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UNITED NATIONS INDUSTRIAL DEVELOPMENT ORGANIZATION

Genetic Engineering and Biotechnology Monitor

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A. POLICY, NEWS AND OTHER EVENTS

UNIDO news

Forum of scientists

The Preparatory Committee on the Establishment of the International Centre for Genetic Engineering and Biotechnology, at its tenth session on 2-4 December 1987 endorsed the proposal of the Panel of Scientific Advisers for the holding of a Scientists' Forum and requested the Director of the ICGEB, Professor I. Gonsalus, to submit a proposal on the organization of the Forum to its next session.

The objective of the forum would be a further elaboration of the research and training activities of the ICGEB, including inputs to the preparation of a five-year work programme; identification of operational means of enhancing information exchange among the ICGEB and its members. It was proposed to hold the forum at Trieste, Italy, from 27 to 30 March 1988. The tentative programme will be plenary lectures by leading scientists on research trends on topics of relevance to ICGEB's work programme and focusing on needs of the developing countries; presentation of the ICGEB research work undertaken at the ICGEB Components and affiliated centres; and parallel sessions of theme-oriented working groups in which written or oral presentation of member country scientists will be made. These will focus on ICGEB's work programme and manifested research needs of the developing countries.

Workshop on biotechnology for Latin American and Caribbean countries (8-12 February 1988, Havana, Cuba)

Cuba, having participated in the activities of UNIDO related to biotechnology and having established its own biotechnology centre in 1982, is undertaking considerable efforts to broaden its basis for biotechnology research and production in selected fields and is prepared to share its experience with other developing countries and join forces especially with those of the Latin American and Caribbean area. During a visit of the Director-General of UNIDO to Cuba in February 1986, further co-operation between Cuba and UNIDO in the field of biotechnology for the benefit of other developing countries was discussed and it was agreed that UNIDO would provide assistance in organizing a workshop on biotechnology in Cuba within the framework of the ICGEB, and oriented towards new research work of developing countries in the region.

The objectives of the seminar are:

(i) To facilitate transfer of know-how in the genetic manipulation of micro-organisms with the aim of contributing to the industrial and socio-economic development of Latin American-Caribbean countries;

(ii) To discuss and analyse existing and planned national programmes in biotechnology in the Latin American and Caribbean regional context;

(iii) To enhance information transfer and technology development through the dialogue of policy-makers, scientists and industrialists from different countries in the Latin American and Caribbean region;

(iv) To discuss and orient biotechnology research in Latin America and the Caribbean, in the light of industrial needs of the countries therein and to establish links between research and industry;

(v) To assess the state-of-the-art and exchange knowledge in the field of biotechnology and genetic engineering through presentations in recent technical/scientific advances; and

(vi) To improve and upgrade the capabilities of researchers in biotechnology in the Latin American and Caribbean region.

Workshop on genetic engineering techniques (Introduction to recombinant DNA) 21-25 November 1987, Kuwait

This workshop, organized by UNIDO and the Kuwait Institute for Scientific Research, was designed to introduce researchers in molecular biology, microbiology, biochemistry and laboratory technologists to the recent developments in the field of genetic engineering, with special emphasis on the potential applications of recombinant DNA to petrochemical industry, agriculture and medicine.

The objectives of the workshop were to familiarize the participants from Kuwait and other Arab countries to the scientific and technical basis of gene analysis and manipulation and the specific techniques for handling and interpretation of isolated genetic material.

The workshop very prudently combined lecturing with practical laboratory work. The participants were also briefed on UNIDO's activities in biotechnology and promotional efforts towards closer regional and international co-operation in this field. The idea was to initiate first steps on future co-operation in biotechnology among Arab countries, particularly the Gulf States.

Seminar on the role of biotechnology and genetic engineering in Saudi Arabian development 5-9 December 1987, Riyadh, Saudi Arabia

At the first Arab Gulf Conference on Biotechnology and Applied Microbiology, held in Riyadh, Saudi Arabia, from 12 to 15 November 1984, it was pointed out how biotechnology and its advanced techniques could be harnessed to solve problems facing countries of the Arabian Gulf. In a paper presented by the UNIDO Secretariat at the above-mentioned conference, it was suggested that these countries could particularly benefit from the applications of biotechnology in the areas of agriculture and hydrocarbon microbiology. For Saudi Arabia, given its extensive coastline along the Red Sea, the Arabian Sea and the Persian Gulf, it appears that the country's potential in marine biotechnology would also be significant. Consequently UNIDO's co-operation was requested to assist the Government of the Kingdom of Saudi Arabia in assessing the potential of biotechnology and genetic engineering for Saudi Arabian development, and in recommending actions to be taken by Saudi Arabia in order to realize this potential and it was proposed to hold a Saudi Arabian seminar on biotechnology under the sponsorship of UNIDO and the King Abdul Aziz City for Science and Technology (KACST).

The recommendations of the seminar culminated in the setting-up of a National Biotechnology Advisory Group (BAG) with the participation of government agencies, industry and universities as well as the Arab Gulf University (Bahrain) plus an active international input through advice and support of UNIDO. It was decided that the main task of the BAG

would be to initiate and co-ordinate biotechnology programmes, develop a biotechnology information base for Saudi Arabia and training programmes/workshops on specific aspects of biotechnology, while promoting interaction between various disciplines and industry.

Positions open for molecular parasitologists and molecular virologists for International Centre for Genetic Engineering and Biotechnology, New Delhi, India

The International Centre for Genetic Engineering and Biotechnology (ICGEB) is an intergovernmental organization being established by 40 countries as a centre of excellence devoted to the application of genetic engineering and biotechnology to accelerate economic development. The United Nations Industrial Development Organization (UNIDO) assists the member countries of the ICGEB in establishing the Centre and is currently implementing an interim programme for a period of three years by which stage the Centre is expected to function as an autonomous inter-governmental organization.

At New Delhi, India, the initial focus is on the molecular aspects of hepatitis virus and parasitology, with special emphasis on protozoan infections.

The Centre is under the directorship of Prof. Irvin C. Gunsalus. The New Delhi component is under the directorship of Prof. K.K. Tewari. Positions are now available as follows:

Research scientists

Research scientists are being recruited at levels from Assistant to Senior Scientist with equivalence to academic attainment of Assistant to full Professor at major internationally recognized universities. Fluency in English is essential. The levels of appointment and the salary will be commensurate with academic excellence, experience and demonstrable leadership.

Please send resumé with three letters of recommendation to:

Prof. I.C. Gunsalus
c/o Mr. R. Croydt, Head
Project Personnel Recruitment Branch
UNIDO
P.O. Box 300
Vienna A-1400, Austria.

Expert missions to ICGEB affiliated centres

A number of expert missions were undertaken to several affiliated centres of the ICGEB and after long discussions between various visiting scientists and scientists of host countries, a pattern of common problems in laboratories of affiliated centres and member countries has emerged. These problems can be summarized as follows:

(a) Consistent problem of ready availability of fine chemicals, enzymes, and radio labelled compounds. These problems, in the most part, are a result of stringent foreign exchange controls existing in the country. Even if the foreign exchange is available there are delays in customs clearance.

(b) Inadequate library facilities, especially timely arrival of new periodicals. This problem keeps scientists in the dark as to the most current state of research.

(c) Lack of scientific interactions with the international scientists. It is not always possible for member countries to support the travel of their nationals to international meetings.

(d) Lack of member country scientist publications in international journals.

It is the intent of the ICGEB to help alleviate some of the above problems by interacting with the affiliated centres and member States in the following ways:

(a) Identify common research problems between affiliated centres and international centres. Develop co-operative programmes that can be funded for chemicals, scientific trips, and journals. The research problem in such cases will have joint co-operation.

(b) Planned international scientific conferences, the first of such a conference on protein engineering is planned to take place between 21-25 March 1988 in Trieste, Italy, prior to the Forum of Scientists to be held from 27-30 March 1988 in Trieste as mentioned earlier in this issue of the Monitor. Participants and scientists from member countries will be invited.

UN and other organizations' news

World Health Organization plans better AIDS management

The World Health Organization (WHO) has set this year's budget for combating AIDS (acquired immune deficiency syndrome) at US$43.7 million and has launched an international study to survey trends in AIDS legislation. By the end of the year, the budget will allow about 32 people, twice as many as now, to work full-time on monitoring the disease.

WHO wants to establish itself as the "worldwide clearing house for reliable information on AIDS". To that end, one of its newest and most important research projects is the global survey examining the trends in AIDS legislation. The results of the study would be expected to be presented to an international forum of public health and legal experts whose brief would be to provide guidelines on the alternative approaches to the notification and reporting of AIDS and human immunodeficiency virus (HIV) infection, the protection of blood supplies and donation of organs.

Most legislation so far is concentrated in North America, Australia and Europe, although the highest incidence of the disease is in Africa. There is growing pressure on WHO from its member States to consider AIDS as a global crisis and to ensure that management to combat the disease is centralized, although each country would be self-reliant in fighting the disease.

The Soviet Ministry of Health has proposed the establishment of an international co-ordinating committee for research on AIDS. Speaking on Moscow television, Dr. Evgenii Chazov, the All-Union Health Minister, said the issue had already been raised with the World Health Organization (WHO), and that the Soviet delegation to the WHO General Assembly in May hopes to discuss it more fully. The proposed committee, Chazov said, would co-ordinate investigations into the nature of AIDS, diagnosis, the development of vaccines, and also preventative

measures. International efforts would be important, Chanov said, in studying AIDS epidemiology. (Extracted from Nature, Vol. 325, 5 February 1987 and Vol. 327, 7 May 1987)

Social issues

School to study the ethics of biotechnology

A four-year, $100,000 programme called "Bioethics in Biotechnology" has been set up by Iowa State University (Ames) which will focus on such topics as the use of growth hormones in agriculture and the long-range ethical implications of biotechnology. The school's programme headed by Daniel J. Zaffarano, the university's vice-president for research, will be represented by the departments of molecular biology, biochemistry and other sciences, as well as economics, history, philosophy, political science, psychology and sociology-anthropology. Members of the Iowa legislature and other state agencies also will participate. Already, the university's Biotechnology Council has asked members of the programme to assist in the selection of the latest biotechnology research projects to be funded with state money. (Source: Chemical Week, 17 June 1987)

Regulatory issues

Battling biofundamentalists

Genetic engineers won a big victory when American regulators after much delay allowed the release of genetically engineered microbes into the open air. But although this represented a setback for the biofundamentalists, they continue to do well on several fronts.

The biofundamentalists' campaign is organised largely by Mr. Jeremy Rifkin, who now runs the Foundation on Economic Trends in Washington, DC.

Mr. Rifkin is now campaigning for a five-year moratorium on the release of genetically engineered material. The impact of a moratorium could be severe. BioTechnica International of Cambridge, Massachusetts, is waiting for permission to do field tests on its nitrogen-fixing microbe, which makes alfalfa plants grow faster. Monsanto, an American chemicals multinational, has waited for two years to test its genetically altered Pseudomonas fluorescens, which produces a natural protein that is toxic to the insect pests which attack the roots of maize plants.

A group of European scientists at Complutense University in Madrid and elsewhere has worked out a way to introduce foreign DNA material into cereals to change their properties, and now hopes to make them more robust. Enzygen in Athens, Ohio, is among the companies working out how to do the same for animals - introducing genes that are responsible for the production of growth hormone into dairy cattle in order to boost milk production, and into pigs to produce leaner meat.

For Mr. Rifkin, all these issues resolve into one big one: manipulating genes for profit, regardless of the ecological or moral consequences.

True, the lack of control over an altered bacterium once it is released poses incalculable risks. The newly introduced genetic information within microbes, plants or animals might somehow seep into neighbouring wildlife with unforeseeable consequences.

Most scientists are more sanguine about the risks. No adverse effects from the release of Frostban or other similar frost-resistant microbes have been observed and the potential savings to the American farmer are plain. Ten years of laboratory tests suggest that the likelihood of genetically altered microbes causing damage to the ecosystem is remote. American agrochemical companies, which have already spent heavily on tests, cannot see what more Mr. Rifkin's five-year moratorium could prove.

Besides, the release of genetically engineered products can be a relatively controlled event.

Scientists manage to mix breeds because even though the number and type of genes differ from animal to plant, their chemical structure does not.

Mr. Rifkin sued the American Department of Agriculture in 1986 in an attempt to stop research involving the transfer of genes between higher animals to breed bigger livestock, but he lost the case. The Recombinant DNA Advisory Committee, which exists to oversee federally funded genetic-engineering research, said that the benefits of such work - finding new treatments for human and animal diseases and the development of more efficient food sources, for example - were too great to ignore.

Since then, scientists at the University of California at San Diego have inserted the gene that codes for an enzyme called luciferase - which is responsible for a firefly's glow - into the genetic material of a plant. The plant now glows in the dark like a firefly, which shows that the genetic equipment of a plant can accept animal genes.

The sort of species integrity that Mr. Rifkin demands cannot be attained. Evolution itself works by forging new genes within species. One human gene added to a bull does not make a Minotaur - nor does it violate the integrity of cattle as a species. More ambitious genetic experiments would anyway fail because the genes would be incompatible, or would result in a creature incapable of reproduction. The geep, a "mosaic" made at Cambridge University by fusing the embryos of a goat and a sheep, was sterile, like the mule.

Similarly, the side-effects of other breeding experiments involving genetic engineering have been little different from those of their classical counterparts. In November 1986, the American Agricultural Department's experimental station at Beltsville, Maryland, announced it had managed to produce a line of deformed, arthritic, rust-coloured pigs by inserting the gene for human growth hormone into the pig's genetic machinery. These pigs produced similarly unfortunate offspring.

Most biotechnologists applauded the technical achievement involved in thus injecting foreign genes into fertilised animal eggs; however, the biofundamentalists immediately seized on the arthritic pigs and claimed that genetic engineering would increase the prevalence of disease in the animal kingdom. Yet such aberrations are quite common during ordinary animal breeding experiments, in which the genes are not manipulated. In fact, one aim of genetic engineering is to increase the ability of animals to resist the diseases to which classical breeding experiments have rendered them susceptible. Battery hens bred to produce more eggs are, for example, sickly creatures. (Extracted from The Economist, 27 June 1987)

Lords call for laws to govern release of gene-spliced organisms

The UK's House of Lords Select Committee on the European Communities in a report said that the Government should consider legislation to control the release of genetically engineered organisms into the environment.

At present, scientists who want to release genetically manipulated organisms must abide by voluntary rather than statutory guidelines. There is no legal requirement for organizations wanting to release such organisms even to notify the Advisory Committee on Genetic Manipulation (ACGM), which is in charge of the voluntary guidelines.

The Select Committee says that the European Community's programmes of research into biotechnology "pay insufficient attention to environmental aspects". The European Commission's own views about regulations to control biotechnology are divided "between member States favouring a low-key approach and those looking for severe restrictions". Meanwhile, the Committee says, "the release of genetically engineered organisms into the environment and the growing of new crops may have unforeseen adverse effects".

In the United Kingdom, the ACGM has approved four projects involving the release of genetically altered organisms: the genetic "tagging" of a caterpillar virus; a similar experiment with tagged nitrogen-fixing bacteria; and two projects with genetically altered potatoes. The Committee expects researchers to submit details of a fifth project, again involving the caterpillar virus, within the next few weeks.

The ACGM says that it wants legislation to force organizations to notify the Committee if they want to release novel organisms. The Department of Environment, however, is waiting for the Royal Commission on Environmental Pollution to report at the end of this year before the Department decides whether wider legislation is needed to control such releases. (Source: New Scientist, 25 June 1987)

Laws should balance safety against speed

The vast majority of large-scale industrial applications use organisms of intrinsically low risk, warranting only minimal containment practice. When it is necessary to use higher-risk organisms, further assessment criteria have been identified; physical containment has long been used to contain pathogenic organisms.

Recombinant micro-organisms of higher risk can also be handled safely with appropriate physical and/or biological containment.

The assessment of potential risk for environmental/agricultural applications is less developed than for industrial applications. Nevertheless, the means for assessing rDNA organisms can be approached by analogy through experience gained from use of traditionally modified organisms.

General:

(1) There is no scientific reason for special laws governing the use of rDNA techniques. OECD member countries should examine their existing oversight and review mechanisms to ensure that adequate controls may be applied while avoiding burdens that unduly hamper technological development.

(2) The process of guideline implementation should not be allowed to impede development in rDNA techniques.

(3) In order to facilitate data exchange and minimise trade barriers between countries, factors such as testing method, equipment design and microbial taxonomy should be considered at both national and international levels. Due account should be taken of ongoing work on standards within such groups as the World Health Organization, the Commission of European Communities, the International Standards Organization, the Food and Agriculture Organization, and the Microbial Strains Data Network.

(4) Special effort should be made to improve public understanding of rDNA techniques.

(5) For rDNA applications in industry and agriculture, OECD member countries ought to follow the development of these techniques. For certain industrial, environmental and agricultural applications, some countries may wish to have a notification scheme.

(6) Recognizing the need for innovation, it is important to consider appropriate ways of protecting intellectual property and confidentiality while assuring safety.

Industrial applications:

(1) Large-scale industrial applications should use micro-organisms of intrinsically low risk. Such organisms can be handled using good industrial large-scale practice (GILSP).

(2) If a micro-organism cannot be handled by GILSP, measures of containment corresponding to the assessed risk should also be used.

(3) Further research to improve the monitoring and controlling of unintentional release of rDNA organisms should be encouraged for large-scale industrial applications requiring physical containment. (Extracted from Recombinant DNA Safety Considerations, published by the OECD, 1986)

Germans claim DNA risk "unfounded"

The risks of using recombinant DNA technologies have been over-estimated, according to the FRG research society Deutsche Forschungsgemeinschaft (DFG). The society claims that there is no evidence that genetic experiments pose any particular threat.

DFG warns that the recommendations of the FRG parliamentary committee looking at the risks could lead to rules that would stifle research efforts. Researchers oppose the recommendation that the current voluntary safety guidelines be made mandatory.

While accepting some of the suggested restrictions, such as a proposed ban on manipulation of human genes, DFG opposes the suggested five-year moratorium on deliberate release. (Source: European Chemical News, 1 June 1987)

General

International biotechnology group to boost third world biotechnology

The application of biotechnology to the needs of the less developed countries (LDCs) will soon be addressed by an organization backed by the Rockerfeller's Resources Development Foundation's newly formed International Biotechnology Group, a "for profit" business development and venture capital management company which will evaluate and finance life science-based ventures in certain LDCs.

IBG is looking first to South East Asia, and countries such as Indonesia, the Philippines, Sri Lanka and Thailand, where it sees the political and economic stability and the infrastructure in which small biotechnology-based business ventures might work.

Initially, it has established an "Asian Fund" consisting of a $15 million pool which will allow investors in developed countries to co-invest with

Asian partners. Money for the fund has come from private investors, from international development agencies and similar donors.

Over the next nine to 12 months it will be looking closely into a number of agricultural projects which could be commercialised. Potential exists, it believes, for projects in micropropagation of selected plants; MAB and nucleic acid-based probes for plant improvement; bioprocessing for organic phosphate fertilisers; integrated shrimp aquaculture; and biotechnology-based inputs in milk production systems. Details of BDF from: Peter Hall, Resources Development Foundation, 2685 Marine Way, Suite 1220, Mountain View, CA 94043, USA or on (415) 960-3550. Details of IBG's activities can be had from Robert J. Parra, Suite 802, 1015 18th Street, NW, Washington, DC 20036, USA or on (202) 537 0138. This side of the Atlantic, talk to Gunnar Wessman, Svartbeckagatan, S-753 32 Uppsala, Sweden, or on +46 18 10 18 80. (Source: Chemistry and Industry, 1 June 1987)

Industrial safety club born

In order to provide industry with information and research on the safe operation of bioprocessing equipment, the UK's Department of Trade and Industry (DTI) and the Public Health Laboratory Service have set up an Industrial Biosafety Club. Ten companies have already joined the club.

At the moment, it appears that very little quantitative research on the possible hazards of industrial bioprocessing has been performed. The only data on human exposure to non-pathogenic micro-organisms used by industry are contained in confidential reports of accidental occupational exposures.

The application of risk assessment methods to bioprocessing is one of the aims of the new club, which will be supported by research at Warren Spring Laboratory (WSL) and the Centre for Applied Microbiological Research (CAMR), which will produce a state-of-the-art report on bioprocessing risk assessment for club members in a year's time.

Even less is known about exposure to high levels of human proteins than about non-pathogenic micro-organisms, since the application of large-scale protein production technology is more recent than basic fermentation methods. The relative novelty of large-scale bioprocessing with genetically manipulated organisms means that there are no quantitative exposure limits.

Despite the lack of risk data and numerical guidelines, some companies are using air samplers designed to measure leakage of micro-organisms from valves and seals. Whatever their reasons for doing this, the data provided could be misleading, according to research on samplers at WSL. It was therefore not realistic to simply put a sampler near a piece of processing equipment and believe the result.

The Health and Safety Executive's Advisory Committee on Genetic Manipulation will shortly publish an updated version of guidelines published in 1979 on fermentation with recombinant organisms. The update will not contain quantitative advice, but will include the Good Industrial Large-Scale Practice (GILSP) concept. GILSP, an idea borrowed from an OECD report on recombinant DNA safety published last year, places responsibility on the operators to make their own risk assessments. (Source: Chemistry and Industry, 1 June 1987)

Preventing genetic erosion

While research is under-way to develop genetic strains that are nearly perfect, an equally earnest counter-movement is being launched in Malaysia. The campaign urges the preservation and use of traditional seed varieties; it is the joint effort of Sahabat Alam Malaysia (SAM; "Friends of the Earth") and the Asia-Pacific People's Environment Network (APPEN), both of whom are working to meet the goals of the Seeds Action Network (SAN), a group started in 1984 to curb genetic erosion.

Citing the Irish potato famine in the mid-1800s as the past we may be doomed to repeat, SAM wants to alert the world to the dangers inherent in relying on only one or two hybrid strains (as happened in Ireland). SAM organizers tell the story of a rice disaster in the Philippines that began with the failure of one of the prized developments of the Green Revolution - a rice strain called IR-8. Growers then switched to two other new hybrids; both proved inadequate. Breeders then decided to try an original Taiwan strain, only to discover that local farmers in Taiwan had eliminated all the original seeds and planted most of their fields with IR-8.

One purpose of the seeds campaign is to keep such events from being repeated. The high-yielding varieties now being developed and marketed by a small number of wealthy and diversified transnational corporations are seen as useful only under optimal circumstances. More to the economic point, however, is that those hybrids can only be multiplied by the corporations that own the parental lines. If traditional open-pollinated varieties disappear, the consequences could be serious.

Genetic erosion is thus a serious and potentially disastrous problem, and one that can only be averted by the co-operation of agriculturalists throughout the third world. To this end, the organizers of the seeds campaign are collecting information about experiences with high-yielding varieties - how the seeds were acquired, how they performed, whether they are still being used (if not, why), and so forth. Those having such information should contact the Seeds Campaign, Sahabat Alam Malaysia, 37, Lorong Birch, 10250 Penang, Malaysia. (Source: BOSTID Developments, Vol. 7, No. 1, Winter 1987)

New warnings sounded on biodiversity crisis

The threatened loss of biological diversity is fast moving into the forefront of issues of concern to the scientific community, policy-makers, and the public. The latest statement of concern comes from the Smithsonian Institution.

In early April, the US Office of Technology Assessment issued a major report for Congress on "Technologies to Maintain Biological Diversity". And just recently, the seriousness of the global decrease in species that is occurring was the keynote theme that opened the annual meeting of the American Association for the Advancement of Science.

Biological diversity as a term covers the variety and variability among living organisms. It ranges from complete ecosystems to the chemical structures that are the molecular basis of genetics. It is a fragile and complex framework, the Smithsonian points out, noting predictions by some experts that at the present rate of destruction, almost one third of the world's arable land and one half of its tropical forests may be destroyed by the year 2000.

The Office of Technology Assessment's (OTA) report notes that biological diversity to the variety and variability among living organisms and the ecological complexities in which they occur. The report identifies diversity at three levels:

Ecosystem diversity: A landscape interspersed with croplands, grasslands, and woodlands has more diversity than a landscape with most of the woodlands converted to grasslands and croplands.

Species diversity: A rangeland with 100 species of annual and perennial grasses and shrubs has more diversity than the same rangeland after heavy grazing has greatly reduced the frequency of perennial grass species.

Genetic diversity: Economically useful crops are developed from wild plants by selecting valuable inheritable characteristics. Thus, many wild ancestor plants contain genes not found in today's crop plants. An environment that includes both the domestic varieties of a crop (such as corn) and the crop's wild ancestors have more diversity than an environment with wild ancestors eliminated to make way for domestic crops.

In assessing the role of Congress in responding to the current threat to biological diversity the OTA report identifies 10 "findings" in five different but related areas:

1. Strengthening the national commitment to maintain biological diversity:

- A comprehensive approach is needed to arrest the loss of biological diversity. Significant gaps in existing programmes could be identified with such an approach, and the resources of organizations concerned with the issues could be better allocated.

- Because maintenance of biological diversity is a long-term problem, policy changes and management programmes must be long-lasting to be effective. But, such policies and programmes must be understood and accepted by the public, or they will be replaced or overshadowed by shorter term concerns. Conveying the importance of biological diversity requires formulating the issue in terms that are technically correct yet understandable and convincing to the general public.

2. Increasing the nation's ability to maintain biological diversity:

- Current technologies are insufficient to prevent further erosion of biological resources. Thus, increasing the nation's ability to maintain biological diversity will require acceleration of basic research as well as research in development and implementation of resource management technologies.

- Many federal agencies sponsor diversity maintenance programmes that are well designed but not fully effective in achieving their objectives because of inadequate funding and personnel, lack of links to other programmes, or lack of complementary programmes in related fields.

3. Enhancing the knowledge base:

- Congress and other policy-makers need improved information on biological diversity. Such information cannot be supplied without improvements in data collection, maintenance, and synthesis.

4. Supporting international initiatives to maintain biological diversity:

- The United States has begun to abdicate leadership in international conservation efforts, with the result that international initiatives are weakened or stalled in the tropical regions where diversity losses are most severe. Renewed US commitment could accelerate the pace of international achievements in conservation.

- Constraints on international exchange of genetic resources could jeopardize future agricultural production and progress in biotechnologies. Such constraints are becoming more likely because developing countries with sovereignty over most such resources believe that the industrial nations have benefited at their expense.

5. Addressing loss of biological diversity in developing countries:

- Existing legislation may be inadequate and inappropriate to address US interests in maintaining biological diversity in developing countries.

- The Agency for International Development (AID) could benefit from additional strategic planning and conservation expertise in promoting biological diversity projects.

- A major constraint to developing and implementing diversity-conserving projects in developing countries is the shortage of funds. Present funding levels are insufficient to address the scope of the problem adequately. (Source: Chemical and Engineering News, 6 April 1987)

Biotechnology in space

Medical spin-offs from the space programme include biotelemetry for intensive-care units and respiratory gas auto-analysers, miniature electronic circuitry as applied to transdermal rechargeable pacemakers and programmable/implantable medication systems, and microminiature implantable human tissue stimulators.

