (Taylor and Francis Ltd.), London.

This new audiovisual package is designed for the school market ('O' level GCE in the UK and senior High School in the USA). The package includes a cassette of the songs and an accompanying booklet which contains the words, a melody line, suggestions for minimal linking music, guitar chords and revision notes/diagrams. Biorhythm 1 is entitled Human Biology and includes basic processes such as excretion, circulation and digestion. Biorhythm 2 is called General Biology and is largely taxonomy, elemental cycles and cell division/genetics.

The authors are very brave to tackle a largely untried educational aid in this way. The musical style is on the whole interesting and might be described as a cross between Lloyd Webber, jazz and various styles from light musicals. The range of almost two octaves is really too great both for the youthful music group the Metabolites, average age 14 years, and relatives of the authors, and also for the average school pupil who might be expected to 'sing along'. The arrangements are interesting to listen to but in places are fussy and interfere too much with the words, e.g. in 'The Plant Kingdom'. The tunes vary in their impact and there is in some over use of syncopation which makes them difficult to sing without skill and practice. The pronunciation of scientific words is excellent and must have taken children of this age group a long time to learn efficiently. (Extracted from Trends in Biotechnology, Vol. 3, No. 6, 1985)

Two new databases: Biolink and Biobusiness

Access to information on biotechnology has been improved with the creation of two new databases that cover this hybrid field specifically. One database, however, has been discontinued.

"Berkeley BioLink" is an on-line directory, boasting all the advantages of a computerized index of biotech companies. BioLink provides information on who is doing what in biotech, for clients like major corporations, investment banks, and venture capitalists. Corporate and academic affiliations, key personnel, and areas of interest are included. In addition to completing its listing of public companies, BioLink is beginning to put research strengths of universities, starting with 11 schools.

BioLink is currently offered only as a service to clients, but there are plans to provide much of the database on-line eventually. Some of the information now on BioLink is proprietary, so many of the details will have to be excised for the public version.

Another new database, this one called Biobusiness a joint effort between database veterans Biosis and Information Access Co., allows literature searches. It is available through Dialog Information Services (Palo Alto, CA) and began this past summer as File 285 in the Dialog system (at a cost to the user of $117 per connect hour). Stressing the business applications of biological and biomedical research, it covers four broad subject areas: agriculture, biotechnology, food and beverages, and pharmaceuticals. The database monitors over 1,000 publications in an effort to provide information to help users predict which research areas have the most potential for commerical growth. It began with some 16,000 records dating back to the beginning of 1985, and will be updated monthly.

The business-oriented "Telegen Alert", from EIC/Intelligence, has been eliminated in favour of EIC's other biotech database, "Telegenline", which stresses research. (Extracted from Bio/Technology, Vol. 3, September 1985)

Food science information available on database from CISTI system

Food science information is available on a database recently added to the CAN/OLE online information retrieval system by the Canada Institute for Scientific and Technical Information.

Food Sciences and Technology Abstracts (FSTA) is an international database produced by the International Food Information Service in Frankfurt. FSTA covers abstracts from 1,200 journals, patents from 20 countries, standards and books in any language. All aspects of food science and technology are covered as well as related areas such as chemistry, biochemistry, physics, agriculture, home economics and engineering, as these relate to food science and technology.

The database contains 270,000 references and will be updated by about 1,500 references monthly. Materials published from 1969 to date are included. (Source: Canadian Research, February 1985)

Contracts to develop biomedical research system

BBN Laboratories Inc. has received two contracts from the US National Institutes of Health (NIH) to develop and implement software for an advanced generation of computer graphics workstations for life science research, and to maintain PROPHET, an existing biomedical research system developed under prior contracts with the NIH Division of Research Resources. Details from: BBN Laboratories Inc., 10 Moulton Street, Cambridge, MA 02238, USA or on (617) 497 2559. (Source: Biotechnology Bulletin, Vol. 4, No. 7, August 1985)

INSPIRE (Interactive Species Information Retrieval)

This is a simple data base designed to assist foresters in the selection of species for plantations, or for specific sites or climatic conditions. It contains details of 173 tropical and sub-tropical species. The species information and programme are described in the publication:

Webb, D.B.; Wood, P.J.; Smith, J.P. and Henman, G.S., 'A Guide to Species Selection for Tropical and Sub-Tropical Plantations', Tropical Forestry Paper No. 15 (2nd edition revised), Commonwealth Forestry Institute, South Parks Road, Oxford, UK, 1984. (Source: Appropriate Technology, Vol. 12, No. 2, September 1985)