Durable, lightweight materials originally designed for space have been incorporated into artificial heart valves and components for dialysis machines, and graphic image analysis techniques are being applied to magnetic resonance imaging, computerised tomography and digitised radiography.

While biotechnology is revolutionising medical diagnosis and treatment with such things as monoclonal antibodies, cloned genes, modified cell sub-populations, natural and synthetic hormones and proteins, some of these substances cannot be produced on Earth in sufficient volume or purity for clinical use.

In space, microgravity minimises three processes that interfere with purification and separation - sedimentation of cells and particles in suspension, thermal convection created by temperature-induced differences in solution density, and zone sedimentation of solutes in solution.

Perfectly uniform latex spheres have been produced under conditions of microgravity for membrane pore sizing, to measure blood flow and standardize drug carriers and tracers.

Space-based bioprocessing appears especially attractive for the following processes:

On Earth, sedimentation and thermal convection interfere with this process by remixing separated substances. Erythropoietin has been purified with a continuous-flow electrophoretic separator aboard a spacecraft. This resulted in 700 times the volume, with four to five times the purity achieved on Earth.

Electrophoresis in space has also been used to isolate cell populations that manufacture pure proteins when cultured on Earth. In early studies, human embryonic kidney cells have been separated into fractions rich in cells producing erythropoietin, human granulocyte stimulating factor, plasminogen activator and urokinase. Pituitary cells have been separated into fractions that produce growth hormone and prolactin. Experiments to separate pancreatic islet cells into their four constituent types will be helpful for research on islet cell interaction, the role of islet cell antibodies in diabetes mellitus, and the development of purified, minimally antigenic islet cell populations for transplantation.

Engineering of natural proteins is possible only after their three-dimensional structure is determined by X-ray crystallography - a process that requires protein crystals of large size and high quality. On Earth, crystal growth is limited by thermal convection forces that mix the crystallizing solution and upset the delicate solute balance. Space experiments have yielded lysozyme crystals 1,000 times as large as those produced on Earth, as well as crystals of beta-galactosidase that are 27 times larger. The structure of purine nucleoside phosphorylase - a bacterial enzyme that produces nucleoside analogs for chemotherapeutic, immunosuppressive and antiviral agents - is of special interest.

Crystallizing cell receptor molecules or hormone receptor ligands in space to determine their structure will allow the engineering of related peptide hormones. These in turn will lead to development of new drugs. Space crystallization experiments may also answer questions about the three-dimensional interaction of proteins and nucleic acids.

Space offers an exceptional environment for growing and studying cells in culture. Oxygen transfer in cell culture is facilitated by the lack of oxygen bubble buoyancy. This, combined with the absence of cell sedimentation, improves stability of the culture media. Further, the absence of gravity at least theoretically increases cell replication by minimizing the expenditure of energy needed for maintenance of surface forces.

Such studies will clarify the role of gravity in cell growth and metabolic energy balance.
(Source: Canadian Research/Biotechnology Canada, April 1987)

Human genome project

A year after the Human Genome Initiative began, biologists are beginning to come to terms with the goals and organization of the project.

In what will be one of its most rapidly produced committee reports, the US National Academy of Sciences is preparing a commentary on the current initiative to map and sequence the human genome. The Academy's committee on the topic, convened under the Board on Basic Biology, plans to publish its conclusions by June.

The committee joins a growing list of national bodies currently contemplating this major project, and this includes the Department of Energy (DOE), the National Institutes of Health (NIH), and the Office of Technology Assessment.

The fact that ideas of structure and organization are now being seriously considered is significant and reflects a real evolution of the biological community's response to the prospect of a megaproject of a scale and cost more familiar to physical scientists.

The principal organizational idea that began to emerge from the Academy committee's discussions was the establishment of about half a dozen research centres that would concentrate on specific aspects of the problem, including mapping, sequencing, technology development, and data analysis. This arrangement would allow the exploration and development of new approaches to the problem to go along with what committee members kept referring to as "real science". The business of ultimately trudging through all 3 billion bases of the human genome would, most agreed, have to be tackled in some kind of factory approach.

Although the Academy committee's discussion gave a sense that the human genome project was at last on its way, there was also a clearer recognition than has been apparent at previous gatherings that the practicalities are going to be even tougher than at first acknowledged. It was not that the committee heard any startling new evidence or covered new territory, but, as one member observed, "people got past the rhetoric" and faced up to the practical limitations of current techniques.

The ideal physical map of the human genome would actually be a line of bottles, each of which would contain DNA fragments about 40,000 bases long, the position of which on the genome would be accurately known. Producing individual fragments of this sort - which are known as cosmids - has been part of biologists' tool kit for some time. The challenge is to blanket the 30 billion bases of the human genome with overlapping cosmids so that there are no gaps in the map. That is a tough task, especially as some parts of the genome, particularly those with long stretches of repeated sequences, will prove very difficult to clone.

The clearly-stated limitations of mapping techniques so far available led to a recognition that a map, however good, might remain patchy for a long time. The discussions also led to the notion of combining cosmid mapping with a restriction fragment length polymorphism (rflp) map, the latter forming a very much coarser scatter of markers that would serve to pinpoint the position of cosmids around the genome.

The development of new techniques both for mapping and sequencing is going to be crucial to bringing the genome project within manageable bounds, and Academy committee members were therefore delighted to hear from Harvard University's George Church about "multiplex sequencing". If it works, this low technology, parallel processing approach has the potential to improve sequencing by a factor of 10. Church and his colleagues are now putting the system to the test, and if it is successful they hope to have sequenced 90 per cent of the *Escherichia coli* genome [which has 3 megabases] within a year.

The very real momentum that is now established behind the genome project nevertheless faces many uncertainties. For instance, proponents' interest in establishing a series of small, specialized centres reflects a recognition of the need for some sort of co-ordination and organization while maintaining flexibility, specifically in technology development. Although the prospect of trudging through the entire genome, whether mapping or sequencing, is widely described as being potentially immensely tedious, there is a fear that if a megacentre is established too soon to take on the job as a production task, then the technology might become frozen in its infancy.
(Source: *Science*, Vol. 235, 13 February 1987)

Biosensors in living matter

Together with the existing devices which react or respond to sunlight, smoke, the presence of metals, etc., a new type of sensor, called a biosensor is in a relatively advanced phase of study. The USA and Japan have been competing since 1962 to develop this type of sensor. Recently, research in this field has been stepped up especially as regards applications in medicine, agrology, the food sector, etc.

Biosensors are the result of inserting an enzyme, a molecule, or a cellular tissue into an electrode. This biological material reacts in the presence of certain chemicals or natural substances by creating impulses which are then transformed into electric signals processed by a computer and displayed on a screen or printer.

To date, only one compound, ferrocene, and its derivatives, has been able to satisfy the criteria for a successful mediator: namely chemical stability, low toxicity and the appropriate redox potential. However, Tony Turner of the Cranfield Biotechnology Centre told delegates of a new compound, tetrathiafulvalene (TTF), which in tests has shown certain advantages over ferrocene. For example, it is more pH sensitive and less oxygen sensitive.

Turner expressed hope that TTF would be able to replace ferrocene as a mediator for amperometric biosensors, the only biosensors commercially available.

According to a study carried out by US experts, the biosensor market, even if limited at present, will reach US$400 million by 1990 with a demand above all from the medical and agrifood sectors.

The Japanese industry is currently the most advanced in the development of this type of sensor. One of the most recent innovations is a device which can determine how fresh foods such as meat, fish, etc. are, as well as their quality. The sensors, inserted in the food under examination, react in the presence of certain chemical elements which develop during the process of decomposition.

Finally, at the Tokyo Institute of Technology the possibility is being studied of inserting various types of enzymes on a chip which are sensitive to numerous substances. In this way sensors could be developed to determine the taste of food, that is the presence and balance of the amino acids proper to them.

Biosensors are currently finding applications in the areas of blood analysis, fermentation analysis and food analysis. In addition to their use in enzyme electrodes, mediators can be used in DNA probes and for immunoassay enzyme amplification.

On the subject of molecular electronics, Professor Peter Day of Oxford University claims that advances in the reduction in size of electronic components had put them on a par with certain biological components, e.g. viruses.

Explaining that silicon-based technology was reaching certain limits imposed by, amongst other things, the sensitivity of microscopic components, Day has outlined the advantages molecular conductors promised, including their sensitivity to impurities, their self-assembly properties and their potential for high-density packing. Molecules also offer the advantage of being able to work in three dimensions. However, research on molecular electronics still faces several obstacles. The synthesis of molecular conductors, their chemical stability and their stability to heat are still problem areas.

As regards biology and pharmacology, advent of biosensors, capable of functioning continuously, even in sterile environments and at high temperatures, will open up a new era in the search for new substances and in the study of cultures and enzymes. (Source: IBIPress Bulletin, 11 May 1987 and Chemistry and Industry, 1 June 1987)

Protein splicing set to soar

Protein engineering, one of the key enabling technologies of biotechnology, will make a quiet but none the less significant impact on the chemical industry by the end of the century. By 1990 the market for protein engineered products should reach $180 million rising to $5.1 billion by 1995 and $15.8 billion at the end of that decade, according to US consultants Business Communications.

The technique, which involves the substitution of key amino acids, can lead to proteins that have improved properties. Of the markets projected, BCC estimates that agriculture and food processing will amount to $3.4 billion in sales by 1995 and $10.4 billion by the year 2000. Although this represents the largest sector, greatest growth will be seen in pharmaceuticals and speciality chemicals.

Growing at an average rate of about 37 per cent/year the market value will rise from $180 million in 1990 to $930 million in 1995 and $4.6 billion by the end of the century. Other applications will grow by about 32 per cent/year, contributing $320 million in sales by the year 2000.

With these rates of growth, protein engineered products will account for about 3 to 5 per cent of the proteins market and 35 to 45 per cent of the total recombinant products market. Nevertheless, the major limiting step in this development is the shortage of qualified scientists. Demand for researchers far exceeds supply, the consultants warn. (Source: European Chemical News, 25 May 1987)

Biotechnology predictions fail to materialise

The enabling technologies of recombinant DNA techniques have still not proved to be the cash flywheel that many had hoped for at the start of the decade. So far, the only individuals making money from biotechnology are shareholders benefiting, particularly in the US, from stockmarket hype.

It appears, according to delegates at the recent Biotech '87 conference organised by Online International, that biotechnology's time has not yet arrived. Nevertheless there are some encouraging signs.

Last year the EEC paved the way for a constructive new alliance between farming and biotechnology by agreeing to bring the cost of agricultural raw materials for the chemical industry down to the world free market price. Before this change of heart, chemical industry consumption of sugar dropped from 100,000 tons/year in 1968 to 62,000 tons/year in 1985/1986.

Cefic, the European Federation of Chemical Manufacturers, estimates that consumption of EEC-derived carbohydrate will now rise rapidly.

With Brussels now contemplating further changes to the common agricultural policy, Europe will become a more attractive location for potential investors. As supplies of cheap hydrocarbons become exhausted, farmers hope to step into the role of suppliers of raw materials for industry. But farmers will find that

they will benefit from biotechnology-derived inventions. Biotechnology will have an impact on animal and plant health, production and nutrition.

One of the most promising areas is the development of biological pesticides. Potentially these products are appealing from a number of different standpoints: they are toxic to target species, capital production costs are low and they degrade within the environment rapidly. However, sales of such products only command about 1 per cent of the $10 billion global pesticides market.

It is ironic that many of the same points that make microbial pesticides so desirable are also commercial weaknesses. These can be split into three general categories: persistence; spectrum of control; and speed of action.

Biotechnology now has opened up the opportunity to address the problem of persistence directly.

Similarly, researchers are now looking for organisms that can express the toxin genes more successfully. At the moment the amount of toxin produced in the "highjacked" organism is not enough to kill the pest rapidly.

One hurdle that will be more difficult to clear is the conservative attitude of the agrochemical industry. Historically, all innovative technologies are viewed more as a threat than an opportunity. (Source: European Chemical News, 25 May 1987)

Biotechnology in Western Europe

According to a two-year study of biotechnology in Western Europe and the US, American biologists neglect research in Europe. The study also warns that European and British scientists struggle to find venture capital and to earn respect for taking entrepreneurial risks.

In 1985, a biologist, Robert Yuan visited London to study British and European biotechnology for the US's Commerce Department. Yuan collaborated with staff in US embassies to compile a report, Biotechnology in Western Europe, to be published soon. It identifies a multitude of problems that block the translation of basic biological research into products.

The Commerce Department undertook the study, along with another on Japan's efforts in biotechnology, to help to make American business more competitive in the field.

In Europe, however, governments tend to set the pace for the exploitation of research. In Britain, for example, the role of the British Technology Group is to translate research at universities into commodities. Several things obstruct the process. Britain has responded slowly to the explosion in biological techniques for tinkering with recombinant DNA.

The report also notes that the UK Government has crippled universities with funding cuts. The result is a "gradual demoralisation of the research community".

The British Government has promoted start-ups of new biotechnology companies such as Bioscot, Biotechnics and Cambridge Life. But reductions in funding for universities have weakened them to the point where large multinationals such as ICI or Glaxo both seek expertise and invest abroad.

There is even the "curious situation", observes Yuan, of the Scottish Development Agency providing £30 million to Damon Biotech, an American company (started by an Englishman educated at Oxford), to establish a production company in Scotland. That company turned out to be an active competitor to Celltech, one of the first biotechnology companies set up in Britain.

Although Britain has a broader spectrum of biotechnology companies than any other country in Europe, many lack the capital to explore such fields as biosensors, gene transfer and expression in plants, or large-scale fermentation. Struggling universities also neglect these fields.

More than any other country, including the US, Britain leads in experimenting with methods of transferring technology, the report states. None the less, Yuan concludes that Britain "is the only country visited where government support of biotechnology-related research is decreasing significantly in real terms". He notes that the quality of British universities and laboratories has until now attracted foreign scientists to everyone's benefit. Fiscal cuts have changed that.

Biotechnology in the US enjoys a stronger industrial base than in Europe. Nevertheless, companies and laboratories in the US have neglected fields such as specialty chemicals, waste treatment and bioelectronics. The American executive's emphasis on rapid return on investment has narrowed industry's focus to biomedical products.

Nor do America's universities prepare graduates for global competition, says the report. Not only do they ignore foreign science, few students in the sciences learn foreign languages. (Extracted from New Scientist, 2 July 1987)

Industry outlook

The biotechnology industry may break even this year, according to financial analyst Linda I. Miller, who presented a financial overview during a February seminar sponsored by the Brookings Institution.

According to Miller, the 50-60 publicly held biotechnology companies now have an overall value of between $9 and $10 billion, based on aggregate stock prices. Last year, investors put $800 million into publicly held companies, and additional private placements pushed the 1986 total for private-sector investment over $1 billion. Although most of the money is concentrated in relatively few companies, altogether the industry has accumulated about $1.5 billion in cash.

Most of the new funds are pouring into companies whose promises for products and profits are largely still to be realized. None the less, total product sales reached almost $500 million in 1986, and that figure could double this year. The industry is still reporting overall losses, but it may break even in 1987 - particularly if several promising drugs, notably tissue plasminogen activator for treating heart attack victims, are approved for use in humans.

Although diagnostic devices receive only about 10 per cent of the overall R&D investment in the biotechnology corporate world, they currently account for about 55 per cent of all sales. Sixty-five per cent of the private-sector biotechnology investment supports the development of products for human therapy, but these pharmaceuticals represent a much smaller fraction of sales because of their more complicated testing and approval process.

So far, biotech-based products have cost about half as much to develop as typical chemical drugs. The new industry has had relative good fortune with regulators, particularly in receiving expeditious review of applications by the US Food and Drug Administration. Patent disputes, state and local regulations, the effect of federal efforts to reduce hospital costs, and accounting rules changes could lead to difficulties. (Source: Biotechnology, Vol. 5, April 1987)

B. COUNTRY NEWS

Brazil

New Biotechnology Centre in Rio de Janeiro

Work is to begin on the construction of the first biotechnology enclave in Rio de Janeiro, Bio-Rio, which will be located on an area of 200,000 square metres on the campus of the Federal University of Rio de Janeiro (UFRJ) on Ilha do Fundao. According to Antonio Paes de Carvalho, chairman of ABRABI (Brazilian Association of Biotechnology Companies), one of the purposes of Bio-Rio is to allow for integration between the university and the business community, so as to strengthen the modern biotechnology sector. A second part of the biotechnology enclave is due to be constructed on an area opposite Fiocruz (Oswaldo Cruz Institute Foundation), on Brasil Avenue. Far-Manguinhos, Fio-cruz' medicine production unit, will gain new space for expansion in the Bio-Rio area.

Mr. Carvalho remarked that Bio-Rio will be devoted to modern biotechnology and that the business firms which are candidates for the enclave must be national, or have the control of their stock in Brazilian hands. He predicted an initial investment of about $10 million and reported that Bio-Rio would be self-remunerative through payment of the services offered to the firms established in the enclave.

The administrative premises should be ready by the end of this year, as well as the large laboratory to render services to the companies and to the company "incubator." This will accommodate micro-businesses with support infrastructure for shared use. (Source: Jornal do Brasil, 14 April 1987)

Danish company plans enzymes facility

Denmark's Novo Industri has revealed plans to build a $5 million food enzymes facility at Curitiba in the Brazilian state of Parana which should be on stream by the end of 1988, according to Erik Sorensen, executive vice-president and head of Novo's bio-industrial group.

The new facility will be run by the Danish firm's wholly-owned Brazilian subsidiary and will produce enzymes "to satisfy initially the potential needs of the Brazilian food industry." Currently enzymes have not had much impact on this region as Brazil and other South American countries have been reluctant to become dependent on imports.

Nevertheless, Novo is confident that the market will soon grow and be equivalent in size to some of the major European markets. (Source: European Chemical News, 18 May 1987)

UNICAMP research in biotechnology

The State University of Campinas (UNICAMP) has formally purchased the country's largest research complex in the fields of biochemistry and agricultural biotechnology. This is the Agricultural Research Centre of Monsanto Industries of Brazil, located in Campinas.

The purchase of the centre is being financed by the State Bank of Sao Paulo (BANESCO), with the approval of the state government. UNICAMP will amortize the loan by including the payments in the institution's future budgets. According to the dean, it would take UNICAMP about five years to build and equip a centre of this size and it would cost about $10 million, at current values. UNICAMP will designate the centre as the Multidisciplinary Research Centre for Biological and Biochemical Research.

Biotechnology firm seeks to expand

One of the first companies in Brazil devoted to biotechnology, Bioferm, a subsidiary of Biobras, is seeking associates to participate in its expansion plan, which will permit ground-breaking activity in the private sector: the provision of services in research and development of technological processes in the area of biotechnology.

According to Marcos Maros Guia, general director of Bioferm, the decision to invite the participation of new business groups is a result of the success of the firm, created to develop technological processes for Biobras.

For the expansion plan, the company must attract several million US dollars to expand Bioferm's activities. According to Guia, the entry of new associates has already been cleared with FINEP (Funding Authority for Studies and Projects), which holds a 36 per cent interest in the company.

For two to three years, Bioferm will continue to hold a majority interest, possibly with 51 per cent of the capital. After this phase, the company plans to go public.

The new resources are needed for the continuity of the company's research projects, including the development of products for diagnosis of human diseases, in a later phase. Meanwhile, Bioferm will continue to do research for Biobras, under service contracts. (Extracted from O Globo, 6 January 1987)

Canada

National Biotechnology Advisory Committee recommendations

In its second annual report, the National Biotechnology Advisory Committee says Canada has yet to mobilise the human and financial resources needed to transform research into commercial reality.

The Committee strongly recommends that the government take steps to fortify the science base underlying future progress. Politicians must also ensure that rules governing the development and application of new technologies are comparable to those of Canada's trading partners. Particular attention is drawn to the need to clarify regulations for the approval of products and processes derived from new genetic techniques.

Future advances will be based largely on the genetic engineering of plants, animals and micro-organisms, so profitability in agriculture and its allied industries will increase with the availability of increased gene pool resources. Food production will be further enhanced by the development of plants with greater nutritional value, earlier maturation, disease resistance and stress tolerance. Development of biocontrol agents and biofertilizers will reduce negative environmental impact and production costs. Crops will be designed to meet specific food product or processing requirements. Opportunities to improve agricultural production, processing and food manufacturing exist at all levels.

To meet this challenge the report says it is important that Canada maintain a strong agricultural research and development base. The benefits of agricultural research carried out by federal, provincial and university laboratories over the past 100 years are evident throughout the world, but the industrial climate is not as conducive to commercial development as it could be. The committee is concerned about the lack of plant breeders' rights,

uncertainty over patentability, inflexibilities in the certification process for new varieties of plants, and unclear and unduly complicated regulations.

Canada has a well-established forestry and forest-product industry. But the industry is facing stiffer foreign competition and higher trade barriers. The potential contribution of biotechnology here is broad, ranging from tissue culture and micropropagation to the development and selection of fast-growing trees, to utilization of special bioreactors for pulp and paper waste treatment. The adoption of sophisticated forest-management strategies such as biological pest control and novel fertilization techniques could provide an excellent opportunity to demonstrate and promote biotechnology. Trials of new pulp treatment methods using micro-organisms and enzymes to improve the brightness and strength of paper are already underway.

Based on the industrial and economic implications of such developments, the committee recommends that forestry be identified as a national priority. Any new resources for forestry and forest-product research should be linked to national strategic objectives, and both government and university research programmes need targets developed in consultation with industry.

The National Biotechnology Advisory Committee was established in 1983 to advise the Minister of State for Science and Technology on biotechnology developments and the effectiveness of the national biotechnology strategy, and to further foster commercial biotechnology. Strategic priority areas have been defined as human and animal health care, plant strain development and nitrogen fixation, cellulose utilization and waste treatment, mining and mineral leaching. Networks have been formed in each field to link researchers from industry, universities and government. Priorities in basic research include developmental genetics of plants and animals, cellular genetics and physiology, microbial ecology, protein engineering, biomaterials, bioelectronics, and bioprocess engineering. (Extracted from Canadian Research/Biotechnology Canada, April 1987)

New institute opened

The Canadian government's $61-million Biotechnology Research Institute (BRI) opened in Montreal in May. When the facility is fully operational in three years, it will have a budget of $30 million, it will employ 225 people, 100 of them scientists, plus an equal number of visiting researchers.

The Institute's directors are already developing ties with Canada's biotechnology firms to conduct research on-site. "We have a mission to promote the transfer of technology to industry," says Bernard Coupal, BRI's director, who began his five-year term last autumn. R&D agreements have already been reached with Labatt Breweries for yeast and Domtar, Inc., a forestry firm, for lignin. Eventually, the Institute plans to get 25 per cent of its support from industry through licensing fees and royalty payments.

BRI was formed two years ago and had been conducting research in rented rooms at the Royal Victoria Hospital. Projects it is currently developing include:

- Pseudomonas strains to degrade polychlorinated biphenyls (PCBs) and pesticides;
- Bacillus subtilis that produces biosurfactant from a peat substrate;
- A synthetic gene for papain, a protease enzyme, inserted into brewing yeast for clarification of beer after fermentation.

The 17,000-m^2 facility, located in Montreal's Cité Scientifique, is the largest of three biotechnology centres established by the National Research Council. It has R&D in protein and genetic engineering, cell fusion and immunology in consultation with industry, universities and public organizations. When completed, its 1,500-m^2 pilot plant will be Canada's largest, with seven fermenters of 20 to 1,500-litre capacity, and a 500-litre continuous sterilizer plant. The other centres are the Plant Biotechnology Institute of Saskatoon and the Biological Science Division, Ottawa. (Source: McGraw-Hill's Biotechnology Newswatch, 1 June 1987)

New tissue culture laboratory

A new tissue culture laboratory is under construction near Upper Canard in the Annapolis Valley, Halifax. When completed in 1987, it will be the only commercial venture of its kind in Atlantic Canada.

The laboratory, built with financial and scientific assistance from the National Research Council, will be operated by Nova Biotechnology Inc. to investigate the production of 20 different fruit, herb and ornamental plant crops. (Source: Canadian Research/Biotechnology Canada, April 1987)

Companies jointly develop technology to minimize risks associated with open heart surgery and kidney dialysis

Allelix Inc. and Continental Pharma Cryosan Inc. (CPCI), have announced the establishment of a research collaboration and manufacturing agreement.

The research collaboration will accelerate the commercial production of Heparinase, an enzyme that alters heparin, a widely used anticoagulant. This restores the ability of blood to clot following heparin therapy which is used in open heart surgery and kidney dialysis and greatly reduces the risk of complications. CPCI holds several patents related to Heparinase production and medical applications of Heparinase.

CPCI's research in the area of heparin management has been conducted over the past several years by researchers at the Massachusetts Institute of Technology. Several products are being developed within this programme, including a heparin assay and a filter for removing heparin from a patient's blood. Research may also result in innovative products of potential use in the field of cancer, atherosclerosis and rheumatoid arthritis.

Large quantities of pure Heparinase will be required as certain of these products enter clinical trials. Presently, these quantities cannot be prepared economically from the current source of the enzyme. Allelix will clone the gene for Heparinase and produce the enzyme from a recombinant organism. (Extracted from Company News Release, 18 June 1987)

Denmark

State support for biotechnology

Danish biotechnology is to receive a governmental infusion of 500 million Danish kroner.

This investment is an attempt to introduce a new element into Danish research policy: an effort to steer research towards fields that promise economic growth.

New research centres will be established at technical universities and private firms at a cost of 410 million kroner. New scholarships will be established for 70 million. Another 20 million kroner will be spent on information and technology evaluation.

The proposal was supported by a relatively large majority in parliament with a call for special appropriations for research in environmentally sound agricultural technology, however. Similar demands for ethical and ecological considerations have been raised by environmentalist organizations. (Extracted from De Telegraaf, 29 January 1987)

European Economic Community

Directives to harmonize biotechnology R&D efforts

The Commission hopes by the end of the year to establish a four-pronged approach that will harmonize Europe's biotechnology R&D efforts. This approach will include the development of EEC-wide regulations covering both health and environmental aspects of the technology, better control of feedstock prices, harmonized protection of intellectual property and development of a co-operative research programme.

The introduction of the starch and sugar regime allowing the European biotechnology industry access to carbohydrate feedstocks at world prices was the start of the effort. So far it is difficult to assess the impact of the changes as accounts have not yet been produced.

The Commission expected to present four directives to the EEC council of research ministers by July of this year.

If all goes well the directives will be considered by the European parliament by March 1988. The new single European act will give the parliament much greater powers.

Development of the regulatory framework involves a number of different commission departments (directorate generals). DG III is responsible for looking at the possible risks associated with micro-organisms affecting plants and animals and the concept of good industrial large-scale practice (GILSP).

A directive for processes involving organisms potentially hazardous to humans, under the auspices of the new article 118A, is being drawn up by DG V.

Rules to contain the risks of industrial accident and waste management are currently being considered by DG IX. Meanwhile, DG VI and DG XI have the difficult task of hammering out a framework for deliberate release of genetically manipulated organisms into the environment.

The Commission is also very conscious of the importance of intellectual property and is hoping to harmonize patent laws within the Community.

Before the Commission can construct a patent protection framework for the whole Community a number of key issues must be sorted out. The EEC has to decide the patentability per se of micro-organisms.

One encouraging move recently was the FRG decision to allow the Dutch firm Gist-Brocades to deposit a genetically modified yeast in order to get a patent. When depositing a micro-organism for patenting, industry must be guaranteed confidentiality. This is particularly important if patent applications are to be challenged.

One crucial area in the patents field is the existence of grace periods to allow academics to publish their scientific findings and still apply for patents. Currently the grace period can vary from six months to as much as two years, as in the US. Some countries within the EEC have no grace period at all.

Brussels also hopes to improve the competitiveness of European biotechnology with its proposal for funds amounting to 3120 million under the auspices of the R&D framework programme. This, however, cannot be put into action until the Council of Ministers sanctions the whole budget for the programme.

At the last meeting of the Research Council, although 10 of the member States were willing to accept a compromise budget, both the UK and FRG were still holding up the plan.

The new compromise suggested by the Belgian research minister will allow for a budget of about Ecu 6.5 billion for the period 1987-1991 although Ecu 843 million of this total will only be committed budgetarily after 1991. Originally it had been planned to have a budget of Ecu 7.7 billion for a five-year programme running from 1987-1992. The Commission is also looking at the possibility of stimulating the industry/agriculture interface.

This plan will look at ways to develop new crops that are better suited to market needs, the biorational use of scientific advances and the development of biotransformation technologies. Italy and Denmark are believed to be showing interest in the concept of whole crop harvesting where agricultural refineries will fractionate useful components for different end products. (Extracted from European Chemical News, 6 April 1987)

EEC seeks harmonization of vaccine regulations

Brussels is planning to extend the directive that harmonizes the criteria for approval and manufacturing of pharmaceuticals and medicines in the EEC to include vaccines and other immunological products.

Article 34 of the original 1975 directive excludes serum-based products and vaccines from the rules governing the rest of pharmaceuticals. This is because it is difficult to guarantee or measure quality control throughout the whole process, as it is not easy to test the end product.

Currently each member State has its own sophisticated systems regulating the use of these products and, although the standards are similar, the quality control requirements differ.

Before the Commission can bring forward its proposals it first has to find a consensus among member States' experts.

The Commission is hoping to meet the deadline set by the framework white paper for the harmonization of the market at the end of the year. (Extracted from European Chemical News, 4 May 1987)

EEC to constrain gene-product releases

The European Commission is to propose new rules this summer governing the release into the environment of genetically altered organisms.

Geneticists will have to convince a committee of experts, picked by the Commission from the countries of the EEC, that the gene-spliced organisms they wish to release will not disrupt the environment or spread out of control once introduced into the open.

Heaviest pressure for the safeguards is from the FRG, where Green politicians claim to have forced a five-year moratorium on releases. The Rainbow Group, a cadre of Green MePs, has called for a Europe-wide moratorium on all releases of manipulated organisms. It alleges that genetically engineered

herbicides for maize have been spilled in the Rhine and that other gene-spliced products have been tested in the Third World.

The only other countries in the EEC that have drafted rules to monitor or sanction releases are the UK and Denmark. In Britain, voluntary guidelines for release were published last year by the Genetic Manipulation Advisory Group (GMAG), a body set up by Britain's Health and Safety Executive to deal with safety issues relating to genetic engineering.

The GMAG will judge applications on a case-by-case basis. If the European committee of experts materialises next summer, then national monitoring bodies such as the GMAG will have to refer each application to it for full approval. (Source: New Scientist, 12 February 1987)

Co-ordinated action

Health ministers of the countries of the EEC have agreed to co-ordinate action to tackle the AIDS epidemic. They will set up a working party of 12 public health officials which will share data on the spread of infection with human immunodeficiency virus and co-ordinate research. One of their first tasks will be to consider ways to speed up exchange of information and means of co-ordinating scientific research in individual countries.

The group will also consider controls on travellers. Ministers said that systematic and obligatory screening of people at frontiers would be ineffective in controlling the epidemic. (Source: New Scientist, 28 May 1987)

Federal Republic of Germany

Commission reports on genetic engineering

Wide-ranging recommendations on the applications of genetic engineering are contained in a report of an FRG parliamentary commission. Although generally approving the use and exploitation of genetic manipulation, the commission calls for a ban on experiments on fertilized human eggs that have the potential to develop into "complete human individuals" and for a five-year moratorium on the environmental release of genetically transformed micro-organisms.

The 400-page report, Chances and Risks of Genetic Engineering, was approved by 16 of the 17 members of the inquiry commission ('Enquete Kommission'), composed of eight experts from industry and science and nine members of parliament.

The report is designed to help the Bundestag to devise new legislation and to inform the public. It applauds the exploitation of genes and the opportunities for more efficient, economic and ecologically beneficial farming. But production of herbicide-resistant plants should be allowed only if the "use is promoted of herbicides that are without ecological or toxicological risk".

The report is not opposed to the application of genetic engineering methods in animal breeding and recommends the "promotion of the use of transgenic animals in biomedical basic research".

More reliable and precise prenatal diagnosis by means of genetic techniques are "welcomed" in the report. But there should be a guarantee that no unacceptable abortion practices will emerge. The "sociological compulsion of abortions of embryos with genetic defects" has to be opposed. But the screening of newborn babies to recognise treatable diseases is a "worthy instrument of preventive medicine", although screening for untreatable diseases was rejected.

The injection of genetic material into human cells is seen as a "basically acceptable form of therapy", but only if the individual is properly informed by a neutral physician or scientist and if the practice is approved by a special 'committee for biological safety' at the Bundesgesundheitsamt in Berlin.

Experiments on human germ-line cells are to be prohibited even if they are aimed at therapy, "if the germ-line cells can grow into complete human individuals".

The "guidelines for protection from dangers through in vitro recombined nucleic acids", created for use in gene laboratories, must be adopted in all production processes, in particular genetic work with retroviruses, cell fusion and hybrid cells. The release of genetically transformed micro-organisms must be stopped for five years and this moratorium should be used for risk analysis and further research into possible ecological dangers. The release of viruses into the environment is prohibited with the exception of vaccines for humans and animals.

Generally, the commission emphasised that the existing guidelines have proved efficient even though they are voluntary, but they should be made legally binding. (Source: Nature, Vol. 325, 5 February 1987)

Factor VIII claim period extension

FRG manufacturers of Factor VIII and their insurance companies have agreed to extend the limitation period for liability claims from AIDS infected haemophiliacs to 31 March 1988. Parties to the agreement are Alpha Therapeutics, Beringwerke, Trepenwerke, Immuno and Travenol along with the Allianz, Alter Leipziger and Colonia insurance firms.

Bayer is facing around 20 liability claims from haemophiliacs who claim to have contracted the AIDS virus after using contaminated blood clotting agents produced by the FRG major's US affiliate.

There are doubts whether liability can actually be established. Haemophiliacs commonly use Factor VIII from a number of producers.

According to Hans-Joachim Kramer of the FRG pharmaceutical manufacturers association, settlement of the claims against German Factor VIII producers is solely in the hands of their insurance companies. Around 60 per cent of the FRG's 3,000 haemophiliacs receiving Factor VIII have been found to be HIV-positive and 56 have developed the full-blown disease.

The FRG pharmaceuticals industry association (BPI) says that the one-year extension will give the producers and the insurance firms time to process all individual claims. Justified claims will be settled "quickly and unbureaucratically," according to a BPI spokesman.

The deal applies to all Factor VIII products sold in the FRG and liability has been limited to DM 200 million/plasma product and DM 500,000/person.

Usually the limitation period for liability suits under FRG drug law is three years but as AIDS tests have only been available since 1984 some victims were facing expiration of their rights to claim before knowing they were affected. Around 50 AIDS positive haemophiliacs have asked for damages so far.

The State prosecutor's office in Bonn is investigating a leading Federal Health Ministry official on charges that his negligence led to the infection of about 2,000 haemophiliacs with AIDS after they had been given contaminated Factor VIII blood plasma products.

Charges of bodily injury and contributing to offences against drug laws were brought by an attorney on behalf of a client. According to the attorney, the health official should have assured that hospitals used only blood products which had been tested for the virus. (Source: European Chemical News, 23 March 1987, 6 April 1987 and 11 May 1987)

Organisations form genetic engineering working group

A "Working Group on Genetic Engineering" has been formed by the Technical University of Darmstadt, the Boehm and Merck companies in Darmstadt, and the Grunenthal company in Aachen. The four partners, who describe their form of co-operation as unique in the FRG to date, want to develop genetic engineering projects ranging from basic research to the production stage of a new material, to jointly utilize expensive research equipment, and to exchange their special know-how. Half of the costs of the working group's research projects is paid by the Federal Ministry of Research and Technology. All the projects of the working group, which has drawn up a co-operation contract, are to be ready for application by the companies within three years if possible and monitored by external evaluators.

In informal research co-operation the four partners have already developed a number of projects, including new drugs to prevent blood clots and inflammation, and for use in shock therapy. Among the first programmes of the working group is the search for an enzyme to help pinpoint the underlying cause of inflammations in patients and research at the Technical University of Darmstadt on factors to stop the growth of lung tumours.

The Darmstadt consortium will concentrate on applications-oriented research, in contrast to other genetic centres. Right from the start, the working group intends to develop all methods autonomously and not to fall back on previous developments from the United States. (Source: Technologie Nachrichten-Management Informationen, October 1986)

Gene-splicing fears halt insulin unit plans

Fears associated with the potential risks of biotechnology have prompted the FRG state of Hesse to deny Hoechst permission to build a gene-spliced insulin plant. The State's Environmental Ministry is to hold a public inquiry before considering whether or not to give the plant the go-ahead. The chemicals major is hoping to test their product recombinant human insulin on an industrial scale at a planned facility in Frankfurt.

Local environmentalists are opposing the plant on safety grounds. Although Hoechst has insisted that sterilization of its waste water guarantees that the genetically modified E. coli bacteria used in the process are not released into the environment, opponents have pointed to recent experiments in the US which they claim suggest the opposite.

Hoechst now has to choose between withdrawing its application, which seems unlikely, or shedding more light on the safety aspect. The State's decision, based on a recommendation by the Environmental Ministry, could delay Hoechst's entry into the genetically engineered human insulin market for several months.

The Frankfurt-based group has been producing porcine insulin since 1983 using an enzymatic process and is currently testing its new genetic technology at the fermentation stage. The test phase before industrial-scale production is projected to last two years. The Hoechst subsidiary Behringwerke hopes to begin broad clinical trials with the new drug this year.

The Hoechst case could form the basis for approving future applications for recombinant DNA projects in the FRG. The Federal Government has developed safety guidelines for biological experiments, but these apply formally only to projects supported with State funds. Although not binding, the rules are generally respected by companies involved in genetic research. (Source: European Chemical News, 6 April 1987)

Bayer, Hoechst link up in AIDS research

In an unusual move, FRG chemical giants Bayer and Hoechst have pooled their research efforts in seeking a means of combating the virus that causes acquired immune deficiency syndrome (AIDS). Although the two companies are rivals in many commercial areas and have no business ties, the decision to combine their expertise in virology and immunology in AIDS research was taken in light of the rapid spread of the disease, the urgent need for an effective antidote, and the high development costs this will entail. If the joint study leads to a viable product, it is unclear as yet whether the partners would market it jointly or independently. (Source: Chemical and Engineering News, 20 April 1987, p. 8)

Finland

Call for financial increase to biotechnology programme

The Finnish Academy presented its proposal at the end of January for a national development programme in biotechnology and molecular biology for 1988 to 1992. The proposal was developed by the Biotechnology Section of the Academy, the chairman of which is Professor Pirjo Makela.

The goal is to achieve a significant improvement in Finland's biotechnology research during the 5-year period. Consequently, an additional 184 million markkaa, or 37 million per year is proposed to be spent on training, equipment and research.

There is already strong interest in biotechnology research in Finland. About 200 projects are now underway at technical institutes and research centres throughout the country. However most of the projects are small and inefficient.

The development programme should double the number of researchers who are capable of using the new biotechnology methods and should also make the application of biotechnology in various fields of industry more efficient. (Extracted from Hufvudstadsbladet, 31 January 1987)

Hungary

UK biotechnology firm enters joint venture

Cambridge Life Sciences, the small UK biotechnology company, will be signing a joint venture agreement which will give it access to the cream of Hungary's biological research. CLS, which is based at the Cambridge Science Park has already taken on board two Hungarian research projects seen as having major commercial potential.

The agreement is with the Hungarian company Vepex, which is owned by the Hungarian Academy of Sciences and two State banks. The two research projects involve a simple blood test to detect the presence of parasitic worms in humans and animals

while the second is an advanced method of extracting and purifying gamma linolenic acid, a potent pharmacological agent used in the treatment of pre-menstrual tension, certain eczemas and rheumatoid arthritis.

CLS and Vepex each have a half share in a new company, Biotechnology International, through which CLS will have exclusive marketing rights to the fruits of up to 90 per cent of the research work in the six institutes under the aegis of the Hungarian Academy of Sciences.

In return, Vepex has access to the complete range of CLS diagnostic products, veterinary and clinical, for marketing in Comecon and Third World markets. And through an existing CLS subsidiary, Cambio, the Hungarians will be able to buy biological reagents to further research. Vepex will also receive regular market research analyses designed to direct research programmes towards needs in Western and Third World markets. (Source: The Financial Times, 12 May 1987)

Italy

Italy boosts biotechnology funds

The government is earmarking L 400 billion ($306 million) for projects between 1988-1992. The funds will be used to support biotechnology research in medicine, chemicals, food and agriculture and environmental protection under the national research programme.

Through this programme, Italy is hoping to corner a 10 per cent portion of the world's biotechnology market by the year 2000. This could mean a market worth around L 2 trillion for the Italians, according to government estimates. (Source: European Chemical News, 27 April 1987)

New biotechnology association

A new association has been formed within Federchimica, ASSOBIOTEC, the national association for the development of biotechnology. Any company interested in biotechnology products and processes in Italy can join this association. Federchimica, which has already shown its interest by publishing a study on "Biotechnology in Italy: an opportunity for industrial development", seeks to help out those companies that work or will work in this field, to solve technical, economic and legal problems. This goal will be achieved by participating with the appropriate ministries in the formulation of national research and development programmes; by preparing proposals favouring biotechnology through financial and tax assistance, and which follow regulations to be issued for the production and marketing of substances resulting from biotechnology. The association will also concern itself with the development and execution of EC sponsored programmes. (Source: BIOTEC, November/December 1986)

Biotechnology industry interests

Italy's pharmaceutical industries are getting set to take part in the biotechnology race. Specific programmes have been developed by Farmitalia-Carlo Erba (part of the Montedison group), Selavo, Sorin Biomedica, Lepetit, Recordati, Sereno and Menarini. Other companies such as Sigma Tau and Biomedica Foscama have also launched major research programmes.

In three or four years, a Farmitalia-Carlo Erba research centre employing several hundred researchers - an estimated 1,800 by the late 1990s - will be established at Nerviano (Milan).

"This facility," says Professor Nasue, who is in charge of research at Farmitalia-Carlo Erba, "will enable us to apply all cloning and DNA recombination techniques. Our technical personnel will include people specially trained in the fermentation of micro-organisms for large-scale reproduction. We will be working on a pilot project involving research on ways to improve production. In addition, we are going to study and try to develop monoclonal antibodies that are capable of attacking tumours without causing major toxic side-effects." (Extracted from Scienza Duemila, April 1987)

Plan to map the human genome?

Italy is planning to enter the race to map the human genome, chiefly because the National Research Council (CNR) believes it has a lot to offer. CNR president Professor Luigi Rossi Bernardini, announcing the decision, said that the council's mind had been made up as the result of a large meeting held in Rome under the chairmanship of Renato Dulbecco of the Salk Institute. The plan is to set up a new institute in Rome. (Source: Nature, Vol. 326, 23 April 1987)

Group organised to pool medical skills

The first molecular genetics co-ordinating group has been established in Italy. The purpose is to create an archive of skills available in Italy in the field of molecular biology which can be used for the diagnosis and prevention of hereditary diseases. In particular, the initiative is aimed at optimizing the knowledge and material available for prenatal diagnosis with an analysis of the DNA through hybridation with probes. There are now various Italian groups that have used these techniques at the research and clinical levels. The initiative, pursued by professors Paolo Durand and Giovanni Romeo as of now includes eight fields of interest, each of which is headed by a co-ordinator:

Mapping of the human genome: M. Rocchi, Genoa;

Coagulation defects: A. Fontani, Rome;

Hyperlipidemia: S. Calandra, Modena;

Collagenopathy: R. Cancedda, Genoa;

Thalassemia and haemoglobinopathies:
C. Camaschella, Turin

Muscular dystrophies and cystic fibrosis:
G. Romeo, Genoa;

Follow-up of prenatal diagnosis: B. Brambati, Milan;

Phenylketonuria and other metabolic diseases:
G. Andria, Catanzaro.

(Extracted from BIOTEC, April 1986)

Italy attracts gene field tests

The absence of laws to regulate the field testing of genetically engineered organisms in Italy appears to be the spur in a deal between Advanced Genetic Sciences of the US and Sicily's Agricultural Industrial Development. The two firms plan to field test the US company's genetically engineered antifrost bacteria Frostban in Sicily and Sardinia.

Italy could, in fact, become the testing ground of Europe. Another move in this direction was made recently by Montedison following its acquisition of

the California-based firm Plant Cell Research Institute. Currently, the EEC is drawing up plans for a directive to regulate the deliberate release of genetically engineered organisms later this year. (Source: European Chemical News, 13 April 1987)

Japan

Biotechnology promotion projects to be supported

The Government is increasing its biotechnology promotion projects to keep up with the US. The Ministry of Finance and the Ministry of Agriculture created the government-industry Bio-Oriented Technology Research Advancement Institute (BRAIN) in October 1986. The Health & Welfare Ministry will set up a similar group in October this year to focus on health science. These groups are modelled after the Key Technology Center, which was formed by the Ministry of International Trade and Industry and the Ministry of Posts in 1985 to stimulate the development of high technology by the private sector. Some 830 firms have joined BRAIN, and 91 have signed up for the Health Ministry's project. The Key Technology Center has already assisted several projects, including some being conducted by the Protein Engineering Research Institute. Several companies including Kirin Brewery, Kyowa Hakko and Mitsui Toatsu Chemicals will form PCC Technology to develop new techniques to efficiently produce substances for drugs, dyestuffs and perfumes.

Japan's Health Ministry is particularly conscious of the need to catch up with the US. Some companies see problems in receiving government assistance, because it is given as loans that may have to be paid back before the companies receiving them can turn a profit. One project participant also points out that companies tend to keep the best research data to themselves. The BRAIN project is to some extent held back because 50 per cent of its 830 corporate members did little more than invest money. The Ministry of International Trade and Industry and the Ministry for Science & Technology are now pushing their Yen 1 trillion, 20-year Human Frontier Science Programme, a multinational effort that will involve research into biomechanisms. (Extracted from Japan Economic Journal, 14 February 1987)

International competitiveness

The United States Government is investing about nine time as much in biotechnology research projects as are the Japanese. This statistic came from Sumiko Ito, vice president for investment banking at Nomura Securities International (New York, NY), speaking at an executive seminar on biotechnology strategic management. Other data, compiled by Nomura Research Institute and presented in table I, show that Japan has spawned only two or three biotechnology specialty firms (compared to 200 in the US), and that since 1984 Japanese researchers have not received a single patent related to gene operation (compared to 24 for US scientists).

At the meeting, Ito noted that most of Japan's biotechnological activity takes place within its established industry. Interestingly, however, the pharmaceutical companies cannot boast the earliest involvement. Nomura's survey of 145 Japanese firms found that greater than 60 per cent of the chemical, textile and pulp, and food companies initiated biotechnology research prior to 1974. Fully half of Japan's pharmaceutical houses did not enter the field until after 1980.

On the finance side, Ito stressed that US ventures can secure funding from a variety of sources, including venture capitalists, wealthy individuals, large institutional investors, R&D limited partnerships, and America's well-developed public equity markets. In Japan, however, financing young companies is more difficult. Only about 3-5 per cent as much venture capital funding is available; Japanese institutional investors are more conservative; and limited partnerships do not exist. Additionally, it is harder for a company to go public: while some 700 firms made initial public offerings in the US last year, only 50 did so in Japan.

Ito said that the sole area where Japan has an advantage over the US is in strategic policies designed to move Japan forward in biotechnology. In general, the Japanese and European governments are more supportive of biotechnology than their US counterpart, added Nigel Webb, president of the Weston Biotechnology Group (Weston, MA), especially in areas like technology transfer, industrial grants and loans, and risk capital (see table II).

Japanese firms do provide a number of business opportunities for US companies, Ito stressed, including research funding, sponsoring Japanese clinical trials, marketing and distribution, and joint ventures. On the financial side, Japanese insurance and venture capital firms might participate in second-round financing of US start-ups, and US firms doing public stock offerings could choose to place some shares in Japanese markets.

TABLE I

COMPARISON OF U.S. AND JAPANESE BIOTECHNOLOGY

	USA	JAPAN
No. of Pure Biotech Firms	200	2-3 (200-300 companies participate as subsidiary)
No. of Publicly Traded Firms	25,500	1,002
Biotech Employment	5,000-6,000	1,000-1,000
1986 Gov. Assistance for Biotech Research	1000 mil.	200 mil.
Percent of Papers (on gene sample molecular biology journals)	30-40%	6-9%
No. of Patents Related to Gene Operation (1980-7)	24	0

Data Courtesy Nomura Research Institute

TABLE II

FINANCIAL SUPPORT FOR BIOTECHNOLOGY

	Europe	Japan	US
PRIVATE SUPPORT			
• Corporations	•	•	•
• Venture Capital	+/-	-	•
• Public Markets	-	-	•
GOVERNMENT SUPPORT			
• Biotech R&D	•	•	•
• Technology Transfer	•	•	-
• Tax Credits	•	•	•
• Industrial Grants/Loans	-	•	-
• Risk Capital	•	•	-

Data Courtesy Weston Biotechnology Group

(Extracted from Biotechnology, Vol. 5, May 1987)

Bioindustry association launched

The Ministry of International Trade and Industry (MITI) approved the launch of the Bio Industry Association (BIA) in late February. To date, 325 companies, 50 academic organizations and 1,300 individuals have joined the new association. Kei Arima, emeritus professor at Tokyo University, is president; Eiji Suzuki, chairman of Mitsubishi Chemical Industries, and Nikio Kato, president of Kyowa Hakko Kogyo Co. are director general and managing chairman, respectively. The new group incorporates BIDEC, Bioindustry Development Center, which had been the central organization of biotechnology industry in Japan, and the Fermentation Engineering Association, to which BIDEC formally belonged. (Source: McGraw-Hill's Biotechnology Newswatch, 4 May 1987)

Sumitomo begins sales in Japan of IFN-α for cancer

Osaka - Sumitomo Pharmaceuticals Co. has begun marketing "Sumiferon," alpha-interferon for treatment of kidney cancer and polymyeloma. The firm has also filed an application with the Ministry of Health and Welfare (MHW) to use the same interferon in hepatitis B treatment.

Sumitomo claims "the world's largest" interferon plant, including an 8,000-litre fermentation tank, which opened in February at Hikawa, Shikoku Island. Its production is based on Namalwa-cell technology (human lymphoblastoid cells of Burkitt's lymphoma), which Sumitomo licensed from Wellcome Foundation Ltd., London, in 1980. (Source: McGraw-Hill's Biotechnology Newswatch, 4 May 1987)

Silk component in bioreactor for enzyme immobilization

According to Japanese researchers, ordinary natural silk may become an important component in biotechnological processes of the future. Silk fibre has proven to be an extremely good material to which enzymes can be affixed. Researchers at the Tokyo University of Agriculture and Technology discovered that natural silk acts as an outstanding immobilization material for enzymes.

Natural silk has been shown to be superior to other materials on one count. Enzymes bound to the fine fibres of natural silk are extremely tolerant to temperature changes and more importantly, they are resistant to high temperatures.

The ability to withstand high temperatures is an extremely important property, since enzymes are usually so sensitive to high temperatures that they lose their ability to function. Because of this insensitivity to heat on the part of enzymes attached to silk, researchers now believe that silk will be a future component in bioreactors. (Extracted from Ny Teknik, 30 October 1986)

Sweden

Biotechnology centre fully functional in two years

In just under two years the new centre for life sciences will be completed at Huddinge Hospital, Sodertorn. Better diagnostic methods and new and better pharmaceuticals and vaccines are some of the results that are expected from this research.

"Gene technology is the main thrust of this medical research," said Professor Jan-Ake Gustafsson, executive vice president of the Centre for Biotechnology. A centre at which basic research and clinical research co-operate with corporations will give new impetus to this research. The biotechnology centre is seen as the motor that will enliven the town of Sodertorn. A research city for advanced scientific work is one of the corner-stones of the new Sodertorn. There are also plans for a university, an airport, a railway station, and new residential areas.

Two parts of the planned centre for life sciences are already established. About 40 people are already working at the biotechnology centre at Huddinge Hospital and work has also begun at the Centre for Dental Technology and Biomaterials. Professor Gustafsson hopes other centres will be established at the research city, as well. The Institute for Medical Technology will be moved from Karolinska Hospital, and in April the new Institute for Molecular Biology will be opened, headed by Professor Henrik Garoff from Heidelberg, FRG. (Extracted from Svenska Dagbladet, 19 February 1987)

United Kingdom

UK releases of engineered organisms

Three of four planned UK experiments involving the deliberate release of genetically manipulated organisms are set to go ahead in the coming weeks. All three had been revised in response to comments from the UK Advisory Committee on Genetic Manipulation (ACGM), which expressed itself happy with the revised plans at a meeting in early May. Revised plans and preparations for the fourth experiment, which involves baculoviruses, have not yet been submitted to ACGM.

Two of the planned experiments involve potatoes, the third involves Rhizobium, the nitrogen-fixing bacterium that forms the root nodules of leguminous plants. The potatoes, to be planted in a carefully monitored field near Cambridge by scientists at the Plant Breeding Institute (PBI) of the Agricultural and Food Research Council (AFRC), have been genetically engineered to contain genes for two bacterial enzymes. Whereas neither gene 'improves' the plant, the experiment is a model for future improvements.

Following consultations with ACGM, the PBI scientists have designed the experiment to avoid any spread of the plants from the experimental plot. The plants will be deflowered, weeding and harvesting will be carried out only by hand, the potato tubers will be handled in isolation from others and the field will be kept fallow for a year.

Similar precautions will apply to the potato experiment at the AFRC Institute of Arable Crops Research at the Rothamsted Experimental Station in Harpenden, Hertfordshire. In this case, the plants derive from cell fusion between a domestic potato and a wild South American species that can resist the potato leaf roll virus. No recombinant DNA technology is involved.