G. MEETINGS

Conferences, Courses, Meetings

20 November 1985	Seminar on Biotechnology Information, London, UK. (Contact: EBIP, 9 Kean Street, London WC2B 4AT).
21-22 November 1985	1st International Conference on Protein Engineering, London, UK. (Contact: Helen Racquet, Oyez Scientific & Technical Services Ltd, Bath House (3rd Floor), 56 Holborn Viaduct, London ECIA 2EX or on 01-236 4080).
27-29 November 1985	BIOTECH '85 ASIA, Singapore. (Contact: Online Conferences Ltd, at address in 21-23 October entry, or talk to Juletta Broomfield on Singapore 732-1861/2).
5 December 1985	Industry/Academic Interfac[illegible] Biotechnology - Its Significance and Development, London, UK. [illegible] Dr. Brian Kirsop, Association for the Advancement [illegible] hnology, AFRC Food Research Institute, Colney [illegible] A or on 0603 56122).
9-13 December 1985 (and 30 June-4 July 1986)	Monoclonal Antib[illegible] (Contact: J E Liddell, Department of Bi[illegible] y College, Cathays Park, Cardiff, Wales [illegible] 2303).
9-21 December 1985	Fundamentals of Fic[illegible] gineering, New Delhi, India. (Contact: Prof. T.K. [illegible], Biochemical Engineering Research Centre, Indian Institute of Technology, Hauz Khas, New Delhi 110016, India).
11-13 December 1985	1st IFAC Symposium on Modelling and Control of Biotechnological Processes, Noordwijkerhout, The Netherlands. (Contact: Congress Office, Royal Institution of Engineers in the Netherlands, P.O. Box 30424-2500 GK, The Hague, The Netherlands or on 070 64 68 00. Telex: 33641).

16-18 December 1985	Getting into Biotech Business, Swansea, UK. (Contact: Christine Roberts, The Biotechnology Centre Wales, Singleton Park, Swansea SA2 8PP or on 0792 296396).
20-22 January 1986	Bio/Technology Looks to the Next Decade, New Orleans, USA. (Contact: Bio/Technology Looks to the Next Decade, Nature Publishing Co. 65 Bleecker St., New York, NY 10012).
20-22 February 1986	2nd Cuban Seminar on Interferon, Havana, Cuba. (Contact: Interferon y Biotechnología) "86", Apartado Postal 6072, La Habana, Cuba, telex: 511072).
22 January - 19 March 1986	Cell Culture Techniques - A Short Course, London, UK. (Contact: Dr. N.L. Morgan, Senior Lecturer in Biotechnology, South Bank Polytechnic, Borough Road, London SE1 0AA or on 01-928 8989 ext 2318).
25-26 March 1986	Symposium "Process Possibilities for Plant and Animal Cell Cultures", Manchester, UK. (Contact: Dr. C. Webb, PAC Secretary, Chemi. Engin. Dept. UMIST, P.O. Box 88, Manchester M60 1QD, GB).
30 March - 2 April 1986	First Conference of Food Science and Technology for Mediterranean Countries, Dokki, Egypt. (Contact: Prof. Hassan Ali Heikal, Food Technol. Dept., Horticultural Res. Center, Giza, A.R. Egypt).
7-10 April 1986	Energy from Biomass and Wastes. This three-and-a-half day conference includes an exhibition and a trade show. It will be held at the Hotel Washington Hilton, Washington, DC. Organized by the Institute of Gas Technology, it includes a technical programme and addresses research topics as well as business and non-technical issues that affect the contributions of biomass and wastes to primary energy demand. Further details from the Institute of Gas Technology, 24 South State Street, Chicago, IL 60616, US.
7-11 April 1986	Controlled Release Technology: Polymeric Delivery Systems for Drugs, Pesticides and Foods, Cambridge, Mass., USA. (Contact: Ms. Maria Clara Suva-Martin, Industrial Liaison Programme, Massachusetts Institute of Technology, Cambridge, MA. 02139, Tel. 617-253-2691, Telex 921473 MIT CAM).
15-17 April 1986	International Conference on Bioreactor Fluid Dynamics, Cambridge, UK. (Contact: British Hydromechanics Research Association, c/o Ms J. Stanbury, Cranfield, Bedford MK 43 0AJ, GB).
4-7 May 1986	Protein Engineering Symposium 1986, Groningen/NL. (Contact: Protein Engineering Symposium, 1986, Lab. v. Chemische Fysica, Nijenborgh 16, NL-9747 AG Groningen
11-16 May 1985	3rd Meeting on Recovery of Bioproducts, Uppsala/S. (Contact: Engineering Foundation, 345 East 47th Street, New York, NY 10017, USA).
3-6 June 1986	DECHEMA-Jahrestagung der Biotechnologen 1986, Frankfurt, FRG. (Contact: DECHEMA, Postfach 970146, D-6000 Frankfurt 97).

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