The Rhizobium experiment, also at Rothamsted, is designed to test the extent to which genes can be transferred between rhizobial strains in soil. It is financed by a European Economic Community programme for risk assessment in biotechnology, as one of the conceivable hazards of deliberate release experiments is the unwanted transfer of genes between strains. The strain that will be released at Rothamsted contains a harmless marker gene whose transfer to natural strains in the soil will be monitored. (Source: Nature, Vol. 327, 28 May 1987)

Biotechnology 'clubs' gaining favour

Now in its sixth year and running a $15 million programme of biotechnology research, the Biotechnology Directorate of the UK Science and Engineering Research Council (SERC) is increasingly using the "club" approach to attract industrial interest and funding. An Animal Cell Biotechnology Club has just been formed, raising the total number of clubs to three, and the possibility of two others is being investigated. Moreover, directorate staff now have access to an independent assessment of the first two years of the Protein Engineering Club, which was the first to be set up and now accounts for almost a quarter of the directorate's spending.

The directorate's main aim is to encourage strategic or pre-competitive research - the kind that UK industry is notoriously unwilling to carry out and which academics cannot necessarily be expected to perform. It encourages industry to participate in two ways. One is for a single company to finance half of a specific programme of research in an academic department. There are about 20 co-operative grants of this kind, the largest of which involves Imperial

Chemical Industries (ICI) in supporting a $170 000 project on immunotoxin construction at the University of Warwick.

The other way to be involved is to subscribe to a club. Each participant is committed to an annual subscription - $40,000 in the latest club - that goes towards financing a programme of research in several academic centres into an enabling technology. All the participating companies have equal access to the results and none has any exclusive influence on the projects that are supported. They do, however, have an overall influence on the programme of research through the club's steering group.

Of the perceived advantages to joining a club early, the most appreciated are access to results and first rights to licenses on discoveries of value, and as a way of ensuring that more potential candidates are trained and that member firms have access to them.

Such a need can only help the Biotechnology Directorate in its aim of filling some of the lamentable gaps in Britain's strategic research. A partner in this pursuit is the government's Department of Trade and Industry which, for example, matches the annual $130,000 put into the Antibiotics and rDNA Club by the four industrial subscribers. (Extracted from Bio/Technology, Vol. 5, June 1987)

Strategy document on molecular sensors

A strategy document setting out the aims and objectives of Science and Engineering Research Council (SERC) £5 million, five-year molecular sensors initiative is now available. Started in 1985, the initiative aims to promote the development of these devices, which combine electronics technology with developments in chemistry and biology. When coupled with advances in signal processing, they will provide compact, low-cost instruments and real-time control systems for a range of uses.

According to SERC, molecular sensors could open up the possibility of using unskilled operators in areas of manufacturing which were previously highly skilled operations, including medicine, biotechnology, chemicals, food and drugs processing, defence and information technology. Copies of the strategy document may be obtained from: Ron Coster, Chemistry Secretariat, SERC, Polaris House, North Star Avenue, Swindon SN2 1ET or on 0793 26222 ext 2263. (Source: Biotechnology Bulletin, Vol. 6, No. 5, June 1987)

The Sainsbury Laboratory

In the largest private gift ever made to support plant science, David Sainsbury, through his Gatsby Charitable Foundation, is giving £15 million over 10 years to create a new international laboratory for research into molecular plant pathology. The Sainsbury Laboratory will be directed by a steering committee chaired by Professor Harold Woolhouse, director of the Institute of Plant Science Research (IPSR). A Scientific Council will include such leading scientists as Professor Heinz Saedler of the Max Planck Institute, in Cologne, and Dr. Brian Staskawitz from the University of California at Berkeley. Funded by the Agricultural and Food Research Council (AFRC), the IPSR is based at the John Innes Institute in Norwich, and will host the new laboratory. The idea, as Professor Woolhouse puts it, is to: "Create a brain drain in reverse."

David Sainsbury, who is finance director of J. Sainsbury plc, personally endowed the Gatsby Charitable Foundation in the 1960s. In the last decade, since the company went public, the combined Trusts set up by members of the Sainsbury family have grown to the point where their assets are valued at over £350 million. But why invest in this field? "The fundamental study of the ways in which plants become diseased through infections with viruses, bacteria or fungi has emerged very strongly in the past three or so years as one of the most interesting areas in plant research," Sainsbury replies. "Unravelling how a bacterium gets into a plant and makes it ill or not is exciting science." Developments in this area are also likely to produce important practical benefits, particularly in the Third World.

The John Innes Institute has been in the forefront of research on viral plant pathogens for many years. Among the areas on which the Institute's work has focused are rhizobia-plant symbioses, while Dr. Jeffrey Davies and his colleagues in the Virus Research Department discovered a reverse transcription process in plant cells, whereby RNA can be copied into DNA; constructed 'pseudo virus' particles to carry genetic information into plant cells; and develop molecular diagnostic kits for the rapid detection of viruses in plant tissues.

More recently John Innes scientists have developed a major project on the bacterium Xanthomonas, a typical example of major crop pathogens. Its main interest for industrial biotechnologists, however, is that it produces xanthan gum, a widely used thickening agent. In addition to work on the pathogenesis of the organism, the Sainsbury Laboratory's work should help develop improved industrial strains. The Sainsbury Laboratory is due to commence operations later in the year. (Extracted from Biotechnology Bulletin, Vol. 6, No. 4, May 1987)

New AIDS committee

The Medical Research Council in Britain is setting up a new committee to oversee clinical trials of new drugs to treat AIDS. One of the aims of the committee will be to ensure that trials are large enough to provide results of strong statistical significance.

The increasing prevalence of AIDS in Britain means that it is now more feasible for the council to have trials with large numbers of people. The committee will also examine ethical problems of the kind posed by the American trial of the drug azidothymidine (AZT) last year. Experts judged it unethical to continue with this study after only six months, because there had been 19 deaths in the group receiving placebo. None of the people receiving AZT, meanwhile, had died. However, some scientists believe that such premature termination is wrong, because it removes the chance of determining the long-term side effects of the drug. (Extracted from New Scientist, 11 June 1987)

Donated blood is an unlikely source of AIDS

Britain's policy of discouraging people at high risk of AIDS from giving blood seems to have been quite effective. Since the National Health Service began screening all donated blood for antibodies to the AIDS virus in October 1985, only 65 donors have been identified as carriers of the virus. This number represents one in every 50,000 donors.

The test for antibodies to the AIDS virus detects all carriers and has a low rate of false-negatives. Even so, if the blood sample gives a positive result, the service goes on to test the donated blood itself before contacting the donor. News of a positive test is never broken over the telephone or by post. (Extracted from New Scientist, 5 March 1987)

R&D support for animal cell culture

The details of an animal cell biotechnology research programme, which has been fermenting in the UK's Science and Engineering Research Council's

pipelines for almost two years, were unveiled at a conference by John Clegg, the programme's manager.

The programme is spending £1 million over the next three years to generate information that will allow animal cell cultures to be used more cost-effectively for producing monoclonal antibodies and recombinant proteins on a commercial scale. The research will be carried out with the support of SERC and five companies: Beecham, Celltech, Glaxo, Porton International, and the Wellcome Foundation.

The largest grants, about £287,000 each, will go to groups at the Universities of Kent and Surrey. Professor A. T. Bull and others at Kent will study the phenotypic and genotypic stability of cells during the long-term culture of mouse hybridomas, including the fidelity of immunoglobulin production. At Surrey, Professor R. E. Spier and colleagues will analyse the physiology of a hybridoma cell line and compare sub-lines with varying levels of immunoglobulin secretion. They hope to gain a better understanding of the complex interactions involved in immunoglobin secretion in order to allow the development of stable cell lines that secrete high levels of antibody.

Two other groups will study energy metabolism by mouse hybridomas. At Oxford University, Dr. K. M. Brindle and others will attempt to identify important enzymes controlling glucose and glutamine metabolism, with an eye to genetically altering the metabolic pathways to improve the productivity of commercial cell lines. Dr. M. Butler and co-workers at Manchester Polytechnic will examine the relationship between the regulatory enzymes and the growth and product release of these cells.

Finally, Drs. C. MacDonald and D. Onions at the Universities of Strathclyde and Glasgow will try to make retroviral DNA vectors that can be used to introduce 'immortalising' genes into white blood cells and so create novel cell lines useful for the production of human monoclonal antibodies. (Source: Chemistry and Industry, 1 June 1987)

New biotechnology advice group

Greater co-ordination of strategic research in biotechnology is the aim of a new advisory committee set up to give research council directors strategic advice on biotechnology research and ease some of the difficulties at the interfaces between the councils' activities.

The committee, called the Biotechnology Advisory Group, is chaired by Professor Roger Whittenbury of the University of Warwick.

The new committee will try to determine what is best scientifically, and then try to sell their vision to research council chairmen. The group includes people from the research councils and universities, as well as ICI and Glaxo.

Among the topics on the committee's agenda this year are the future of protein engineering, the safety aspects of industrial facilities and the environmental release of genetically-engineered micro-organisms, and the use of biotechnology in food engineering. For example, the advisory group will address itself to linking basic research on protein engineering at the MRC's Cambridge laboratory with the kind of strategic research funded by the SERC's protein engineering initiative. (Source: Chemistry and Industry, 18 May 1987)

New biochemical engineering centre planned

University College London (UCL) is now trying to raise industrial funds for an advanced centre for biochemical engineering - a new facility to be built on a World War II bomb site in central London. The Wolfson Foundation has already donated £0.5 million and another £0.5 million for special equipment for the centre has been given by the Science and Engineering Research Council (SERC).

UCL, along with the University of Birmingham, were chosen last autumn by the SERC as centres for research in biochemical engineering. While Birmingham is to modify an existing chemical engineering facility, UCL wants to start from scratch with a purpose-built facility.

UCL hopes to raise the money from UK-based companies before having to approach foreign-based multinationals. Building may be finished in 1990-91. (Source: Chemistry and Industry, 18 May 1987)

United States of America

Success or controversial field test reported

Advanced Genetic Sciences (Oakland, CA) reported that the engineered "ice-minus" bacteria it sprayed on strawberry plants in its recent controversial and historic field test seem to have survived despite the fact that 80 per cent of the plants had been uprooted by vandals before the bacteria was applied. In addition, the company said that no recombinant bacteria were detected outside the northern California test site.

BioTechnica International (Cambridge, MA) received a set-back, however, in its attempt to field-test recombinant Rhizobia that may increase alfalfa yields. The US Environmental Protection Agency (EPA) extended its review of this test for 60 days. The company, which remains hopeful of going to the field this summer, reports that EPA has determined that the trial would not pose "an unreasonable risk", but rather that the agency will use the time for public comment and to specify conditions imposed on the test. (Source: Bio/Technology, Vol. 5, June 1987)

Experimental drug proposal

Industry trade associations have been quick to comment on the US Food and Drug Administration commissioner Frank E. Young's innovative but controversial proposal to allow the sale of promising investigational drugs to desperately ill patients. The Industrial Biotechnology Association voiced support for the plan, urging, however, that the new procedure not delay the normal drug approval process. While also endorsing the idea, the Association of Biotechnology Companies called for further definitions of some key terms in the proposal. Both groups also stressed that compassionate approval should only be granted after sufficient clinical trials have been performed to indicate some therapeutic effect.

The Pharmaceutical Manufacturers Association (PMA), which represents the powerful drug firms that would be least helped by the change, endorsed the proposal as well, but with reservations. Specifically, the PMA questioned whether clinical trials might be more difficult to complete with an experimental drug available for sale, and it pointed to the ethical dilemma of withholding that drug to control patients in such trials. (Source: Bio/Technology, Vol. 5, June 1987)

Poll results on biotechnology

The first survey of American attitudes toward genetic engineering shows that the public is generally both interested and confident in the science. The full report, was due in June, but summary results released by the Office of Technology Assessment (OTA) show that while Americans still favour strict regulations, they also strongly support continued research into genetic engineering.

The survey of 1,273 Americans, which is one of six studies comprising OTA's 2 half-year assessment of biotechnology, was designed to find out what people think they know, not to measure their level of scientific expertise.

Two-thirds of the respondents think that genetic engineering will enhance life for all; 52 per cent of them believe that genetically engineered products are somewhat likely to pose some danger to people or the environment. If there were no direct risk to people and remote risks to the environment, 82 per cent of the respondents say, they would favour small-scale testing of genetically altered organisms. As for testing in their own communities, 53 per cent would favour such testing; 14 per cent would not care, but only 42 per cent support the idea of a company releasing genetically altered organisms into the environment on a large scale.

The study results are viewed as mostly positive. People seemed to express most confidence in the technology when confronted with specific situations. Even with evidence that the public does support biotechnology, however, there seem to be conflicting views on how such support will influence federal funding for biotechnology. Congressional staff also doubt that the report's message will actually translate into increased funding over present plans. The 1987 allocation for biotechnology research by all federal agencies is estimated to be more than $2 billion, a significant portion of the federal research effort.

For the biotechnology industry, however, the impact of the report could be positive because public perceptions may play a big role in the purchase of biotechnology stocks. (Extracted from Chemical Week, 10 June 1987)

FDA rejects genetically engineered TPA

Genentech's genetically engineered tissue plasminogen activator (TPA) - an enzyme that dissolves blood clots - should not be approved for treatment of heart attacks, says the US Food and Drug Administration's (FDA) cardiovascular and renal drug advisory committee because Genentech failed to prove that TPA extended the life of heart attack patients after dissolving blood clots. The ruling, however, is not the last word on the subject. Genentech plans to submit new evidence to the agency, and analysts expect that the drug will receive approval in a year or so. (Extracted from Chemical Week, 10 June 1987)

Vector vans bring biotechnology to teachers across the nation

Functioning as vectors do, mobile laboratories from Cold Spring Harbor Laboratory will shuttle information about DNA to high school and college teachers across the country. Throughout the summer of 1987, 14 schools in 11 states, among them Indiana, Alabama, and Wisconsin, hosted week-long biotechnology workshops.

Two "vector vans", one acquired this year with a $415,000 grant from the National Science Foundation, carry micropipettes, centrifuges, spectrophotometers - everything necessary for genetic engineering experiments, including microbial culture, gel electrophoresis, restriction analysis and transformation.

Laboratories for students, says Dave Smith, co-ordinator of the project, will depend on the teachers and facilities. "The greatest difficulties will be in rural areas with low tax bases, where there's maybe $600 for the entire science programme." Outfitting a school laboratory "really well" can be done for $6,000 to $8,000. Smith notes, "What happens in the classroom will probably be ... more for the student who is not going to become a scientist. It's to give a background, prepare them for when issues come up."

And "because high school students do talk to their parents some, this will be a way to get information about biotechnology to adults", anticipates Steven Burke, communications manager for the North Carolina Biotechnology Center. In the belief that "people are resistant to learning, once out of high school, and can't be expected to read easy books or go to science museums", Burke will go where the people are next autumn - to shopping malls. (Extracted from McGraw-Hill's Biotechnology Newswatch, 1 June 1987)

EPA approves IMC's r-DNA E. coli for growth factor

A day after the US Environmental Protection Agency (EPA) gave International Minerals and Chemical Corp. (IMC), of Northbrook, Ill., permission to manufacture a microbe that makes insulin-like growth factor, IMC announced formation of a new subsidiary, ENCERA Bioproducts, Inc., to make and market the product. IMC genetically engineered a crippled strain of Escherichia coli to secrete the growth factor, somatomedin, which it is now offering "to the research industry", as a substitute for animal sera in synthetic culture media.

At least half a dozen biotechnology companies worldwide are developing the insulin-like growth factor for clinical use, in diagnostic kits for cell growth, culturing skin cells for burn injuries, and wound-healing generally.

In granting approval to commercialize the recombinant microbe and growth factor, EPA noted that IMC would produce it solely in fermentation systems, not for environmental use. The firm's transformed E. coli K-12 strain, the agency points out, "does not pose human health concerns ..." (Source: McGraw-Hill's Biotechnology Newswatch, 1 June 1987)

US plans massive trial of AZT

A large trial involving 1,500 patients is about to begin in the US to determine whether the drug azidothymidine (AZT) helps to delay the onset of AIDS in people who are infected with human immunodeficiency virus (HIV). Doctors in 19 American cities, co-ordinated by the National Institute of Allergy and Infectious Disease in Bethesda, Maryland, will begin enrolling patients into the trial next month.

The trial, which is expected to run for about two years, will have three "arms": patients will take either of two different doses of AZT, or a placebo. The results of the trial should help doctors to decide whether it is better to give AZT to patients while they are still relatively healthy and so better able to withstand the anaemia that the drug can cause, or whether it is too toxic to give to people who have not yet developed AIDS.

An independent board of experts will review the data from the trial at intervals of four to six months to see if any groups are doing so well or so poorly that the trial should be stopped. (Extracted from New Scientist, 11 June 1987)

Biotherapeutics to establish cancer research facility in Newport Beach

Biotherapeutics Incorporated, a patient-centered cancer research company has announced the establishment of a cancer research laboratory in Newport Beach, California in conjunction with Hoag Memorial Hospital

Presbyterian. The new laboratory, Pacific Coast Biotherapeutics Inc., will provide Orange County, California with research services focused on the development and application of custom-tailored therapeutic options for cancer treatment employing biologicals including interleukin-2 (IL-2). The services to be offered will enable cancer patients and their physicians to obtain access to promising technologies.

The research programmes to be offered are based on the belief that cancers among individuals are more different than alike and that each tumour in each patient is different. This approach to cancer research and treatment is based on the perception that effective cancer management strategies require collaboration between laboratory scientists and clinicians to better understand the individual characteristics of each patient's tumour.

This approach is manifested in the first two research programmes to be offered by Pacific Coast Biotherapeutics. The Tumor Acquisition, Propagation and Preservation (TAPP) Programme establishes the patient's tumour in the laboratory for analysis and future therapeutic options. This programme is designed for tumours that can be partially or completely removed and where there is a greater than 20 per cent chance of recurrence.

The second, and major therapeutic programme to be offered in Newport Beach, is Biotherapeutics' Cellular Component Development (CCD) Programme currently incorporating interleukin-2 and lymphokine activated killer cells (IL-2/LAK).

Interleukin-2 for Biotherapeutics' studies is provided free of charge to the patient by the Cetus Corporation. Patients that are enrolled in Biotherapeutics' CCD research programme do not pay for IL-2, but rather fund the laboratory research services required to activate the LAK cells. Biotherapeutics provides research services to patients on FDA approved protocols utilising regulated investigational drugs.

Financial support for the costs associated with Biotherapeutics' IL-2/LAK cell studies will come from individual patients or from their insurance companies. This concept of "patients as partners" in the clinical research process is one of the underlying principles of Biotherapeutics. The partnership of investor, patient, physician and research laboratory working together in the private sector to increase the patient's access to new technologies in cancer treatment represents a powerful new method for developing cancer therapeutics. Biotherapeutics is the first to establish this partnership which offers a new mechanism for providing seriously ill individuals access to the most promising scientific developments and the funding of cancer research. Further, this move is consistent with the FDA's recent Group C designation of IL-2 and their revised provisions relating to the use and sale of investigational new drugs. These proposed procedures are designed to facilitate the availability of investigational new drugs to seriously ill patients and would authorize the sale of an investigational drug in clinical trials.

Biotherapies are different from conventional chemotherapies. Traditionally, physicians have been able to utilize manufacturer's formulated chemotherapeutic agents in the treatment of patients right off the shelf. However, many biotherapies require intensive laboratory manipulation. This is true not only in the activation of cells for interleukin-2 but also for other adoptive cellular therapies, custom-tailored monoclonal antibody/immunoconjugates, autologous vaccines and the rational selection of combination lymphokines and cytokines based on tumour sensitivity. (Extracted from Company News Release, 26 May 1987)

C. RESEARCH

Research on human genes

Evolution of an inherited disease

Phenylketonuria (PKU) is one of the commonest genetic disorders that is inherited recessively among northern Europeans. It is caused by a defect in the gene that codes for the enzyme phenylalanine hydroxylase. People with two copies of the mutated gene do not produce the enzyme and become mentally retarded unless they eat a diet free of phenylalanine. Children born in Britain are routinely tested for the disorder at birth by a simple biochemical blood test.

Now researchers in Houston, Texas, have identified two mutations that together account for half the cases in people of northern European origin. The discovery makes it possible to screen the DNA of adults to identify 90 per cent of the people who are carriers of the disorder.

The discovery also sheds light on the evolutionary origins of the disease. It is surprising that a genetic disorder as common as PKU can be traced back to just a handful of mutational events. Before the new research geneticists suspected that PKU is common because the gene mutates at a high rate. However Anthony DiLella and colleagues at Baylor College of Medicine have shown that more than half the people with PKU are directly descended from two people who experienced the initial mutations. Such evidence suggests that being a carrier (heterozygous) might now be, or in the past have been, advantageous in some unknown way, allowing the mutated genes to spread through the population by "balancing selection". (Source: New Scientist, 4 June 1987)

Gene for cystic fibrosis

Molecular biologists in London have now identified a region of chromosome 7 that carries the gene for cystic fibrosis. They may well have found the gene itself.

Bob Williamson and his colleagues at St. Mary's Hospital in London used a new technique to isolate the candidate gene underlying cystic fibrosis which affects one in every 2,000 children born in Britain each year. The researchers sought to distinguish the gene itself from neighbouring noncoding sequences.

They worked on the idea that many genes are associated with regions of DNA rich in unmethylated dinucleotide CpG, called HTF islands. Using enzymes that recognise such regions and cut the DNA there, the researchers isolated clones fragments of DNA from chromosome 7 that contained an HTF island. The biologists then zeroed in on the gene by selecting a clone with an HTF island lying between two genetic markers already known to flank the gene for cystic fibrosis.

Molecular analyses of children suffering from cystic fibrosis will soon determine whether Williamson and his colleagues have at last found the gene itself. Better ways of treating the disease and diagnosing carriers of the genetic defect should follow. (Source: New Scientist, 14 May 1987)

Search for gene responsible for NF narrows

The disease von Recklinghausen neurofibromatosis (NF) remains one of the world's most common genetic disorders, afflicting roughly one in 3,000 people, including an estimated 100,000 in the United States, although few victims develop severe disfigurement. A variety of bone and central nervous system complications are commonly associated with the ailment and until recently scientists knew little about its etiology.

Now two teams of scientists have identified the approximate location of the gene apparently responsible for NF, sparking hope that early detection and treatment of the disease may be possible in coming years. Moreover, their research suggests that although it can manifest itself in a number of ways - ranging from minor skin discoloration to solid tumour malignancy - the disease is probably the result of a defect or defects in a single gene. That finding, along with the fact that about half of all NF cases are the result of new mutations found in offspring of genetically normal parents, has led some of the scientists to theorize that the gene may be unusually large and therefore susceptible to more mutations.

Research teams from the University of Utah in Salt Lake City and Massachusetts General Hospital and Harvard Medical School in Boston report respectively that they have narrowed the location of the NF gene to a region close to the central constriction of chromosome 17. Working independently the two groups traced previously mapped genetic markers that are typically inherited along with the disease - a technique that has been used to pinpoint the genes responsible for cystic fibrosis and muscular dystrophy, making possible the development of prenatal tests for such defects. (Source: Science News, Vol. 131, 6 June 1987)

Cataract genes

Some types of cataracts may be due to defective genes, according to a report in the Proceedings of the National Academy of Sciences. Canadian, British and Dutch researchers say people suffering from Coppock-like cataract, which is present at birth, have a unique genetic profile involving genes that code for crystallin, the protein found in the lens of the eye. A mutant crystallin gene might cause the protein to fold improperly, making it no longer transparent and clouding the lens. (Extracted from Science News, 7 February 1987)

French scientists closer to schistosome vaccine

Scientists at Transgène, in collaboration with Institut Pasteur, have moved closer to developing a cheap vaccine for schistomiasis. The chronic debilitating disease affects about 250 million people in the world's tropical regions and although it can be treated by drugs such as praziquantel, produced by Miles Pharmaceuticals, they do not prevent reinfection.

A team headed by Jean-Pierre Lecocq at Transgène and André Capron of Institut Pasteur has managed to clone and express a gene for an antigen that induces immunity to schistomiasis. Using a recombinant 172 amino acid 25K fragment, the researchers found that rats and hamsters recognise the antigen and respond by producing specific IgG and IgE antibodies which can kill the schistosome larvae.

Vaccination trials show that protection is produced in rats and hamsters. In addition, vaccinated baboons produce cytotoxic antibodies similar to those found in rats and hamsters suggesting that the vaccine is also effective in these primates.

More encouraging is the news that the antigen occurs in four species of Schistosoma: S. mansoni, S. haematobium and S. japonicum that infect humans and S. bovis that infects cattle. This suggests that a broad-spectrum vaccine could be developed.

Further experiments are still to be conducted on primates but Transgène is hoping to be in a position to start human trials by the end of 1988. Immunity to the disease is thought to be very complex involving at least four cell types. The mechanism of the experimental vaccine is believed to involve IgE bound to eosinophil cells. Other cell types associated with the immune response include mast cells, macrophages and platelets and several kinds of immunoglobulin.

A final vaccine may actually involve the eliciting of these cell types by being multi-antigenic. Transgène plans to work in close co-operation with the World Health Organization to develop a vaccine for young children to avoid primary infection. But even if such a product is unable to eradicate the disease in endemic areas it is still likely to reduce the parasite burden and contribute to control measures. (Source: European Chemical News, 6 April 1987)

More clues into the workings of leishmania

Two scientists now believe they may have uncovered the way in which a parasite not only gets into a macrophage, but also avoids death once inside. David M. Mosser and Paul J. Edelson of Cornell University Medical College in New York City have found that Leishmania major, which causes parasitic diseases common to the tropics, uses one of the body's nine components of complement - proteins that help destroy foreign invaders - to stay alive. Leishmania, which first live in an insect before changing form and transferring to a warm-blooded host, often affect children and are responsible for mild to fatal lesions and ulcers on the body. The diseases caused by leishmania have been cited by the World Health Organization and others as one of the five major health parasitic scourges worldwide.

The trick for a parasite is to get past the cell's defence mechanism and into its new home. Although it has been known that leishmania and other organisms, such as Toxoplasma gondii, have learned how to enter a macrophage without triggering a burst, Edelson believes this is the first time scientists have shown how leishmania achieve that feat.

Edelson speculates leishmania are successful perhaps because not all receptors trigger the respiratory burst, and leishmania have figured out which one bypasses the deadly process. Edelson believes the third component of complement (C3) is responsible for getting leishmania into the cell and decreasing the effects of respiratory burst once there. By binding to a specific receptor, leishmania are able to trigger the unlocking of the door. Complement normally works, in part, by coating an invader for ingestion by a macrophage. In this case, the parasites have learned to change complement from adversary to ally. If successful in disarming the cell, leishmania multiply to the point where they burst their host.

Mosser and Edelson believe it could be common practice for leishmania and perhaps other intracellular parasites to activate C3 and gain entrance into cells.

The findings might be used to help researchers discover ways to prevent invading organisms from picking up the complement they need to penetrate the cell or to help programme cells to initiate a respiratory burst against any invader. (Source: Science News, Vol. 131, 6 June 1987)

An extra defence against parasites

Of all the proteins in the body, the group of polypeptides known as the serine protease inhibitors, or "serpins", is among the most obscure. But according to two researchers in Scotland, serpins could form the basis of a powerful defence against invading parasites.

Serpins act as suppressors of certain enzymes, such as the digestive enzyme trypsin, and thrombin, the blood-clotting enzyme. Each serpin has a sequence of amino acids, called the reactive centre, which is an ideal substrate for the enzyme to attack. Once the enzyme is "lured" into close contact with this reactive centre, it is "frozen" into a complex that it can cleave only very slowly.

Although these inhibitors are interesting, the function of most of the polypeptides remains a mystery. Robert Hill and Nicholas Hastie, of the MRC's Clinical and Population Cytogenetics Unit in Edinburgh, have found that the genes that code for these protease inhibitors are evolving at an unprecedented rate, but only at the reactive centre. The reason may be that serpins are an important first line of defence against invading parasites.

Hill and Hastie compared the messenger RNA sequences of four serpin genes, one for the alpha-1 inhibitor of chymotrypsin, a human enzyme; one for the equivalent protein in mice (contrapsin); and two rat serpins. Although the gene sequence of the chymotrypsin inhibitor is almost identical to that of contrapsin, the mouse protein inhibits trypsin rather than chymotrypsin, because there are major differences in the gene (and so also in the protein) sequence in the reactive centre. When the researchers looked at the gene and protein sequences of the two rat serpins, they found a similar story: the two were very similar to the mouse contrapsin and human anti-chymotrypsin proteins, except in the reactive centre, where they were completely different.

For closely related protein genes to differ so much at the sequence that codes for the "working" part, means that these changes, which can accumulate only by mutation, have been selected. Such accelerated evolution is encouraged by evolutionary pressures. Hill and Hastie suggest that the protease inhibitors are rapidly changing their specificity for target proteases because their main function is to block the action of foreign proteases introduced by invading parasites and bacteria. Pathogens such as Pseudomonas, bacteria that commonly infect the lungs of people suffering from cystic fibrosis, seem to use serine proteases to increase their virulence. So the serpins may keep not only our own enzymes in check, they could also form a system of defence similar to the immune system's production of antibodies.
(Source: New Scientist, 2 April 1987)

New malaria parasites

Novel forms of malaria parasites have been generated through cross-fertilisation of gametes in mosquito vectors. In studies described by D. Walliker and colleagues of the National Institutes of Health, genetic recombination - reassortment of genes and exchange of genetic markers between chromosomes - between distinct Plasmodium falciparum parasites took place within mosquitoes. Anopheles freeborni mosquitoes were permitted to feed on mixtures of gametocytes of two cloned lines of P. falciparum, the most pathogenic human malaria strain. Sporozoites soon appeared in the mosquitoes' salivary glands, chimpanzees were infected with the sporozoites, and parasites were later isolated from the chimpanzees' blood. Genes from the two original clones were present in new combinations in the progeny: this was apparent in patterns of drug sensitivities, forms of several proteins (an enzyme, two antigens, and certain other proteins), hybridization patterns with DNA probes and altered chromosome sizes. Control measures (vaccines and therapies) for malaria must take into account and overcome the ability of malaria genes to recombine and produce new pathogenic strains.
(Extracted from Science, Vol. 236, 26 June 1987)

The gene that makes cancers immortal

Most scientists agree that cancer cells are abnormal in at least two, and sometimes three, ways, but they understand only one of these. First, cancer cells grow out of control; this happens when something activates any member of a family of genes that controls the various steps in the pathway of cell division. Cancer cells are also abnormal in that they become immortal and can carry on dividing forever. (Normal cells usually die after about 50 divisions.)

As with uncontrolled cell division, immortality can be conferred by activating any member of an entire (but different) family of genes. Some of these genes also inhibit the process of differentiation and freeze cells in the early stages of their development, a state called "arrested maturation".

Until now, no one knew how the second family of genes functioned. But recently, two groups of researchers found that one of the immortalizing genes seems to code for the nuclear receptor for thyroid hormone.

This gene, called erb-A, is one of two genes contained in a virus (avian erythroblastosis virus) that causes cancer in chickens. The second gene in this virus, erb-B, codes for one member of the family of genes that controls growth. Both genes must be activated for the virus to cause cancer. The two viral genes resemble genes expressed in many normal cells, which are called c-erb-A and c-erb-B (to distinguish them from the viral v-erb-A and v-erb-B).

Researchers knew from earlier studies that the structure of v-erb-A is similar in many ways to the structure of genes that code for receptors for steroid hormones. This led Jan Sap and colleagues, at the EMBO laboratories in Heidelberg, and Cary Weinberger and colleagues, at the Salk Institute in San Diego, to examine whether the c-erb-A gene coded for a known receptor. The researchers isolated copies of the human c-erb-A genes and used them to produce the corresponding protein. They then examined the protein's ability to bind known hormones. Both teams found that the protein specifically bound 3,4,3'-triiodo-L-thyronine (T3), one of the major thyroid hormones (Nature, Vol. 324, p. 635 and p. 641).

The product of the v-erb-A gene, however, could not bind thyroid hormones. So although v-erb-A and c-erb-A genes are structurally similar, the viral gene appears to lack a region critical in the specific binding of thyroid hormone.

Two important questions arise from these studies. First, how do these genes work. And secondly, might thyroid hormones be involved in cancer. The answer to the first question is likely to be that the thyroid hormone receptors, like receptors for steroid hormones, may bind directly to specific regions of DNA and allow transcription of adjacent genes. Many scientists think that binding proteins to DNA in this way is an important mechanism in the control of the processes of differentiation.

Both groups of researchers suggest that the failure of the v-erb-A protein to bind thyroid hormone might mean that the normal mechanisms regulating this protein do not operate, and that the v-erb-A gene turns on processes that otherwise would occur only in the presence of thyroid hormones. In support of this view, Sap and his colleagues point out that thyroid hormone can promote the growth and spread of several types of cancer, and that the transformation of cultured cells by radiation or viral infection is aided by thyroid hormone.

These results may help researchers to understand how cancer cells become immortal. (Source: New Scientist, 5 March 1987)

Colorectal oncogenes found

Using new methods to find genetic mutations, two groups of scientists have found more evidence that oncogenes are a significant cause of cancer. Oncogenes have been found to transform normal cells into cancerous cells. Scientists at the State University of Leiden in the Netherlands and Johns Hopkins University School of Medicine in Baltimore report that over one third of the colon and rectal tumours they studied contain the ras oncogene. Another group at the State University of New York in Stony Brook and the University of Alabama at Birmingham found similar results using a different assay method that also detected gene mutations, which apparently convert normal ras genes into the oncogenes found in malignant cells. (Source: Science News, Vol. 131, 30 May 1987)

Tumour cells fight cancer

Scientists in the US are hoping to combat deep skin cancers with the help of irradiated cells taken from the tumour itself. Fred Seigler and colleagues at Duke University, North Carolina, hope to use the "renegade" cells as a vaccine to stir the body's defence system into fighting against the tumour.

Already Seigler has found that a patient's white blood cells can kill skin cancer, or melanoma cells in laboratory cultures. He hopes to establish whether the killing power of white blood cells can be amplified.

He removes melanoma cells from the patient, alters them by radiation, then injects them back into the body to help the patient build up immunity.

Because the injected cells cannot grow, they are harmless. The theory is that they induce the immune system to produce more white blood cells which then attack any live cancer cells in the body.

Seigler says that preliminary results from several centres where the "vaccine" is being tested are good. If the technique works, it will be used to combat deep skin tumours, which invariably kill.

Melanoma, one of the major skin cancers, can be cured in up to 90 per cent of cases if the site is small and detected early, but about 90 per cent of people with deep-seated tumours die. (Source: New Scientist, 12 March 1987)

The body fights back against cancer

Training the body's immune system to fight cancer is an increasingly promising therapy that is winning adherents. Steven Rosenberg of the US National Cancer Institute produced more evidence that his unique treatment destroys advanced cancers. Rosenberg treated 157 patients with advanced cancers, either with interleukin-2 (IL-2), a protein of the immune system or with a combination of IL-2 and special killer cells grown from the cancer victim's own white blood cells. Several researchers have treated cancer with IL-2 alone, but Rosenberg reported last year that the combination therapy seems to be superior.

Rosenberg creates special killer cells for each patient, by drawing lymphocytes from them and incubating them for several days with IL-2. Strengthened by the association, these LAK cells are infused into the patient with IL-2, which helps the killer cells to multiply in the body.

Rosenberg's latest findings do not dispel concern about side effects but they affirm the potency of the therapy. Of 106 patients taking a course of IL-2 with LAK cells, 8 experienced complete remission. Fifteen showed a "partial response" with their tumours shrinking to half their size or smaller. Another 10 showed a "minor response", with tumours shrinking by 25 to 49 per cent. Of the 46 patients who took a course of IL-2 alone, one has complete remission, 5 a partial response and one a minor response.

Of the different types of cancers treated, 12 of 36 kidney cancers and 6 of 26 melanomas showed partial or complete remission. Of the 9 patients whose bodies were rid of cancer, 2 developed tumours within a year.

Rosenberg emphasizes that the treatment is experimental. Patients suffer a range of severe side effects and four died as a result of the treatment. However, as Rosenberg points out, all other treatments had failed these patients and this was a last attempt at therapy. (Source: New Scientist, 16 April 1987)

New hope in breast cancer fight

The Imperial Cancer Research Fund in London has developed an agent that recognizes and binds to breast-cancer cells exclusively. It could be the key to developing a technique to detect and destroy human cancers.

The agent, a monoclonal antibody, does not bind to healthy cells. Joyce Taylor, whose team developed the antibody, said that in laboratory tests the antibodies found their targets, breast cancer cells, in 95 per cent of the experiments.

The antibodies identify the cancer cells by recognising features on cell surfaces. The features occur in mucin molecules that are thought to protect individual cells.

Researchers may soon be able to use the monoclonal antibody to attach a toxic agent to the tumour cells and destroy their surfaces. These are thought to provide lubrication and protection.

Cancer cells also bear mucines, but unlike normal mucines, these have a gap in their coating of sugars which leaves their protein core exposed. Taylor developed a monoclonal antibody that homes in on the exposed core protein of the mucin of breast cancer cells. It ignores normal breast cells, she said, because their mucin core protein is shielded from attack by an intact coat of sugars.

The monoclonal antibody developed by Taylor to seek out breast cancer cells has shown some attraction towards other cancer cells. In pilot studies, it reacted to lung-cancer cells but not to normal lung tissue. It also showed some selectivity for colon and ovarian cancer cells.

Taylor now plans to test the antibodies in women with breast cancer. By injecting the new monoclones, marked with a radioactive tracer, into a patient's lymphatic system, she hopes to be able to pin-point any cancerous nodes. Surgeons will no longer have to dissect out all the breast lymph nodes to be sure of eliminating breast cancer, she hopes. (Extracted from New Scientist, 23 April 1987)

Research on oncogenes may provide better cancer diagnosis

Research on oncogenes might provide better diagnosis and treatment of cancer. L.E. Schnipper of Beth Israel Hospital (Boston) says oncogene-based diagnostics could be worth $650,000 - $5 million by

1992. Drugs to counteract the proteins produced by oncogenes could be available as well. Oncogenes are already being used to diagnose and select therapy for neuroblastoma, chronic myelogenous leukemia and lung cancer. Oncogene profiles may be used to stage breast cancers and follicular lymphomas to type tumors that are otherwise indistinguishable. Oncogenes may even be able to explain why a given therapy works better in some patients than in others or to help develop new therapies. An oncogene-based probe for leukemia is already in clinical trials. (Extracted from Medical World, 23 February 1987)

Cancer patients to benefit from better 'bullets'

Immunologists at the Scripps Clinic in Southern California have successfully exploited advanced antibody techniques to target immune cells to the site of a tumour. They produced monoclonal antibodies that recognize two antigens simultaneously, one on the surface of leukaemic white blood cells and the other on T lymphocytes, cells that are part of the body's own cellular defence against disease. This is the first time that "bispecific antibodies", developed in Britain more than 10 years ago, have found a clinical application.

The researchers from Scripps found that in culture the monoclonal antibodies bind to both killer lymphocytes and cancer cells and stimulate the T cell to kill the cancer cells. They proved so efficient that two billionths of a gram of the monoclonal antibody was enough to direct T lymphocytes to kill one third of the cancer cells. In future, cancer patients could receive a "challenge" to stimulate the production of cytotoxic T cells, followed by an injection of the targeting antibody to focus them rapidly to the site of malignancy.

The results of clinical trials in the near future should establish the value of both these approaches to cancer chemotherapy. If they are successful, patients with tumours would need smaller or less frequent injections and so suffer less from the side effects of these highly poisonous drugs.
(Source: New Scientist, 11 June 1987)

Liposomes to carry drugs against cancer metastases

Liposomes could carry drugs to activate macrophages to kill metastases, according to I. Fidler of Anderson Hospital & Tumor Institute (MD). Liposomes containing the activating drugs are scavenged by the macrophages, releasing the activators inside the cells. The technique has been used in mice whose primary tumours had been removed surgically. Metastases normally kill the mice in 80 days. Intravenous injections of the liposomes were successful in preventing death in 75 per cent of the treated animals. Similar results were obtained using the technique on dogs at the University of Wisconsin (Madison). The dogs suffered from osteogenic sarcomas, which is generally diagnosed only after metastases have implanted themselves in the lungs, leading to death within 90 days. The treatment, with liposomes containing muramyl tripeptide, has allowed six of nine dogs to survive 200 days after the primary tumour was removed. Even better success was obtained when mice in the study were treated with radiation to increase inflammation, since macrophages home in on inflammation. (Extracted from Science News, 4 April 1987)

Swapping mouse for human moiety makes safer, more deadly, monoclonal

To make monoclonal antibodies more human is the aim of a protein-engineering strategy reported by International Genetic Engineering, Inc. (Ingene) of Santa Monica, Calif., in concert with Oncogen Ltd., Seattle. A drawback to using monoclonals in cancer therapy is that the hybridoma cells that generate the antibodies are half mouse in origin. Injecting murine protein into a patient triggers an anti-mouse immune response, which may make a second treatment useless, or even dangerous.

Oncogen scientists had found an antigen, abundant on the surface of "most" carcinoma cells - lung, breast, colon, ovary - but only trace-present on normal cells. Ingene isolated the gene sequence encoding the monoclonal antibody. Oncogen had raised against this target glycoprotein. Then it exchanged the murine constant domain - the highly immunogenic three fourths of the antibody molecule not involved in specificity - for human constant-region sequences.

The chimeric antibody Ingene cloned and expressed proved less immunogenic and more anti-tumour efficient than its mouse precursor. It bound to the tumour cells' target antigen as efficiently as the original mouse monoclonal, and - in vitro - killed "a greater fraction of target cells at a 100-fold less concentration". Moreover, the chimera killed melanoma cells that resisted the original murine version of the antibody.

Studies with human tumours implanted in nude mice are now under way, and Ingene's vice-president for corporate development, Arup Sen, expects clinical trials to start in 1988. (Source: McGraw Hill's Biotechnology Newswatch, 4 May 1987)

Peptide synthesis set to go fully automatic

Imagine a machine that, at the touch of a button, turns simple organic compounds into complex, biologically important molecules - one all with the minimum human intervention, in a fraction of the time and cost it takes for conventional chemical synthesis. Such a machine is the goal of chemists who are attempting to make, from scratch, the basic building blocks of life - peptides, proteins and nucleic acids.

Chemists at the Medical Research Council's Laboratory of Molecular Biology in Cambridge can now closely monitor the progress of peptide synthesis on solid supports. This means that a series of chemical reactions in which amino acids are strung together sequentially while dangling from a polymer can at last be fully automated.

The trick that Bob Sheppard and his team used was to activate the reacting C-terminus of an amino acid with a special group which, when it comes off, gives an intense yellow colour. So as the amino acid attaches itself to the polymerbound peptide, the support becomes stained yellow. This colour persists while the activated amino acid is reacting. But as soon as all the amino acid has reacted, the yellow colour begins to wash through and out of the polymer.

By monitoring this decrease in colour intensity, the chemists at Cambridge have found that most amino acids have completely reacted in about 20 minutes. A few have bulky side groups that get in the way of the reacting N- and C-termini. This makes their reacting more sluggish and they require much longer reaction times - in the order of 24 hours. By being able to detect these slow steps, Sheppard and his colleagues were able to hold off addition of the next amino acid until the sluggish one had finished reacting. Otherwise, the synthesis most certainly would have failed.

It is only a formality to programme a machine to detect the colour change as the reaction happens, and to dispense the next batch of protected amino acids when the colour has disappeared. In this way, the

process can accommodate even amino acids that take their time reacting, without introducing impurities into the final product. In other words, feedback control has, for the first time, allowed chemists to make peptide synthesis fully automatic. With a similar, automated, solid-phase synthesis of nucleic acids already up and running, biotechnology industries should be rubbing their hands with glee. (Extracted from New Scientist, 12 March 1987)

Enzyme therapy

Workers at the Duke University of Nebraska Medical Center have reported what they call the first successful treatment of a genetic disease by means of enzyme replacement.

The disease is adenosine deaminase (ADA) deficiency, a disorder that afflicts 20 or 30 newborns in the world each year. In the absence of ADA, the DNA precursor deoxyadenosine triphosphate accumulates in cells, blocking the normal synthesis of DNA. The effect is most pronounced in lymphocytes, or immune cells. Victims of ADA deficiency have a drastically underdeveloped immune system and unless they are treated they usually die of an infection within two years of birth. Only one in five can be treated effectively with transplants of lymphocyte-producing bone marrow from a sibling or parent.

Injections of the purified enzyme would seem a straightforward solution. The problem has been that ADA, like most enzymes, normally functions inside cells; when it is injected into the bloodstream, it is broken down rapidly, before it can be effective. Another difficulty is that at present the only economical source of ADA is animal tissue. Animal ADA would be expected to provoke an immune reaction in human patients, particularly once their immune function has improved.

The Duke and Nebraska groups appear to have circumvented both difficulties, although the results they report in the New England Journal of Medicine are preliminary. Instead of injecting pure ADA into the blood-streams of their two patients, the workers injected ADA that had been chemically combined with polyethylene glycol (PEG), a waxy, nontoxic substance with a variety of medical applications. Because PEG-coated ADA is protected from breakdown by other enzymes, its half-life in the blood-stream is two or three days rather than a few minutes. The PEG also seems to prevent an immune response, probably by blocking the binding of antibodies to the enzyme.

After two children had received weekly doses of PEG-ADA for several months, the workers report, "the principal biochemical consequences of [ADA] deficiency were almost completely reversed", and normally functioning lymphocytes appeared in the patients' blood. More important, the children have shown distinct clinical improvements: neither of them has had a serious infection, both have gained weight and both are more active than ever before.

The technique for modifying enzymes with PEG, developed by Enzon, Inc., of South Plainfiled, N.J., might be applied to other genetic and nongenetic disorders, including atherosclerosis. (Extracted from Scientific American, May 1987)

Research on animal genes

Recombinant hormone challenges pig protein for super-ovulating cows

Thirty cows in a research herd in Texas started a four-day course of injections with a genetically engineered hormone that causes super-ovulation. The multiple eggs each bovine releases - six transferable ova, on average - will be artificially inseminated and the embryos implanted into surrogate-mother cows. This field test of the first recombinant bovine follicle-stimulating hormone (bFSH) follows by six weeks permission to test the product, granted by the US Food and Drug Administration.

The cloned bFSH was produced by Integrated Genetics, Inc., Framingham, Mass., and is being field-tested by Granada Genetics (GG) of Bryan, Texas, an embryo-transfer subsidiary of Granada Corp., Houston. GG has worldwide marketing rights for the commercial hormone. (Extracted from McGraw Hill's Biotechnology Newswatch, 4 May 1987)

DNA fingerprinting of birds

Using genetic techniques developed in the last two decades, scientists have been able to detect differences fairly well between species in the animal world and between general populations of animals, but they have had far less success in making the finer distinctions of parentage within a given population or species.

Two papers appearing in Nature on 14 May 1987, however, show that "DNA fingerprinting" - an extraordinary sensitive genetic technique developed for humans and used in forensic identification of individuals as well as paternity and maternity questions - can have in on genetic relations among wild sparrows as well as it does for humans. Other papers in press suggest that the technique applies to cats, dogs and mice as well.

In the fingerprinting technique, scientists essentially count the number of times a particular sequence of DNA base pairs (the chemical building blocks of the DNA molecule) repeat in sections of DNA. The base-pair arrangement of these sections varies so much among individuals that even close relatives can be distinguished with this technique and since parents pass down part of their variability patterns to their offspring, parentage can also be accurately determined. In research being carried out in Canada, snow geese are being investigated.

These birds (Anser caerulescens) come in two varieties, snow white and slaty blue. The colour is controlled by a single gene, with blue dominant to white. But sometimes white adults look after blue goslings. Either the female indulges in matings with another gander, not the one she is paired with, or the pair is parasitized by another female who has laid in their nest. In fact, both happen, according to a new analysis of snow goose DNA by Fred Cooke and his colleagues at Queen's University in Kingston, Ontario.

Thomas Quinn and Bradley White has previously created a DNA library of the snow goose and used it to look for so-called restriction fragment length polymorphisms. These are the much vaunted DNA fingerprints, which are unique to individuals and can be used to establish maternity and paternity with great certainty. Having found probes that would isolate the fingerprints, the researchers turned to DNA samples taken from all the members of four particular goose families. All the adults were white, but two of the families were chosen because they contained one blue gosling each.

Only one of the families proved to be quite proper, all four goslings having inherited all components of their individual genetic fingerprints from their parents. The others were suspect. The fingerprints confirmed what the researchers already believed, that neither of the blue goslings belonged to both of its adult attendants. Unfortunately, the DNA could not distinguish between brood parasitism by another female and insemination by another male.

Even the white goslings were not pure. Three of them had DNA fingerprints that could not have come from either adult, so these must have been left in the nest by a passing female. A fourth white gosling could have arisen either by brood parasitism or by female infidelity.

In total, of the 17 goslings checked, six were of obscure parentage. Four of these were in one family, which might indicate either that some pairs are more likely to be parasitized than others, or that the adults took over an abandoned nest with eggs. This figure is higher than that estimated from previous studies of the inheritance of colour, which had suggested that brood parasitism accounted for between 5 and 12 per cent of the hatchlings. To account for the difference, Cooke and his colleagues point out that two of the families were chosen specifically because they contained suspect goslings, and in the year the samples were taken the field observers noted a particularly high level of parasitism.

This is one of the first examples of DNA fingerprints being used to explore in detail the provenance of individual animals in the wild. As the techniques are refined they will enable a definite distinction to be drawn in this case between parasitism and matings with other males. No one can predict what they will turn up in other cases. (Source: Science News, Vol. 131, 30 May 1987 and New Scientist, 9 April 1987)

The cheetah's future is rosier

The survival of African cheetahs in the wild is threatened by a population crash that happened 10,000 years ago. So say researchers who have been studying the genetic variation of free-ranging East African cheetahs, Acinonyx jubatis raineyi. They found that the gene pool is extremely small and the population highly inbred. They date the reduction in variation to the Pleistocene epoch.

Stephen O'Brien and colleagues at the National Institute of Cancer in Bethesda, Maryland, and Richard Leakey of the National Museums of Kenya looked for genetic variation by analysing isozymes. Isozymes are different forms of an enzyme arising from different forms (alleles) of the gene that codes for the enzyme. Allelic variation within a species is a measure of genetic variation, or polymorphism.

Only two of the 49 alleles the researchers looked at were polymorphic, giving an index of variation of 0.14. This compares with 0.26 for lions, tigers and leopards. Although this variation is small, it is larger than that of captive South African cheetahs, Acinonyx jubatis jubatis, which have an index of 0.0004. A comparision of the polymorphisms in the two subspecies led the researchers to conclude that the cheetahs suffered a population crash about 10 000 years ago. After the cheetahs became geographically separated, the South African subspecies lost yet more of its variation. This process may have been speeded in the past century by overhunting and destruction of the cheetah's habitat.

The discovery that the East African cheetah is genetically more diverse than the South African form, offers hope that careful breeding programmes might improve the gene pool in the South African subspecies. Unfortunately, neither form is very fertile and low fecundity is probably a feature of cheetah biology. Loss of habitat could be the factor that sees off the cheetah. Without space to expand, the population might never reach the numbers required for healthy outbreeding. (Source: New Scientist, 9 April 1987)

New genes cure a shivering mouse

Genetic surgery has been used for the first time to cure a normally fatal neurological disease in mice. The disease, called shiverer mutation, is caused by the absence of a protein that insulates nerves in the brain and spinal cord. Mice suffering from the disease, which is inherited, die from uncontrollable shaking.

Researchers at the California Institute of Technology and Harvard University reported they had prevented onset of the disease by injecting a piece of DNA coding for the missing protein - myelin basic protein - into 320 fertilised eggs. Only one of the resulting offspring was born without the disease, but, even with such a low success rate, the research is hailed as an important advance in genetic engineering.

Three generations of mice bred from the "cured shiverer" mouse are free of the disease. This is significant because it shows that the gene became fully integrated into the genome and can be transferred to subsequent generations like all normal genes. Some of the mice have lived for nine months, well beyond the three-month life expectancy of a shiverer mouse.

The research, proves that insertion of a missing gene can be effective therapy, but the low success rate and the possibility of causing other genetic damage will deter its use on fertilized human eggs. However, the insights the research provides into gene regulation will be useful for gene therapy involving somatic, or nonreproductive cells. It could also become a model system for studying diseases in humans that are caused by a defect in a single gene, such as thalassaemia and cystic fibrosis. (Extracted from New Scientist, 5 March 1987)

Tuna growth hormone cloned

Taiyo Fishery Co. Ltd., Tokyo, has isolated the cDNA of tuna growth hormone. Working with fisheries Professor Shinji Kawauchi at Kinsato University, the company has also extracted two other "cDNA eqivalents" of the hormone. They are now developing dosing methods for the fish-growth stimulator. (Source: McGraw-Hill's Biotechnology Newswatch, 4 May 1987)

Research on plant genes

Birch seedlings cloned

Researchers at three Finnish firms are hoping to plant cloned birch seedlings this summer. Enso-Gutzeit, Kemira and Oy Metsa started co-operation two years ago on the development technology for seedling production through cloning. The problem is not yet solved for pine and spruce, but cloning of birch seedlings is near use, the partners say.

The companies are hoping to develop an economical way of reproducing selected samples of forest trees to ensure that each district has the most productive seedling. While the production of genetically identical trees is helpful for yield predictions it does have the disadvantage that all plants are equally susceptible to disease. Mass production of trees is still a long way off and requires further research and development. (Source: European Chemical News, 20 April 1987)

Fresh orange juice from the test tube

A plant geneticist at the US Department of Agriculture's Fruit and Vegetable Laboratory in

Pasadena has learnt how to grow the juice sacs of citrus fruit in laboratory dishes. Brent Tisserat stumbled on the technique while testing the effects of nutrients, hormones and other chemicals on the taste and other properties of the fruit. He also succeeded in growing the fruit without the tree. Tisserat takes pieces of fruit and its skin from the tree and grows fruit tissue on a special medium with correctly balanced nutrients and hormones.

The cultured sacs are grown in special cabinets where light, warmth and humidity are controlled by a computer. The tiny segments sprout from the surfaces of the fruit and multiply. Cultures of citrus usually die off after a few weeks or months as their growth medium becomes polluted with waste material from the plant cells. But the new cultures survive for as long as a year without having to be recultured (the laboratory equivalent of repotting). The technique is so successful that the juice sacs outgrow the culture flasks. Tisserat's success is not confined to oranges. He has also cultivated laboratory lemons and grapefruits.

According to Tisserat, more research is needed to scale up the process into orange sac "factories", but it might be possible. (Extracted from New Scientist, 4 June 1987)

Monoclonals characterize nitrate reductase

Nitrate reductase (NR) is a key enzyme controlling the rate of inorganic nitrogen assimilation in plants. The Long Ashton Research Station, Bristol, UK, is using monoclonals to characterise monoclonals and locate the enzyme in the apical regions of maize roots before and after NR induction by exogenous nitrate. Details from: Dr. Roger Atkin, Scientific Liaision Officer, Long Ashton Research Station, University of Bristol, Long Ashton, Bristol BS19 9AF or on 0272 392181. (Source: Biotechnology Bulletin, Vol. 6, No. 5, June 1987)

Bacteria come to the aid of wounded plants

British botanists have developed a novel way to protect plants from attack by pests. Rather than breeding resistant strains of crop plants, the researchers, based at the University of Durham, have pressed into service a bacterium that produces a biological pesticide.

The bacteria live in close association with plants and produce their own pesticide only when stimulated by a plant at risk of attack. The bacteria produce the pesticide in small, controlled amounts, while in intimate contact with the plant. This form of protection will be cheap and eliminates the environmental damage caused by conventional pesticides. One way is to bolster a plant's natural resistance to disease by manipulating its genetic make-up. Teams of researchers around the world are inserting into crop plants genes coding for proteins that might act as insecticides.

This technology has great potential, but so far it works only for broad-leaved plants (dicotyledons). Most important crops are cereals, which are monocotyledons. Scientists in the FRG and Britain recently found a way to introduce genes into maize (a monocot) but their technique has no practical applications yet. Another drawback to this approach is that, to be effective, the insecticidal gene should be "switched on" at all times in all tissues. Synthesis of protein at such a high level would probably place a metabolic burden on the plant and lower its yield.

A second approach is to introduce a "pesticidal gene" into bacteria that live in the rhizosphere, the narrow zone immediately surrounding the root. These microbes provide protection without draining the plant's resources. Moreover, the bacteria can colonize the roots of broadleaves and cereals. However, permanent expression of the gene would handicap the bacteria, reducing its ability to compete with other microbes in the rhizosphere. Natural selection would weed out the gene, thus limiting the system's lasting effectiveness.

A better approach is to manipulate the bacterium so that it produces the pesticide in small amounts close to the plant and only when the plant is at risk. This is the idea the researchers at Durham are working on. Alison Ashby, Charlie Shaw and Martin Watson, with Andy Richards of the ICI Biological Products Business at Billingham, have patented just such a "microbial inoculant" and are now developing it in collaboration with ICI's Plant Protection Division. The aim of the research at Durham is to protect plants from opportunistic pathogens, mostly fungi, which take advantage of pre-existing damage to invade the plant. Clearly, some form of protection during the crucial time just after wounding would be invaluable.

Rhizosphere bacteria, such as *Agrobacterium*, are attracted to wounded plants by minuscule amounts of fluids leaking from the wound. Bacteria respond to these chemical signals by swimming towards the site of the wound. Once concentrated in the area around the surface of the wound, higher concentrations of the chemical attractants stimulate expression of a set of the bacterium's genes. To adapt these organisms as microbial inoculants, the researchers insert into *Agrobacterium* a gene that codes for a protein that acts as a pesticide. A range of "pesticidal genes" could be employed in this system, but to minimise the impact of altered organisms on the environment, the scientists chose genes that code for biological pesticides with highly specific actions. They are now testing the system with the enzyme chitinase as the pesticidal protein. This enzyme attacks and destroys the cell walls of fungi (and insects and nematodes) and inhibits their growth.

Using recombinant-DNA techniques, Ashby and colleagues insert the chitinase gene into *Agrobacterium* and inoculate the bacteria into the soil. The bacteria swim towards the plant and accumulate at wounds, where they express the pesticidal protein. This protects the plants until they have healed, when it ceases to release the activating chemicals. At this stage, expression of the pesticide is switched off.

In this system, the pesticide is produced exactly where and when it is needed, so eliminating waste, reducing environmental impact and placing only a small metabolic burden on both plant and bacterium. And, as *Agrobacterium* is attracted to both monocots and dicots, the system can protect all types of crops. (Source: New Scientist, 2 April 1987)

Ice-minus micro-organism tested outdoors, still three years from market okay

For a day late last April, Bremwood, a tiny farming community 40 miles northeast of San Francisco was the biotechnology field-trial capital of the USA. Being tested was a cocktail of two live microbes, *Pseudomonas syringae* and *P. fluorescens*, each with the same DNA sequence deleted. That missing gene codes for a single protein that causes ice crystals to form on plants. If the genetically spayed ice-minus bacteria can colonize plant petals and leaves at the

expense of native ice-plus microbes, farmers can save millions of dollars a year in frost-damaged fruits and vegetables.

The bacterial mixture, trade-marked Frostban, is produced by Advanced Genetic Sciences Inc. (AGS), Oakland, California. It took four years of regulatory ups and downs for Frostban to reach this initial outdoor test.

AGS originally licensed the concept of ice-minus bacteria six years ago from the University of California, Berkeley, where it was developed by Dr. Steven Lindow. Lindow's own field tests, using similar altered bacteria, took place at Tulelake, Calif. some 280 miles north of Berkeley. His tests differ from AGS's in several respects: potatoes instead of strawberries; leaves rather than flower-petals; P. syringae alone, rather than with P. fluorescens. Also, Tulelake, unlike Brentwood, has natural frost-spells the year round.

Lindow's team began their trials by planting potato tubers coated with the anti-freeze microbes. No protesters were present. Three weeks later, when the plants began to sprout, their leaves were sprayed, and the experiment continued along the same general lines as AGS's strawberries, where the initial trial was to last six weeks, after which the 2,500 strawberry plants will be destroyed. The test site - soil, weeds, other vegetation and insect life - will be monitored for another three months.

Beginning five or six days after the initial spraying, leaves, flowers and whole plants will be taken to AGS laboratories and exposed to artificial frost, to determine the degree of protection achieved. They will be monitored to determine Frostban's ability to survive and compete with ice-plus and other native bacteria.

AGS hopes to conduct additional tests on Frostban during freezing weather in the autumn and believes these will probably require Environmental Use Permits. Next spring, expanded tests - from strawberries to peas, almonds, peaches and apricots - will certainly demand such permits.
(Source: McGraw-Hill's Biotechnology Newswatch, 4 May 1987)

Trypsin inhibitor confers pest resistance

British plant scientists funded by Agricultural Genetics Company (AGC, Cambridge, UK) have endowed the tobacco plant with a gene from the cowpea. The gene encodes a protein that is a natural inhibitor of insect trypsin (a digestive enzyme), so the engineered tobacco plants are relatively pest resistant.

This approach, while similar in concept to the introduction of the gene for Bacillus thuringiensis toxin into plants, has the advantage of producing a much broader spectrum of resistance. The inhibitor itself was isolated by Donald Boulter and his team at the University of Durham from a variety of cowpea bred by the International Institute for Tropical Agriculture in Nigeria to combat the problem of stored beans being attacked by beetles. After the inhibitor had been identified two years ago, AGC agreed to fund the cloning of its gene and attempts to express it in tobacco. The company holds patents on the gene and its use.

The transformation work was performed at the Agricultural and Food Research Council's Plant Breeding Institute (Cambridge, UK), using one of its agrobacterial Ti plasmid vectors, in which the inhibitor gene is placed under the control of a constitutive cauliflower mosaic virus promoter.

At present, the gene exists only in immature tobacco plants, and there is no proof - although every expectation - that it will be stably inheritable. Nor is it yet certain that the inhibitor expressed in plants has as broad an action against insects as it does when added directly to their feed. Lack of transformed plants has so far limited tests to the bud- and army worm. Both fail to grow and eventually die when fed on the plants.

One problem that would no doubt have to be faced were food crops to contain the gene is whether the insect trypsin inhibitor has any inhibitory action on human trypsin. In Africa cowpeas are sometimes eaten raw without apparent harm, and that rat feeding experiments have not shown the inhibitor to be harmful either.

For the commercial success of the project, AGC is banking on the adaptability of the technology to major monocotyledonous crops: the rice cutworm, the corn ear worm, and the boll weevil are among the pests that are sensitive to the trypsin inhibitor, at least when it is fed to them. Prospective commercial partners in rice, corn, and maize will need to be able to offer seed marketing facilities, since AGC has none. The company's main hope in that direction lies in the UK Government's long-promised sale of the National Seed Development Organization together with a part of the Plant Breeding Institute. (Extracted from Bio/Technology, Vol. 5, May 1987)

Anti-sense genes

This article by John Newell, Science and Industry Editor, BBC External Services first appeared in Spectrum 15, No. 208, 1987.

A scientist working in the Biotechnology Centre at Imperial College, London has developed and begun to test a revolutionary new way to protect crop plants against virus diseases, using genetic engineering. In work supported by the Biotechnology Directorate of the UK Science and Engineering Research Council, Dr. Conrad Lichtenstein uses what he calls anti-sense RNA, to cancel out the message contained in the viral RNA, which would otherwise order the infected cell to make more virus. RNA is a long sequence of nucleic acid units that embodies the genetic code for making protein.

The technique involves first isolating and cloning a viral gene that produces a protein essential for replication of virus in an infected cell. This gene is then, in effect, turned back to front. It is done by removing part of the sequence called the promoter, which normally initiates the copying of the gene along its length to constitute the genetic message, and the part called the terminator, which normally stops the copying process at the other end of the gene. Their positions are then transposed, so the gene is copied backwards.

Pairing off

The hope is that when such an 'anti-gene' is inserted into a crop plant, using one of the several techniques now being developed, it will then be copied along with the plant's own genes into the form of messenger RNA. Suppose, then, that the plant is subsequently infected with the virus from which the original gene was taken: the virus will insert its genes into the plant's cells in the normal way and the viral genes will, as usual in infection, also be copied as single strands of messenger RNA along with the plant's own genes. If the plant were undiseased, the next step would be for the viral messenger RNA to be transcribed into new viral protein, as part of the process of making new virus particles. But if the

'anti-sense' RNA made by the artificially-inserted gene is present in the cell, its strands pair off chemically with the strands of viral RNA all along their length. This will happen because every sequence along the length of the anti-sense RNA will be complementary to, and so able chemically to bond with, the opposite sequence along the length of the viral RNA.

This pairing off will mean the viral RNA cannot be transcribed in the ribosome of the cell, which requires a naked, single strand of RNA to build up the corresponding protein. The viral message will have been cancelled out.

In its elegance the idea resembles that of the rather similar noise-cancelling technique, in which unwanted sound is silenced by measuring its waveform and then broadcasting a precisely similar sound signal with a waveform precisely out of phase with the unwanted sound, so that the peaks of one wave coincide with the troughs in the other. That sounded like science fiction a few years ago, but it is now in every-day commercial use.

Used naturally

Before anti-sense genes can be used to protect plants against virus infections a great deal remains to be done, in particular to ensure that the anti-sense genes have no harmful effects in the plants they are supposed to protect. But Dr. Lichtenstein points out that he has found at least one organism, a bacterium, which uses anti-sense genes naturally as a genetic mechanism, though not to defend against virus.

Very recently Lichtenstein carried out an experiment which gave exciting indications that the technique may work. He cloned the gene for a bacterial enzyme called chloramphenicol acetyl transferase, CAT for short, and made an anti-gene from it by reversing the positions of promoter and terminator. Then he inserted the CAT gene into tobacco plant cell cultures and measured the levels of the enzyme produced. Next he inserted the anti-gene into the same cultures. The levels of CAT produced fell sharply. So far, Lichtenstein has no hard evidence that this is due to the formation of duplexes, as the double strands of RNA are unknown, but it is the most likely explanation.

If the technique works, it may be possible to implant whole batteries of anti-genes into plants to protect against a number of different virus diseases. The technique would have the advantage of avoiding the use of chemicals and of providing protection even after a virus had gained access to plant cells. Anti-sense genes could also be used to delete a plant's own genes so as to create new mutants or to prevent plants from making poisons.

The value of Lichtenstein' technique depends on being able to insert other anti-genes into those plants used for crops. Recently British and Swiss scientists have shown that it is possible to insert foreign genes into monocotyledons, the class of plants to which nearly all important crops belong. Major problems remain to be overcome before the technique can be used commercially, but it now seems likely that it will soon become possible to create new varieties of crops such as wheat, rice, maize, millet and sugar cane with improved properties such as resistance to insect pests, drought and herbicides.

Agrobacterium

Dr. Jeffrey Davies and Dr. Margaret Bolton at the John Innes Institute near Norwich and their Swiss colleagues in the Friedrich Miescher-Institut in Basle have shown that the bacterium called Agrobacterium, which causes a condition analogous to cancer when it infects plants, can be used to transfer foreign genes into the nuclei of cells of maize, a monocotyledonous plant. Agrobacterium inserts a portion of its own DNA, deoxyribonucleic acid, into the nuclei of cells it infects so as to force the cells to make food substances on which the bacterium feeds. This provides a natural system for plant genetic engineering, but until recently it was proved possible to use it only to transfer foreign genes into dicotyledons, not into monocotyledons.

What the Anglo-Swiss team have done is demonstrate that when the genes of a virus which infects maize cells, called the maize streak virus, were inserted into that part of Agrobacterium DNA which is naturally integrated into plant cell nuclei, and maize plants were then inoculated with Agrobacteria which had been so treated, the maize plants became infected with the virus. This could have happened only if the viral genes had become integrated into the host cell nuclei with the bacterial DNA.

The next step will be to insert useful genes, such as those for resistance to insect pests or to herbicides used to kill weeds, into the viral DNA before inserting it in turn into the bacterial DNA and inoculating maize plants. The scientists hope it will be possible to use infection with the virus as a marker, to show that foreign genes have been integrated into the maize cell nuclei.

Before the technique can be used for commercial genetic engineering, a way is needed to regenerate maize and other monocotyledonous plants from single plant cells into which foreign genes have been implanted. This is the only way to ensure that the foreign genes are to be found in every cell of the regenerated plant. A team led by Professor Ted Cocking of Nottingham University has recently succeeded in regenerating rice plants from single cells, and believes the same technique will work for other monocotyledons. The way now seems clear for the genetic engineering of crop plants, including the insertion of anti-genes to protect against virus diseases.

Engineering a route to better corn

Two biologists at the University of Toledo (Ohio) have developed a genetic process that might lead to genetically engineered strains of corn that have better nutritional value, higher yields and resistance to herbicides. The researchers, Professors Stephen L. Goldman and Anne C.F Graves, say that for the first time genes carrying the codes for such superior traits can be incorporated into one-seed leaf plants, such as corn, by infection with a virulent strain of a soil bacterium. The process involves making a "wound" in an area of a very young corn seedling that contains rapidly dividing cells; that area is inoculated with a bacterial strain. The bacterium contains an agent capable of transferring a portion of its genetic code into the chromosomes of the corn seedling's cells. The transferred genes are then expressed in the host plant, where they become traits that can be inherited in the regular fashion. (Source: Chemical Week, 20 May 1987)

Research on bacterial genes

Mapping entire E. coli genome

New techniques could allow sketching the entire E. coli genome in two-three weeks, and pave the way to mapping the human genome. The E. coli work was done by C.R. Cantor of Columbia University in just over one year. The bacterial genome is only 10 per cent the size of the smallest human chromosome, however. Teams

at Columbia are trying to map human chromosome 6 and researchers at Yale are working on chromosome 4. Center says the work has so far indicated that genes for related functions are clustered together much more than originally thought. Mapping might help diagnosis and treatment for over 3,000 known genetic diseases. Just to process the data produced by mapping the human genome would require a huge computer base. C.P. Bolisi of DOE says the entire human genome could be mapped by the year 2000, and the Japanese are already building a robot to decode DNA 1,000 times faster than is now possible. (Extracted from Science News, 28 February 1987)

Drug firms are developing a new class of antibiotics that uncoil the DNA of bacteria

The 4-quinolones interfere with the enzyme that allows long strands of DNA to curl up to fit inside the bacterial cell. DNA gyrase mediates the twisting of DNA 1,300 microns long so that it fits inside an E. coli cell only two microns long. The curling requires 'nicking' of the DNA to make it more flexible. A sealing enzyme (part of the gyrase complex) then repairs the nicks. Quinolones interfere with the sealing enzyme, so the DNA code is not repaired and the bacterium cannot replicate. The damaged DNA induces production of destructive enzymes (endonucleases) that break up the DNA and kill the cells. The mode of action of the quinolones will make it hard for bacteria to develop resistance. Because quinolones are synthetic, there is no natural enzyme to destroy them, and there is no known mechanism that would prevent their entry into cells. There may be 25 quinolones at various stages of development, according to R. Finch of the University of Nottingham. (Source: New Scientist, 15 January 1987)

Bacterium produces thermostable cellulase

Scientists at Solar Energy Research Institute (SERI) in Golden, Colo., have found a cellulase enzyme system exhibiting activity and stability at temperatures far higher than for any previously known cellulase. The cellulase system is produced by a newly discovered bacterium, Acidothermus cellulolyticus, found by the team at Yellowstone National Park.

The SERI biochemists and microbiologists' research is funded by the Department of Energy's alcohol fuels programme.

A search for a highly thermostable cellulase system is part of the group's research aimed at finding economic methods to produce fuel ethanol from cellulosic biomass materials. In such a scheme, cellulase would convert woody biomass and agricultural wastes to fermentable sugars, in particular glucose. An appropriate yeast would then ferment the sugars to ethanol.

A highly thermostable cellulase would also greatly interest the food and fruit industries. Cellulases produced by fungi are currently widely used for clarification of fruit juices, for example. However, the relatively expensive fungal cellulases are unstable at temperatures greater than 60°C. Hence, process schemes operating at 50 to 60°C must either use high initial concentrations of enzyme or must make constant additions of it. A more thermostable cellulase would allow food processing at temperatures as high as 70 to 75°C, which would result in fewer bacterial contamination problems for producers.

The SERI team sought cellulolytic bacteria that are not only thermophilic but also acidophilic. Ethanolic fermentation occurs under acidic conditions (pH 3 to 5), and so the team wanted bacteria that will produce cellulase enzymes with optimum activity at an acidic pH.

The team sought such bacteria in Yellowstone's hot springs, many of which are highly acidic. Under a collection permit from the Biological Research Station at Yellowstone, the group last year isolated 12 bacterial strains from the upper Norris Geyser Basin area, where springs have a pH of 4 to 5.5 and temperatures of 45 to 85°C.

The SERI scientists have identified one of these strains as a new species, cellulolyticus (meaning cellulose dissolving), belonging to a new genus of thermophilic bacteria, Acidothermus (meaning acid and heat loving). The new genus and species have been officially recognized.

The new bacterium is moderately thermophilic, with optimal cell growth at pH 5 and 55°C. It is aerobic and can grow on a wide variety of substrates to a high cell density - vital factors for commercial application. Most important, however, A. cellulolyticus secretes a complex of cellulase enzymes into the surrounding medium that shows the highest temperature-activity optima and stabilities yet found for cellulase systems.

Crude culture broths from the new bacterium show optimal temperatures of 75°C for total cellulase activity and 83°C for endoglucanase activity. Even at 95°C, 38 per cent of total activity and 60 per cent of endoglucanase activity remain.

The team contrasts these results with those for Trichoderma reesei, a well-studied cellulase-producing fungus, some strains of which are used commercially. A wild type of T. reesei secretes cellulase enzymes with optimal temperatures of 45°C for total activity and 55°C for endoglucanase activity. And after just one hour at 60°C, the cellulase from this T. reesei loses half its total activity.

The SERI scientists are now working on isolation and characterization of the cellulase enzymes secreted into the broth. As yet, standard methods have failed to dissociate the large component into active subunits. The team will continue to pursue this work. It will also seek better understanding of the enzyme's thermal stability by carrying out kinetic studies, and analysis of its amino acid sequence and secondary and tertiary structures, in particular mapping the active site. (Source: Chemical and Engineering News, 6 June 1987)

Glow-in-the-dark biosensors detect toxins

Bacteria, genetically engineered to glow in the dark, can be used as living biosensors for the "detection of virtually any class of toxic agents", according to McGill University microbiologist Michael S. DuBow. Quantifying environmental toxins usually involves complex hardware. DuBow's approach is to link an easy-to-monitor indicator gene to a structural gene that is turned on or off by a mutagen, for example, cigarette smoke, or poisons such as lead or polychlorinated biphenyls. The level of gene expression of the marker will reflect the expression of the target gene.

The idea is eventually to mobilize the recombinant strains on dipsticks that could be used to assay for pollutants in the St. Lawrence River, for example, and get a luminous readout within 30 seconds.

Initially, DuBow fused the lacZ gene, which encodes the readily assayed beta-galactosidase enzyme, to the transposase operon of the transposable element

Hu, and inserted the vector into Escherichia coli. If the mutagen he was testing repressed the Hu element or induced it to move, it would change the expression of the operon, leading to changes in cellular levels of the assay enzyme. Recently, he has inserted genes for the luciferase enzyme from a marine bacterium into his library of Hu-LacZ vectors that respond to different toxins. When the toxin-target gene is turned on, so is production of luciferase, which catalyzes an oxidative light-emitting reaction.

Bioluminescence, the emission of light by bacteria or other organisms may have applications in clinical and other assays and development of anticancer drugs and insecticides. Microbics is developing a broad-spectrum test for mutagenicity based on a mutant strain of luminescent marine bacteria. Mutant bacteria that cannot produce light regain their bioluminescence in the presence of a mutagen. The new test is expected to compete with the Ames test, which takes over one day to complete. The microbics test provides results in under four hours. Microbics has also developed an assay for toxic waste based on Photobacterium phosphoreum, a marine bacterium. The decrease in luminescence is proportional to toxicity. The test provides results in under one hour and can be used to detect toxins such as PCBs, phenols, mercury and lead. Biosyne has developed a similar assay for toxic waste based on genetically engineering E. coli. Test methods that employ bioluminescence are nontoxic and do not cause storage or environmental problems, unlike tests based on radioactive materials.

Lederle Laboratories uses dark variants of Photobacterium leiognathi, a luminescent marine bacterium, to prescreen fermentation broths for anticancer antibiotics. The anticancer agents bind to the DNA of the dark variants of the bacteria. University of Wisconsin researchers are studying the function of luminescent soil bacteria (Xenorhadus luminescens) in nematodes, which carry the bacteria and release them when they bore into insects. The bacteria destroy the insects and produce a pigment that causes the carcasses to turn red, which may attract other insects to the nematode.
(Source: McGraw-Hill's Biotechnology Newswatch, 18 May 1987 and Chemical Week, 4 February 1987)

Research on viral genes

'Monkey virus' may trigger multiple sclerosis

Researchers at the University of St. Andrews in Scotland and the Charing Cross Hospital, London, have found fresh evidence that a virus is involved in some cases of multiple sclerosis. There is little doubt that an infectious agent plays a part in the disease, which destroys the myelin sheath around the nerves of the central nervous system, but the identity of the agent remains elusive.

William Russell and Kamal Goovani at St. Andrews and Leo Lange at Charing Cross found that a significant proportion of people with multiple sclerosis have antibodies to a virus called simian virus 5 (SV5) in the fluid that bathes the brain and spinal cord. SV5 belongs to a family of viruses called the paramyxoviruses, which includes measles and mumps. The virus was first recognized as a monkey virus but it often infects humans. Only around one in 1,000 of those infected develops multiple sclerosis.

As part of the body's reaction to viral infection, the immune system produces antibodies which bind to antigenic proteins on the surface of the invading virus.

Earlier studies found no difference in the levels of SV5 antibodies in patients with multiple sclerosis and those without. Those studies were based on analyses of antibodies in the blood serum. Goovani and Russell took a different approach. They reasoned that antibodies would appear close to the site of infection, so they analysed the cerebrospinal fluid rather than blood serum. If SV5 triggers multiple sclerosis only when it has crossed the blood-brain barrier, it might produce an immune response only within the central nervous system. If the virus remains outside the central nervous system, antibodies might show in the blood but the patient would not suffer multiple sclerosis.

A second reason for the team's success is that it made its analyses with a very sensitive assay called autoimmune precipitation. The antigens on SV5 and another human virus, parainfluenza virus, cross-react - that is, antibodies to SV5 will combine with parainfluenza virus and vice versa. This means that it is impossible to identify SV5 specifically. The researchers solved this problem by testing samples of cerebrospinal fluid with individual proteins from SV5 rather than with the whole virus. They found that 56 per cent of patients with multiple sclerosis had antibodies to an important glycoprotein from the surface of the SV5 virus.

This result is controversial. Other scientists have found that the cerebrospinal fluid of multiple sclerosis sufferers contains antibodies to most common human viruses. They argue that the disease causes a malfunction of the immune response in the central nervous system.

If this is true, then production of antibodies would not indicate a reaction to any specific virus. So the presence of SV5 antibodies might be a red herring. If SV5 is the agent of multiple sclerosis, scientists still have to find out how it causes the disease. (Source: New Scientist, 4 June 1987)

'Retrofection': a new role for retroviruses

Retroviruses have become infamous as the class of viruses responsible for AIDS and some types of cancer. They are unique in that an enzyme in the retrovirus copies the viral RNA genome into DNA, which is then integrated into the genome of infected cells. This gives retroviruses the opportunity to change the genetic material of cells. Maxine Linial, of the Fred Hutchinson Cancer Research Center in Seattle, has found evidence of a second way in which retroviruses might reshape the genomes of their hosts. They may transport cellular messenger RNA (mRNA) from one cell to another, and then deposit a DNA copy of that RNA into the genome of an infected cell.

A retrovirus is a simple chemical package containing the viral RNA, along with a few molecules of the enzyme *reverse transcriptase*, which copies the viral RNA into DNA as soon as the virus infects a new cell. The DNA then integrates into cellular DNA, from where it orchestrates production of both the mRNA that codes for viral proteins, and new copies of the viral genome. Eventually, newly made viral genomes and proteins are assembled into new viruses, which escape from the cell.

Sometimes, however, cellular mRNAs, copied from genes belonging to the cell, are accidentally packaged into the virus. This raises the question: Can the mRNAs be copied into DNA and then inserted into the cell genome of the next host cell in the way that viral RNA is? Maxine Linial's new work suggests that the answer is yes.

To have a chance of observing this process in action, Linial worked with a mutant retrovirus which packaged cellular mRNAs more often than usual. And to follow the progress of the mRNAs it gave rise to, she inserted a new gene into the infected cells artificially. Linial obtained good evidence that mRNA from the gene was packaged into the viruses, and then was copied into DNA in other infected cells and deposited into their genomes.

Linial suggests that what she observed in this modified situation also happens routinely, though less frequently, in normal retroviruses that are infecting normal cells. So it seems that retroviruses may be able to transfer genes indirectly between different cells and different organisms. Linial has called this transfer process "retrofection".

There is good evidence that much of the genome of higher organisms was formed by the copying of mRNA back into DNA. Scientists estimate that 5 per cent of most genomes of the cells of higher organisms may be derived from such a process. Most of the genes concerned have been altered during the process, turning them into "pseudogenes" that are no longer functional. But such pseudogenes might provide the raw material for the evolution of new genes with new functions.

Many researchers believe that pseudogenes were formed by the reverse transcription of a cell's own mRNAs. Linial's work suggests that much of it may have been transferred from one cell or organism to another. The idea that viruses play a major role in evolution, by transferring genes between cells, organisms and even different species, is gaining support. (Source: New Scientist, 14 May 1987)

Viral mutation rate alarms AIDS researchers

The virus that causes AIDS is mutating much faster than previously thought. It may be transforming itself as much as five times faster than the influenza virus.

According to a computer analysis of 17 samples (isolates) of the virus from Africa and the US, some genes show divergence of up to 30 per cent from their point of common ancestry about 20 years ago. The isolates were taken from AIDS patients between 1983 and 1985.

These results also revealed that there is little genetic difference between the AIDS virus first described by French investigators in May 1983 and the group of isolates cultured by Robert Gallo at the National Institutes of Health (NIH) in Bethesda, Maryland. This confirms the findings in 1985 by American and French researchers that genetically, viral isolates from France and from Gallo's laboratory are almost indistinguishable.

The discovery that human immunodeficiency virus (HIV) is mutating so rapidly may delay considerably the development of a vaccine for AIDS, according to Gerald Myers, a molecular geneticist associated with Los Alamos National Laboratory.

He performed the genetic analysis. Like expanding galaxies, the AIDS isolates are "splitting apart". According to Myers' calculations, each isolate's genome is transforming itself every year at a rate of about 1 per cent. Thus, any two isolates could be diverging genetically from one another at a rate of about 2 per cent annually.

Eventually, isolates might diverge so far that a single vaccine might not work for all of them.

Moreover, the frantic rate at which the virus mutates suggests that it has only recently entered an evolutionary niche, says Myers. Being in its evolutionary infancy, HIV could still improve its "fitness", or adaptation to its host, as it nears evolutionary equilibrium. That, says Myers, could mean a drift to new host cells other than the peripheral lymphocytes that the virus now favours.

Myers and his collaborator, Temple Smith, of the Dana Farber Cancer Institute in Boston, Massachusetts, reported their findings in the first edition of a new database of HIV sequences.

They will update the database quarterly.

Exactly how long the virus has taken to accomplish this quick change is still unknown, says Myers, but he reckons the span to be about 12 to 20 years.

Some of HIV's genes have changed by more than 30 per cent. By comparison, the NS1 gene of the influenza A virus changed itself by 18.7 per cent over 50 years.

Myers hopes to analyse an isolate taken from an infected patient in Zaire in 1976. It is now in the possession of the biotechnology company Genentech. The isolate could be an ancestor to anchor the "trees". (Extracted from New Scientist, 4 June 1987)

Researchers want trials with anti-antibodies

Doctors in Britain are considering whether to begin tests on humans of a method of stopping the human immunodeficiency virus (HIV) from binding to the blood cells that it attacks. Doctors at Northwick Park Hospital in Harrow, Middlesex, hope to test the safety of the treatment on six patients infected with HIV who are at high risk of progressing to AIDS.

The technique involves the use of "anti-idiotype antibodies". An idiotype is the variable part of the antibody molecule, the part that recognises a particular antigen. In this case, the idiotype is that found on the antibodies that recognise the molecule to which HIV binds, the T4 receptor. Most of the cells that have the T4 receptor are a type of white blood cell called T4 lymphocytes.

An anti-idiotype antibody is an antibody to an antibody. When the tests on humans begin, doctors will inject patients with antibodies produced by mice. These antibodies recognise the T4 receptor. The patients may then make their own antibodies (anti-idiotype antibodies) against these mouse antibodies. The mouse antibodies are structurally like a plaster cast of the T4 receptor, so the human antibodies produced will mimic the T4 receptor. Because of this similarity, these human antibodies should bind to HIV just as the T4 receptor does.

Scientists know that this kind of approach can be successful from work on other diseases in other animals. Several years ago, Ronald Kennedy of the Southwest Foundation for Biomedical Research, San Antonio, Texas, developed a vaccine based on anti-idiotype antibodies. The vaccine protects chimpanzees against hepatitis B.

At Northwick Park, the focus is now on treatment rather than a vaccine to protect people against infection. To be effective, anti-idiotype antibodies must bind to HIV. This binding must prevent the virus either from entering cells or from replicating in infected cells. Researchers therefore need to be sure that HIV binds only to the T4 receptor.

Several scientists, including Angus Dalgeish and Mirek Malkovsky at Northwick Park, Robin Weiss at the Institute of Cancer Research in London, and Richard Axel of Columbia University, New York, have failed to find evidence that HIV can bind to any receptor but the T4. Some researchers have observed that HIV can infect some cells that normally do not have T4 receptors. Dalgleish and Malkovsky, however, have found that all cells that HIV is capable of infecting have either the T4 receptor on their surface, or messenger RNA that has the potential to make T4.

Tests in animals have been even more promising. Kennedy said at the Third International Conference on AIDS in Washington DC that his group had injected baboons with antibodies against the T4 receptor. These animals produced anti-idiotype antibodies which in the laboratory were able to bind to HIV and partially neutralize the activity of the virus.

All three groups have shown that the antibodies produced by the experimental animals can neutralize, or inactivate, several different isolates (strains) of HIV. This ability to knock out a cluster of strains is important because many researchers have managed to produce neutralising antibodies against HIV, only to find that these inactivate only one strain of the virus.

The next step will be to find out how humans react to the treatment. The hope is that blocking the T4 receptors may prevent viral replication. In addition, the patients may make anti-idiotype antibodies to the antibodies injected, which may then neutralize any remaining virus.

If this approach is successful, researchers may be able to modify the technique to induce a stronger response from the patients' own immune systems. This line of investigation could underpin a programme to develop a vaccine.

Humans do not have antibodies against their own T4 receptors. Some scientists at the Washington conference asked whether antibodies that block the T4 receptor would themselves suppress the immune system. (Source: New Scientist, 11 June 1987)

Marrow suppression hampers AZT use in AIDS victims

A group of researchers at New England Deaconess Hospital in Boston has discovered why the AIDS virus suppresses bone marrow. The finding is important, says Jerome Groopman, who heads the group, because patients with poorly functioning bone marrow are unable to take AZT, which is the only anti-AIDS drug that has been proven useful in a randomised controlled clinical trial.

Groopman's evidence leads him to propose that the AIDS virus infects certain bone marrow cells. Then antibodies to the AIDS virus bind to those cells and prevent them from growing. It is the patient's own immune response to the AIDS virus that suppresses the bone marrow. There is at least some hope that this suppression can be overcome by a newly available class of hormones that stimulate the bone marrow. Groopman and his colleages reported their findings in the 12 March issue of Nature. (Extracted from Science, Vol. 235, p. 1,463, 20 March 1987)

GM-CSF controversia in AIDS victims.

Given that the depression of the human immune system, with anaemia being one of the symptoms, is at the heart of the AIDS syndrome, the news from the New England Deaconess Hospital in Boston is welcome. The protein GM-CSF was synthesised by Genetics Institute and used in hospital trials financed by Sandoz Inc. Jerome Groopman treated 16 AIDS patients and reports that their white blood cell counts resumed normal levels. Side effects included mild aches, chills and fever. Phlebitis, an inflammation of the veins, was reported in four patients.
(Source: Biotechnology Bulletin, Vol. 6, No. 4, May 1987)

Prototype AIDS vaccine tested

The first tests in humans of an experimental vaccine against human immunodeficiency virus (HIV) suggest that the prototype vaccine may stimulate the production of antibodies that are effective against the virus. Daniel Zagury, of the Pierre and Marie Curie University in Paris, recently inoculated himself and a small group of African volunteers with a vaccine based on the vaccinia virus. All of the participants were healthy individuals who were not infected with HIV.

Zagury announced his first results at the Third International Conference on AIDS, held in Washington DC. Zagury said that vaccination, followed by a booster, induced antibodies which appear to inactivate or "neutralize" HIV in the test tube. These antibodies seem to be effective against many different strains of HIV, Zagury said.

The vaccine that Zagury used for the initial inoculation is based on the vaccinia virus, which provides immunity to smallpox. Genetic engineering techniques have made it possible to insert different genes from HIV into the genetic material of vaccinia, to make so-called "recombinant vaccinia". In this case, the vaccinia carried the gene coding for the envelope protein of HIV.

Zagury followed the initial inoculation with a booster of what he described as "disabled cells". These cells were themselves infected with vaccinia virus carrying the gene for the envelope protein of HIV. The cells manufacture the envelope protein, which appears on the surface of their membranes. Scientists believe that this presentation may be more effective than unattached proteins in provoking an immune response.

Zagury's results are promising because the antibodies produced were "group-specific neutralising antibodies". The term neutralising means that the antibodies neutralise, or inactivate, the virus.

The antibodies are called "group-specific" because they neutralize many different strains, or isolates, of HIV, as opposed to just one. So far, most researchers working on vaccines against HIV have managed to induce the production of antibodies that can only neutralise a particular strain of HIV.

Zagury's statement said it would not be possible to boost immunity with disabled cells infected with recombinant vaccinia on a large scale. The search is

now on for a more practical way of deliver : booster. Zagury said: "Without a practi- ooster shown to be efficacious in the laboratory, no candidate vaccine could undergo any field trials".

Scientists would test any promising candidate for a vaccine in people at high risk of HIV infection. This approach would eliminate the problem of deliberately challenging the immune systems of people who had been vaccinated against the virus. According to some researchers, a trial which involved vaccinating 1,000 uninfected people at high risk of infection might supply an answer about the vaccine's effectiveness within a couple of years.

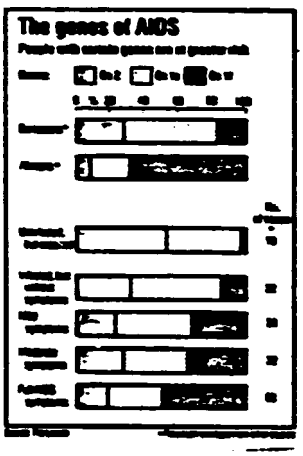
William Jarrett, of the University of Glasgow Veterinary School, said that he has tested a prototype vaccine against HIV in primates. This type of vaccine is based on artificial virus particles called ISCOMS. These are small honeycomb-like structures into which the viral proteins sit. The vaccine appears safe in primates and stimulates the animals' immune systems to produce the necessary antibodies. Jarrett said that he is prepared to test the vaccine on human volunteers, including himself, within a year. (Source: New Scientist, 11 June 1987)

Why some people get AIDS and others don't

Seven British scientists have found one reason why not all people exposed to the AIDS virus get AIDS, and why many of those infected show no symptoms for so long. This is not just the biggest mystery about AIDS, it is one of the abiding puzzles about all infectious diseases. Why, for example, did influenza kill 20 million people immediately after the first world war, whereas now it simply sends you to bed for a few days? What controls the virulence and infectiousness of diseases?

The answer that the British scientists give is genes. Just as some people have blue eyes and some brown, so some people have genes that resist infection with the AIDS virus and others have genes that do not. It has long been realized that, over the generations, bugs and their victims come to an evolutionary accommodation, in which the resistance of the victim increases and the virulence of the pathogen declines. Until recently, most people thought the pathogen's genes were more important than the victim's in determining virulence. The British findings show that both matter.

To guess that genes are involved is easy. To find the relevant genes is difficult. Dr. Anthony Pinching, Dr. Keith Mye, Dr. Lesley-Jane Eales and their colleagues at St. Mary's Hospital in London stumbled on the right gene almost by accident. They were looking to see if certain genes were more common among AIDS patients than among people at large. The ones they chose were not, but Dr. Mye noticed that a different gene he had studied before was, indeed, more common. The gene, called "Gc", comes in three forms: 1f, 1s, and 2. Since humans have two copies of every gene, there are six combinations of the Gc variants that people can have: 1f-1f, 1f-1s, 1s-1s, 2-1f, 2-1s, and 2-2. Dr. Pinching's team found that people with the 1f variant are far more likely than average to catch the AIDS virus and those with the 2 variant are far less likely. Those with 1f-1f are worst off and those with 2-2 are best off. Their study included only 375 people, so it may not be representative. None the less, for their sample the statistics are striking.



The Gc gene makes a protein that sits on the cell surface and plays a role in transporting vitamin D into the cell. The main difference between the 1f, 1s and 2 versions of the protein is that 1f has more of a chemical called sialic acid on the outside of the cell membrane than Gc 1s, while Gc 2 has none. Dr. Pinching speculates that the sialic acid somehow helps the AIDS virus get into the cell by assisting it through the membrane.

The study shows that the same genes also influence the severity of AIDS in those infected with the virus. Those with Gc 1f are more likely to go on to develop the full disease soon after infection, and those with Gc 2 less likely than the average. Probably, again, the sialic acid helps the virus go from cell to cell.

This is more surprising than the previous result, for scientists had long suspected that the only things that triggered the awakening of the dormant virus - and so of AIDS itself - were time, or another infectious disease. Certainly, stimulating the body's immune system to fight a different disease seems to increase the risk of waking up the virus.

The fact the Gc gene affects the virulence of the disease is good news. For the first time it suggests that present estimates of how many of those infected will go on to develop the disease may be exaggerated. It shows that there is a genetic difference between those who are likely to develop symptoms quickly and those who are not. This implies that many of those who do not develop symptoms quickly might never do so. It also implies that death rates will be highest in the earliest years of an epidemic of AIDS, for those most likely to catch the virus are also most likely to develop symptoms.

The discovery involves some good news for Europe and America, and some bad news for Africa. Among people from Central Africa, the Gc 1f gene is much more common and the Gc 2 gene much scarcer than among people of European origin. So the average African may be genetically more susceptible to the AIDS virus than the average European, which may partly account for the fact that the disease seems to have spread faster in Africa than in Europe or the United States. This may also partly explain why a disproportionate number of cases of AIDS in America in some high-risk groups are among blacks: black Americans also have a higher frequency of Gc 1f. Most Asians lie between Europeans

and Africans in the frequency of the Gc 1f version of the gene.

For the moment, however, this discovery offers no relief from the growing epidemic - only some valuable new knowledge of the virus's vulnerability. (Extracted from The Economist, 23 May 1987)

Scientists uncertain about new drug

Researchers in Europe and the US have expressed severe doubts about a new treatment for AIDS which about to begin trials in Sweden. Doctors at the Karolinska Institute in Stockholm intend to treat 18 patients with a substance called peptide T.. Yet scientists elsewhere in Europe and the UK say that they have been unable to repeat the basic experiments to confirm that peptide T can indeed prevent human immunodeficiency virus (HIV) from infecting white blood cells.

A peptide is a short chain of amino acids, the building blocks that make up proteins. Peptide T is a chain of eight amino acids. Five of these amino acids have names beginning with T, hence the name peptide T. The same sequence of amino acid also occurs in the viral protein known as gp 120. Gp 120 is attached to the virus's envelope, and is involved in binding to the white blood cells called T4 lymphocytes.

Peptide T was discovered last year by Candace Pert and her colleagues at the National Institute of Mental Health in Bethesda, Maryland. They say that it can block the receptor on the T4 lymphocyte to which HIV binds, preventing the virus from infecting these cells. In their paper published in the Proceedings of the National Academy of Science in the US, they say that their discovery should help in the development of vaccines. "Perhaps even more important, peptide T, or a derivative, might be useful clinically to half or attenuate the spread of the virus in infected individuals."

Yet, at a meeting last month, organized by the University of California, Los Angeles, in Keystone, Colorado, many researchers told Pert that they had been unable to reproduce her results. Several groups at the Keystone meeting believed that there was a desperate need for independent groups to confirm the data on peptide T. (Extracted from New Scientist, 28 May 1987)

Plasma treatment tried on AIDS patients

A trial will begin at two London hospitals within the next few weeks of a possible treatment for AIDS. Doctors from the Westminster and St. Stephen's hospitals will give AIDS patents blood plasma derived from healthy people who have high levels of antibodies to the virus. The doctors want to see whether the antibodies present in the plasma can help the AIDS patients to recover. The trial will involve about 40 AIDS patients.

People with the human immunodeficiency virus (HIV), but without AIDS, have large amounts of neutralising antibody to the virus that can mitigate the effects of HIV.

The plasma of these people also has other antibodies that help to fight off the infectious diseases that result in full-blown AIDS. Transfusing AIDS patients with plasma derived from people infected with HIV may therefore help them to recover from the disease. The plasma is treated with the chemical agent betapropiolactone to inactivate any viruses that could be present, including HIV. It is also heated to 56°C for 30 minutes to kill any other pathogens within the plasma.

The trial has the approval of the ethical committees of the London and Cambridge hospitals. The patients must be made aware, the hospitals stipulate, that they may receive either plasma containing the neutralizing antibodies, or commercial plasma which does not contain neutralizing antibodies to the AIDS virus. The committees say that if the patients receiving the plasma improve noticeably, "a moral judgement must be made to determine if the change is due to the treatment, which should then be made available to all". (Extracted from New Scientist, 11 June 1987)

WHO derides vaccine scare

Reports of a link between the successful global smallpox eradication programme and the emergence of AIDS have been dismissed by the World Health Organization (WHO). Dr. Jonathan Mann, director of the WHO AIDS programme, said that allegations that the smallpox vaccine, vaccinia, may have activated HIV infections "join many other unproven and speculative ideas about the origin of AIDS". Mann is anxious that unfounded speculation could jeopardize other vaccination programmes, and called for work that links smallpox vaccine with AIDS to be submitted for scientific scrutiny.

It was emphasised at the 40th WHO Assembly meeting in Geneva that the world should concentrate on action to prevent the spread of AIDS, rather than speculating on its origins.

The British aid organization War on Want says up to 75 million Africans could soon be affected by AIDS. Using figures from the WHO conference, the group predicts that the virus will spread along Africa's lines of transport to Zimbabwe, Mozambique and Angola, and that South Africa "may face a major and widespread epidemic in the near future". (Nature, Vol. 327, 14 May 1987)

New virus, growth factor found for AIDS

Yet another virus that apparently causes AIDS - along with a growth factor in the AIDS-associated Kaposi's sarcoma and a role for leukemia viruses in the AIDS scenario - were among the new findings presented by scientists during the Third International Conference on AIDS held in Washington, D.C.

According to Robert C. Gallo of the National Cancer Institute (NCI) in Bethesda, Md., his research group and other collaborators have recently found the following:

- In addition to the previously described HIV-1 and HIV-2 viruses, there appears to be a third, distinct retrovirus capable of causing the fatal disease. The scientists found the virus in blood samples from 10 Nigerian patients with AIDS or AIDS-like syndrome. Tests using the patients' serum and known AIDS viruses showed that the newly isolated virus is a separate human retrovirus that causes AIDS, says Gallo, who expects more such viruses will be found. He says the discovery increases the risk of infection by an AIDS-causing virus, but that "we should not panic" since the virus seems to be less virulent than the other AIDS viruses.

- Although the bluish or reddish skin nodules of Kaposi's sarcoma are frequently associated with AIDS, NCI scientists have determined that the syndrome probably is not directly caused by the HIV virus. Gallo says his group has regulated the growth of Kaposi's sarcoma cells in the laboratory for the first time, by manipulating the one or more growth factors

released by retrovirus-infected lymphocytes. The factors, which cause new blood vessel growth and support long-term cultures of sarcoma cells, were produced in vitro by lymphocytes infected with HTLV-II, a retrovirus that does not cause AIDS. Despite the dramatic effects of these growth factors on the sarcoma cells, the same cells do not respond to other, well-known growth factors as do normal cells, says NCI scientist Shuji Nakamura.

Based on the data, Gallo says the sarcoma "is not a true malignancy, and should be easily controlled by interrupting the growth factor effects". Although it is found in only 40 per cent of AIDS patients and is not in itself life-threatening, systemic Kaposi's sarcoma can cause widespread problems including severe diarrhea, says Nakamura.

- New studies of patients with coinfections of both an AIDS virus and a virus thought to cause leukemia suggest that the leukemia virus may advance the progression of AIDS. The virus, called HTLV-I, has been present in the United States for many years and is not considered very contagious. However, unpublished results from NCI say that HTLV-I is spreading through urban populations of intravenous drug abusers, a group considered at risk for AIDS. According to Gallo, the HTLV-I virus may lie dormant in infected cells for perhaps 30 years, but "it should not be forgotten" as a possible cofactor in AIDS. Because of their possible roles in AIDS, Gallo says HTLV-I and II should be included in planned AIDS vaccines and in screening tests for donated blood. (Source: Science News, Vol. 131, 6 June 1987)

Different viruses may trigger infection

One of the puzzling quirks of the human immunodeficiency virus (HIV) is its ability to lie low for years and then kill its host. What happens during this dormant phase of the virus's life cycle? How does it spend its time? What eventually awakens it?

Several scientists at the US National Institute of Allergy and Infectious Diseases (NIAID) and various universities are pursuing answers to these questions. Anthony Fauci, director of the NIAID, proposes two hypotheses for the behaviour of the virus when it first invades the immune system.

HIV attacks the white blood cells (lymphocytes) called T4 cells. The virus binds to the CD4 receptor molecule that these cells bear on their membranes. Fauci's first hypothesis is that HIV may interact with these cells of the immune system without infecting them. At this point, the virus would not have integrated its genes into those of the host cell. Alternatively, the virus may infect the cells, incorporating DNA of viral origin into the cells' chromosomes, but fail to replicate and kill these cells.

Scientists have observed that when HIV comes into contact with T4 cells, the immune system quickly alters. Normally, the T cells would spring into action at the appearance of a foreign object - an antigen. Once they have met HIV, however, they lie dormant when challenged.

Laboratory experiments at NIAID suggest two possible reasons. First, says Fauci, contact with HIV may alter the pathway through which the receptors on the cell's membrane send signals to the nucleus. Fauci calls this a defect of the "post-antigen receptor signal transduction process". It signals never get beyond these receptors, the cell cannot mount a proper response to antigens.

Interestingly, Fauci found that T cells exposed to HIV still respond to provocation with mitogens. These are substances that normally induce cell division. Fauci says that the cellular pathways through which messages about mitogens pass are different from those for antigens.

The other reason why T cells might stay dormant after coming into contact with HIV is that the virus might block or modulate the CD4 receptor molecule. HIV's proclivity for CD4 is well known; it seeks out cells that sport these molecules on their surfaces.

Normally, the CD4 molecule helps in the immune response controlled by the major histocompatibility complex. This complex is involved in the recognition of self. For example, it directs the rejection of transplants by recognizing antigens from foreign tissue. In the team effort that is characteristic of the immune response, certain cells called macrophages envelop foreign bodies and exhibit parts of their victims on their surface. The macrophages then present these antigens to the CD4 receptors on T cells to elicit their response.

Fauci says that he has not yet proved which of his two hypotheses might be to blame for HIV's effect on the T cell.

Fauci and colleagues at NIAID and Duke University have found that when HIV infects a cell, it proceeds to eliminate some of the cell's regulatory activities. For example, certain mitogens normally induce T cells to produce interleukin-2, a substance that helps to regulate the growth and maturation of T cells. When researchers stimulated infected T cells with such mitogens, they failed to produce interleukin-2.

HIV can commandeer several parts of a cell's machinery. Further evidence has emerged from experiments with another type of white blood cell called a monocyte. Monocytes can be infected with HIV but they do not die. Some researchers suspect that these cells may form a circulating reservoir of infection.

Fauci and his colleagues, Thomas Folks of NIAID, have created clones of monocytes that are infected with HIV but do not produce it. When provoked with a mitogen, these monocytes produced a substance called interleukin-1 beta, which can modulate cell function, Fauci says. HIV "upregulates" interleukin-1 beta, yet "downregulates" interleukin-2. However, no one yet knows what advantages this control confers on the virus.

Latency can continue for months or years until some event activates the virus to start replicating. Several researchers have tested the idea that other viruses can activate the latent HIV. Paul Luciw at the University of California at Davis and his colleagues at the Centers for Disease Control in Atlanta have managed to get HIV to replicate in T cells by introducing either herpes virus, cytomegalovirus (also one of the herpes family) or a mitogen.

In a variation to this approach, Howard Gendelman at NIAID has introduced certain genes from herpes simplex virus and two genes from HIV into cells cultured in the laboratory. The function of the genes from HIV is to help in switching on viral replication. Gendelman found that the addition of the herpes genes sharply stimulates the two HIV genes.

Yet more evidence on the influence of such coexisting infections comes from the brains of people who had died of AIDS. In patients infected with both HIV and papovavirus, a relative of papilloma virus, the level of HIV was markedly higher than in those infected with HIV but not papovavirus. In further experiments, Fauci says, genes from this virus had the same effect on HIV as the herpes genes did.

Fauci has begun studies to judge whether internal signals from the immune system can switch on HIV. The signals he is looking into are called cytokines. These are ubiquitous substances in the body that stimulate cell growth and differentiation. Interleukin-2 is a cytokine, for example. Fauci exposed infected cells to cytokines, and found that this stimulated the virus in these cells to begin to replicate.

Researchers have revealed a little more about HIV's influence on the immune system. Although they are still far from applying this knowledge in the clinic, this work provides a scientific basis for the advice that many doctors give to infected people: Avoid other infections! (Source: New Scientist, 25 June 1987)

Vaccine breakthough by British Bio-technology

British Bio-technology Ltd., the Oxford-based health science company, has made a breakthrough which could lead to a safe and effective vaccine against AIDS. This follows on from work by an Oxford University research team led by Drs. Alan and Susan Kingsman. At the heart of their discovery is a cellular protein which has the unique property of assembling into structures resembling viruses. Working with the company, these researchers have now manufactured an artificial form of the AIDS virus. Since the surface of the AIDS-like particle, or pseudovirus, mimics that of the true AIDS virus, British Bio-technology's scientists believe that it could be used as the basis of an effective, non-infectious vaccine. There is no experimental evidence of this yet, however. Details from: Dr. Keith McCullagh, chief executive, British Bio-technology Ltd., Brook House, Watlington Road, Cowley, Oxford OX4 5LY or on 0865 718817. (Source: Biotechnology Bulletin, Vol. 6, No. 4, May 1987)

Research instrumentation

A production-scale bioreac or system

Verax (Lebanon, N.H.) is marketing a continuous-culture, fluidized-bed bioreactor system that produces kilogram-per-year quantities of biomolecules. The System 2000 operates on a process - for which a patent application has been made - in which cells are cultured in the reactor after immobilization in weighted, porous microspheres. A recycle flow through the reactor vessel suspends the cell-populated microspheres in a thick slurry, while a separate flow continuously adds medium and removes harvest liquor containing the desired cell products. The recycle loop that provides fluidization velocity also conditions the culture liquor. It adds oxygen, removes carbon dioxide, and maintains pH and temperature. (Source: Chemical Week, 22 April 1987)

Miniature electrophoresis system for rapid scanning of samples

A new miniature electrophoresis system for the rapid scanning of small samples has been developed by LKB-Produkter AB, the Swedish manufacturers of instruments and reagents for biosciences and chemistry. Designated LKB 2050 Midget Electrophoresis System, it is said to work three times faster than conventional methods.

Using a wide variety of high-resolution techniques, including zone, disc, gradients, SDS and 2D electrophoresis, the new system is claimed to cut running costs by up to 90 per cent. The complete system includes multiple gel casting units, an electrophoresis tank, an electrophoretic transfer unit, a laser densitometer, digital power supply and various accessories.

With the LKB 2050 Midget, up to 14 gels can be cast at one time. Because of very efficient heat removal, two gels containing 5, 10 or 15 samples each can be run in less than 45 minutes. A complete analysis including casting gels, sample application, running electrophoretic transfer and densitometric scanning can be made in under two hours, LKB says.

Staining and destaining of the thin 8 x 10 cm gels can be achieved in about one hour. This is also the case with transfers to membranes. Automated analysis is possible with the aid of the laser densitometer with 50 micrometer resolution. (Source: SIP, Stockholm, Sweden, May 1987)

Automated DNA extraction

Over the past decade, molecular biology has provided many powerful new techniques for in vitro recombination of DNA molecules and translation of mRNA into proteins, as well as methods for cloning genes into micro-organisms. In the years ahead, potential applications encompass a variety of ambitious projects. Among the most prominent are plans to map the complete human genome; to detect and perhaps treat genetic disorders (gene therapy); and to engineer gene products for pharmaceutical, immunological and agricultural use.

Although the applications are of a diverse nature, there remains an underlying necessity to isolate the gene of choice. This requires the isolation of genomic DNA of high purity and high molecular weight, capable of being cleaved by restriction endonucleases, cloned into appropriate vectors, and hybridized to unique DNA probes. Alternatively, mRNA may be isolated and used as a template to synthesize cDNA strands.

Until recently, genomic DNA has been purified by manual methods - often tedious and time-consuming, and which at times give low recoveries.

Applied Biosystems' (UK), model 340A Nucleic Acid Extractor has been designed to automatically extract and purify genomic DNA and RNA from tissues, bacteria and viruses. The Nucleic Acid Extractor uses a unique ethanol precipitation system to isolate DNA and RNA. First, a solution of ethanol and sodium acetate is automatically added to the extraction vessel, and the nucleic acid allowed to precipitate at ambient temperature. DNA is efficiently recovered by ethanol precipitation at temperatures ranging from -20° to 25°C, with no increase in recovery at lower temperatures. Since at concentrations greater than 10 µg/mL, recoveries in the 85 to 90 per cent range are obtained after a 15-minute incubation period, no cooling is required for precipitation. The insoluble material is then isolated, not by centrifugation, but by entrapment on a teflon filter. The cartridge which houses the teflon filter is constructed to mate directly with the extraction vessel, and is attached after the last extraction step, while the vessel is still on the model 340A. The aqueous extract then passes through the cartridge, and the precipitated DNA

is trapped on the teflon filter, washed with a series of ethanol washes, and then dried.

The cartridge is then taken off the extraction vessel, the housing is opened and the filter - with the purified nucleic acid material collected on it - is removed and placed in an appropriate buffer for final re-suspension. As much as 85 per cent of the material quickly redissolves in 15 minutes if a low vacuum and gentle heat is applied to the immersed filter.

The extractor runs as many as eight samples simultaneously through a user-programmed method designed with a flexible software package provided. There are three vessel sizes available: 15, 7 and 3.5 mL, which accommodate sample volumes from 1 mL to less than 5 µL.

Due to automated control of experimental conditions, DNA product quality and yield is highly consistent. Coefficients of variation within a method are typically between 0.02 and 0.10 for yield and absorbance ratios A230/A260; A260/A280.

Initial applications provide DNA product from biological sources such as blood, Chorionic villi or tumour cells for genetic disease tests. Diagnostic tests using DNA restriction-site markers exist for sickle-cell anaemia as well as thalassemias and Lesch-Nyhan syndrome. More recently, restriction fragment length polymorphisms (RFLPs) have been found to co-relate with Huntington's disease and cystic fibrosis. The 340A has been employed to routinely isolate DNA from human blood samples, as well as occasional isolation of DNA from Chorionic villi biopsies. Five milliliters of human whole blood is easily treated to prepare crude nuclei samples with a lysing agent such as Clay Adams Ultralyse II or 1 per cent Triton X-100 to lyse red blood cells as well as leukocyte cell membranes. Nuclei are isolated by centrifugation, and are either directly injected into a 14 mL 340A vessel or stored at -70° C before use. Chorionic villi biopsies are rapidly rinsed with standard phosphate buffered saline, then injected into a vessel. Blood nuclei or Chorionic villus are cycled through a standard 340A method utilising a 45-minute sample digestion step at 50° C, two ten-minute phenol/chloroform extractions, one ten-minute chloroform extraction, and ethanol precipitation. Total cycle time is three hours and 20 minutes.

DNA product quality was then determined by absorption spectra, restriction and molecular sizing. Absorbance ratios from A230/A260 and A260/A280 are consistently found to be in the range of 0.4 to 0.5 and 1.80 to 1.95, respectively. These ratios are typical for clean DNA product. (Extracted from Canadian Research/Biotechnology Canada, April 1987)

Biocatalysts offers bulk dextranase for tissue culture

Bulk quantities of dextranase are now available from Biocatalysts. Dextranase is a non-proteolytic enzyme which can be used to harvest mammalian cells from dextran-type microcarriers. In the past, enzymes such as trypsin have been used for this purpose but, due to their proteolytic action on the cell adhesion plaques, they have often damaged the cells. Biocatalysts say they are offering dextranase at 10 per cent of the previous cost. Details from: Stuart West, Biocatalysts Ltd., Main Avenue, Treforest Industrial Estate, Pontypridd CF37 5UT. (Source: Biotechnology Bulletin, Vol. 6, No. 3, April 1987)

General

How resistance to antibiotics is increasing

In the first study of its kind, more than 100 scientists from 30 nations have just completed a study shedding some light on a worldwide increase in antibiotic resistance among human pathogens. The three-year study, headed by Stuart B. Levy, professor of medicine and molecular biology at Tufts University (Boston), examined the frequency of antibiotic resistance and how worldwide patterns of antibiotic use may contribute to the spread of drug-resistant bacteria. The study found that in some developing countries, 20-30 per cent of the prevalent strains of bacteria that cause diarrhoea or pneumonia are resistant to penicillin or tetracycline. In many cases, the only alternatives are costly and rare drugs that are usually unavailable in those countries. Additionally, the study shows that new strains of resistant bacteria continue to appear, and that existing strains are developing resistance to multiple drugs. (Source: Chemical Week, 17 June 1987)

Biochemists chase leaping electrons

Transfer of an electron from one site to another in a molecule or between molecules is one of the most fundamental and ubiquitous processes in chemistry. In many relatively simple systems, the process is well understood. But that is not true in biological systems where, until recently, some pretty basic aspects of electron transfer - such as the maximum distance an electron could travel between two redox centres - were a matter of dispute.

Although all the details of biological electron transfer have by no means been sorted out, chemists are developing elegant experimental and theoretical techniques to answer fundamental questions about this critical process.

Electron transfer is an essential component of biological oxidation-reduction reactions, such as the metabolic reduction of dioxygen in a stepwise series of reactions mediated by metalloproteins, mainly the cytochromes. Based on the crystal structures of these proteins, scientists proposed almost 20 years ago that biological electron transfer reactions could occur across distances of 10 to 20 Å. However, inorganic chemists largely doubted that such long-range transfer reactions could occur at the potentials involved in most biological systems.

The intense interest in biological electron transfer stems from the fact that "it is, conceptually, a very simple process - just getting an electron from point A to point B - and therefore, we can think about it in straightforward terms".

About three years ago, four independent research groups - those of Harry B. Gray at California Institute of Technology, Stephen S. Isied at Rutgers University, Brian M. Hoffman at Northwestern University, and George L. McLendon at the University of Rochester have demonstrated that long-range electron transfer could take place at biologically significant rates. Electron transfer in biological systems is one of the "hottest" areas in bioinorganic chemistry today. The questions being asked involve not only mechanisms of electron transfer in specific donor-acceptor pairs, but how these metabolic pathways evolved. (Extracted from Chemistry and Industry, 18 May 1987)

Mathematical model predicts AIDS spread

The AIDS epidemic, according to Robert May of Princeton University, is much less predictable than people think. Although it is possible to project how many people will develop AIDS in the next year or two, for example, there is no way of knowing how many will be infected in five years. Crucial data are missing, but it may be possible to estimate some important features of the epidemic indirectly from mathematical models of how the disease spreads.

May and his colleague Roy Anderson of Imperial College in London have developed a model of the AIDS epidemic which not only provides rough estimates of such things as the length of time between infection with the AIDS virus and onset of actual disease, but which also suggests questions about the epidemic that can lead to a much clearer picture of how AIDS will spread, particularly among heterosexuals. They reported on their model in the 12 March issue of Nature.

Among their conclusions are that it is by no means clear that the AIDS epidemic will be the Black Death of our age. AIDS may die out naturally. In particular, May and Anderson conclude that whether an AIDS epidemic among heterosexuals can be sustained depends on how long infected people remain infectious, how likely it is that an infected man will give the disease to a woman, and how likely it is that an infected woman will give AIDS to a man. If everyone infected dies within 10 years, for example, the epidemic will look quite different than if only 30 per cent die and the rest go on infecting others for the rest of their sexually active lives.

AIDS is an epidemic, and so May and Anderson's model focuses on the rates at which people are being infected and on how to predict the total number of cases.

The model brings into sharp focus a number of important unanswered questions about AIDS. For example, it is not known for certain how long people are infectious. Nor is it certain what fraction of those who are infected will eventually get AIDS. And it is unclear whether people who are infected but never get AIDS will be infectious for the rest of their sexually active lives. Yet, says May, "The long-term view of what's going to happen is crucially dependent on these answers, and we just do not have them".

The AIDS epidemic is still in a phase of exponential growth, but May and Anderson predict that it will slow down and the number of cases will increase linearly; in fact, there is evidence from San Francisco that this is already happening. At first, when essentially everyone in the sexually active homosexual population of large cities such as San Francisco was vulnerable, the AIDS infection rate took off. But now, those populations are already infected and it takes longer for the virus to spread to less sexually active groups. For this reason, the epidemic is slowing.

The problem in modelling this epidemic is that it is nonlinear and no simple mathematical formula predicts how the number of cases will increase. Public health officials who are trying to predict the AIDS epidemic curve-fit - they use today's data to decide what will happen in the next few years. But because the shape of the curve is changing, this approach will not be accurate for projections of even five years in the future, May says. The only way to make long-term predictions is to have answers to some of the crucial questions about the course of the disease.

According to their model and the San Francisco data on infection incidences, it takes more than five years from infection with the virus to the disease AIDS - a time that agrees with other estimates that come from clinical data.

In the end, May and Anderson's model raises more questions than it answers. But its importance lies in its new approach to the AIDS epidemic. Says May, "Population models can give insights into the dynamics of an epidemic and can help people think about the disease more clearly". (Extracted from Science, Vol. 235, 20 March 1987)

Serum-free media are cultures with a future

Cell culturing, a type of fermentation that works by combining plant or animal cells in vitro to obtain hybrid cells for making selected bioproducts, is rapidly becoming a process of choice for pharmaceutical and biotechnology companies. Traditionally, cell culturing involves growing cells in a medium enriched with a bovine serum that provides vital nutrients to foster cell growth and metabolism. But because bovine serum is extracted from animals, cost and availability can fluctuate; quality can be erratic; and the presence of impurities from the serum in the finished product could increase the cost of the product, or even raise regulatory questions about its safety.

Now, to avoid these problems, some dozen companies are in various stages of marketing new media products that lack whole serum while providing key nutrients.

Mammalian cell culturing is expected to aid in mass-producing many key biochemicals - including Factor VIII tissue plasminogen activator (TPA) - that are expected to receive Food and Drug Administration (FDA) approval within the next few years. Technology Management Group (New Haven, Conn.), which tracks the biotechnology industry, estimates that $23 billion worth of products will be produced by this method in 1991.

Propelling that growth is the switch by more and more biotechnology companies from using yeast and bacteria in fermentation processes for making products such as insulin to cell-culturing techniques using higher, more complex mammalian cells. These techniques open the door to a broader range of therapeutics. Mammalian cells require more care and are particular about how they are grown and what they are fed. But bacteria and yeast lack the sophistication to produce natural therapeutic proteins. Animal and insect cells either have the machinery to but produce them, or can be engineered to produce them.

Another driving force behind the increasing use of mammalian cells, which will require a serum-free tissue culture medium, is the increasing importance of monoclonal antibodies, which have already won notice as potentially important therapeutics for cancer and infectious diseases.

One attraction of serum-free media is that they contain fewer unknowns that have to be painstakingly filtered out of the final product before it can be sold as a drug. At present, few cells will grow in basal media, so protein or serum may be added during the growth phase, the stage in classicial cell growth when cells multiply and divide.

Although serum-free media could cut production costs, the first cost of serum-free and serum-containing media is now roughly comparable. The savings for the serum-free version come from

elimination of costly downstream purification and filtration.

Direct cost comparison of serum-free and serum-enriched media is impossible, however, as costs vary, depending on the type of cell line being grown and the particular additives required.

Costs aside, biotechnology companies say that the more closely defined media reduce the potential regulatory problems associated with preparing human pharmaceuticals.

Certainly, the serum-free media will free biotechnology companies from dependence on the price and quality fluctuations of serum. (Extracted from Chemical Week, 1 April 1987)

RT speeds screening for new drugs

Drug design has moved into a new era. In the past, drug research was a kind of alchemy, with researchers randomly screening compounds in animals in the hope of discovering effects against such specific diseases as cancer or hypertension. But a far more rational approach has evolved. Researchers are now using cell membrane receptors isolated from organs, such as the brain and peripheral nerves, the heart, blood vessels, lungs and intestines. The upshot is that they are able to screen compounds in test tubes instead of in animals.

The technique that permits researchers to do that is known as receptor technology (RT). It allows them to determine quickly whether a compound is active in the body and, if so, where it acts. It also is far faster and cheaper than animal testing which can require days to test one compound, while RT allows daily assaying of hundreds of compounds for activity with scores of receptors.

RT is sweeping through the pharmaceutical industry and is generating activity outside the pharmaceutical industry. Sales of radioactive chemicals - used in measuring the binding of a compound to a receptor - have increased at laboratory supply companies.

Receptors are proteins on cell surfaces that bind messenger molecules like hormones or neurotransmitters to let a cell communicate with the whole animal. For example, the hormone adrenaline causes a muscle cell in the heart to contract more rapidly and vigorously.

Drugs often mimic those molecules by binding to specific cell receptors. The drug can then react in two ways. It can cause a cell to respond, in which case it is known as an agonist. For instance, a drug that increases the rate of heart muscle contraction is an adrenaline agonist. If the drug prevents the cell from responding, it is known as an antagonist. A drug, for example, that binds to the heart cell receptor for adrenaline, blocking the receptor, is an antagonist because it makes the receptor unavailable for adrenaline.

An RT assay measures a compound's affinity for a specific receptor. One such test is called a radioreceptor assay, in which the receptor is exposed to a radioactively labelled molecule before exposure to a test compound. The test compound's affinity for the receptor is measured by the extent to which it displaces the radioactive molecule.

Besides greater efficiency and cost savings, RT has several other advantages.

- By screening directly for a drug's activity at its binding site.
- RT provides a simple way to determine the likelihood of side effects.
- Using RT, researchers can precisely tailor a drug to fit its receptor by adding or substituting functional groups to change the drug's shape or charge.

Researchers, in recent years, have discovered new receptors that are providing novel strategies for treating disease. Discovery of the receptor for bradykinin, a peptide that causes pain, has led to new approaches for the treatment of a variety of ailments. Genetic engineering also has improved RT by facilitating the sequencing of numerous receptors, including those for insulin, adrenaline and the neurotransmitter acetylcholine.

PET studies. At the same time, RT tools are being improved. Researchers have recently used positron emission tomography (PET) - a medical imaging technology that studies brain metabolism and activity - to map brain receptor sites.

RT also will play a role in the use of computers to design drugs. A prerequisite for computer-aided design of drugs, researchers declare, is an extensive data base on receptor structure and function. (Extracted from Chemical Week, 15 April 1987)

D. APPLICATIONS

Pharmaceutical and medical applications

Self-assembling drugs hit the spot

A method of making drugs and pesticides more discriminating is under development. The method, developed by Darryl C. Rideout, an assistant member at the Research Institute of Scripps Clinic (La Jolla, Calif.), focuses on the slight biochemical differences that exist between types of cells - between, for instance, healthy and diseased cells. Rideout administers two precursor compounds that are nontoxic and that selectively enter diseased cells because of an affinity for what makes those cells different from healthy cells. The compounds assemble inside the diseased cells by means of a covalent bond to become toxic. Because neither precursor is toxic alone, the method should not harm healthy cells.

PPG Industries has an exclusive worldwide license to Rideout's technology for agriculture and biomedical applications. The work was supported as part of a 15-year research programme between PPG and Scripps in plant molecular biology.

Applications for Rideout's work are not expected in the near future, but the first successes are likely to be in pharmaceuticals, particularly cancer drugs. (Extracted from Chemical Week, 17 June 1987)

SmithKline, British gene synthesizer join to make a 'third-generation' TPA

Two transatlantic partners in a R&D venture view TPA (tissue plasminogen activator) as merely a passing phase on the way to creating the optimal cardiovascular clot-dissolver. SmithKline Beckman Corp. (SKB), Philadelphia, and British Biotechnology Ltd. (BB), Oxford, agreed to collaborate on protein engineering of second- and third-generation thrombolytic agents for treating acute heart attacks and blocked blood-vessels.

British Biotechnology will design, clone and express the genes for ultra-TPA peptides that SmithKline will formulate into patentable therapeutic

agents. These, SKB will test in animals and humans, bring to approval, and market worldwide, with AB collecting royalties on sales.

The British gene-synthesizing firm was formed last December by scientists and executives who had staffed the G. D. Searle research laboratories at High Wycombe, U.K., until Searle was sold to Monsanto, which has its own genetic engineering facilities in the USA. (Extracted from McGraw-Hill's Biotechnology Newswatch, 1 June 1987)

Mabs in improved radioisotope imaging

Immunomedics (Newark, NJ), has improved radioisotope imaging techniques for cancer patients. In the procedure, monoclonal antibodies are attached to a radioisotope and injected into the body. The antibodies home in on 70 per cent of the known types of cancer. Viewed under a nuclear camera, a patient's tumors are highlighted. However, the picture can sometimes be blurry because not all of the isotopes latch onto cancer cells. Those that are still floating produce background radiation making images difficult to distinguish. Immunomedics uses a second set of antibodies to mop up those that do not attach to cancer cells. The antibodies, along with the excess radioisotopes, are excreted through the urine within a few hours. The new technique produces a clearer picture and minimizes radiation damage to normal tissues and organs. (Extracted from Business Week, 9 February 1987)

Celltech launches new blood typing reagent

Celltech has launched a new monoclonal antibody for use in blood typing reagents. BRIC-8 anti-C3d offers a significant improvement in the detection of complement. When blended with a polyclonal anti-human IgG, BRIC-8 produces a potent polyspecific anti-human globulin reagent, which gives fewer false positives than do conventional anti-human globulin reagents. Details from: Ian Nicholson or Nick McCooke, Celltech Ltd., 230 Bath Road, Slough SL1 4EN or on (0753) 77866. US enquiries to Susan Dexter on (301) 483-5139. (Source: Biotechnology Bulletin, Vol. 6, No. 3, April 1987)

Birth control vaccine

The world's first human trial of a synthetic birth-control vaccine is under way at Flinders Medical Centre, a collaborating Centre of the World Health Organization (WHO). The trial, part of the WHO's Special Programme on R&D and Research Training in Human Reproduction started in February 1986 and will last nine months to determine the safety and side effects of the vaccine in already sterilized women. After this phase, the vaccine will be tested on fertile women to determine its efficiency as a birth control method and its duration which is foreseen to be between one and two years. (Source: Biotechnica '87 Hannover Journal No. 3)

Heparin product poised for launch

KABI-VITRUM, the Swedish drugs concern, is poised to launch a new thrombosis treatment on to the European market. Applications for approval to sell the low molecular heparin product have now been filed in all the major markets.

Using conventional heparin, the company cuts up the molecule with chemical agents. The fragment which holds the biological activity is then pulled out and forms the basis for the treatment.

A company spokesman claims that the heparin fragment is easier to control, requires only one daily injection and has fewer side effects than the conventional product. (Extracted from European Chemical News, 23 March 1987)

Gene probes locate waterborne diseases

Researchers at the University of Arizona are using gene probes to detect viruses in water. The test is so sensitive that it can detect 1" viruses in 1,000 litres of water.

The team has developed probes for dozens of types of viruses, including polio, meningitis and childhood diarrhoea. Next year, says Charles Gerba, a professor of microbiology at the university, more than 100 probes will be available.

Hardly a city in the world currently tests for the presence of viruses in its drinking water. Gerba, whose laboratory in Tucson has tested water for local communities for years, knows why such testing is almost never done.

Present methods involve concentrating virus on membranes, then using cell cultures to prove their existence. They both take days or weeks to give results, and are very insensitive.

Gerba's new kit, using gene probes, gives results in less than a day. The kit will be on sale later this year, and new kits providing results within two hours will be available next year.

The gene probe itself is a snippet of nucleic acid - either DNA or RNA - that binds to the corresponding sequence of base pairs of a gene in the sample of the target virus. A single kit can contain many individual probes.

The probe is at least 1,000 times more sensitive than serological tests, Gerba reports. In one case, his probe detected 1 femtogram (10^{-15} grams) of the nucleic acid of polio virus, enough to infect a human.

One of the reasons that Gerba envisions a large market for his kits is viral hardiness: they are far better than bacteria at withstanding chlorination and other water treatments. He mentions several studies that show virus recovered from water where treatment had killed all bacteria, and some viruses can survive in the presence of free chlorine ions.

Besides municipal utilities, Gerba sees his customers as industrial water users who want to monitor their outflow, and the shellfish industry, where even a suspicion of viral contamination can shut down packing houses. (Source: New Scientist 28 May 1987)

Protein process developed

Scientists at the central research laboratories of Japan's Ajinomoto have developed a vector that will boost mass production of proteins. The vector is based on the N-terminal 21 amino acids of the human interleukin-2 protein. Initially the target protein is produced in a fused form with the IL-2 portion.

This fused protein forms a granule which is treated with protease enzymes, such as kurikurein, to hydrolyze the peptide link between the target protein and the vector. This process promotes the accumulation of the target protein 10-fold, according to the company.

Ajinomoto has now improved the system to allow for the production of large amounts of the vector-containing plasmid in the enteric bacterium Escherichia coli. During cultivation of the bacteria, the addition of indole acetic acid was found to enhance the expression of the plasmid and the fused protein genes.

So far the technology has been applied for the preparation of murine IL-2 and human biosubstance P2 at the laboratory scale. Ajinomoto plans to use the

method for the production of other proteins which are difficult to produce in large amounts. The company has still to decide whether or not it will license the technology to others but has filed for patents in Japan. (Source: European Chemical News, 27 April 1987)

First authentic human growth hormone developed by Swedish pharmaceutical company

An authentic human growth hormone, which will be used to treat children of short stature suffering from total or partial growth-hormone deficiency, has been developed by KabiVitrum, the Swedish State-owned pharmaceutical company based in Stockholm. The new drug is identical, in both chemical and biological terms, to the growth hormone naturally produced by the human pituitary gland. Using recombinant DNA technology, the company managed to "copy" the growth hormone down to the final amino acid, a world-first for KabiVitrum and a significant breakthrough in the treatment of hormone deficiencies, according to the company.

The new growth hormone is registered in Sweden under the name of Genotropin. Registration is pending in a number of other countries and clinical trials are under way as well.

New research indicates that biosynthetic growth hormone has an effect in children of "normal variant short stature" who would previously not have been classified as growth hormone deficient. It also appears that girls with Turner's syndrome may be able to reach normal adult height with the aid of growth hormone. All girls in Sweden with this syndrome are either already taking part in a clinical project involving treatment with biosynthetic growth hormone or will be invited to do so. According to endocrinologists, the results so far have been very encouraging. (Source: SIP, Stockholm, May 1987)

Increase in growth-hormone treatment

While growth hormone does not promote growth in persons who have passed the age of puberty, it has been shown that adults previously treated with such hormones feel better and build up firmer sets of muscles if treatment is continued in the form of regular "maintenance doses", KabiVitrum says. There are also theories that growth hormone could be used to speed up healing of broken bones. It is therefore thought that the new drug will bring about a dramatic increase in the number of patients who could directly benefit from growth hormone treatment.

KabiVitrum in 1971 began producing growth hormone retrieved from the pituitary glands of deceased people. Known as Crescormon, this pharmaceutical became a world leader in many markets. Production of Crescormon was discontinued in 1985 after the discovery that four young people in the United States and England had died in Creutzfeld-Jakob's disease, which might have been transmitted during treatment with rival brands of growth hormone extracted from human glands.

By that time, KabiVitrum was already on the way to developing a biosynthetic growth hormone and in the summer of 1985 introduced Somatonorm, which contains the complete chain of 191 amino acids that make up the original hormone molecule and an additional amino acid, methionine. Its American counterpart Protropin is produced by KabiVitrum's U.S. partner Genentech Inc. and today Somatonorm is used to treat over 5,000 children worldwide.

In the manufacturing of Somatonorm, the entire content of the cell is removed, which means that the hormone is mixed with other cell proteins. In the case of Genotropin, however, pure growth hormone is secreted into the space between the membrane and the wall of the cell and is thus retrievable in the form of a "package", KabiVitrum says. This technology is based on a discovery made at Genentech.

In the field of recombinant DNA technology KabiVitrum is currently engaged in a number of research and development projects. An insulin-like growth factor (IGF1) has already been developed and work is progressing on the CRF protein, which liberates growth hormone in the body. Another project involves the epidermal growth factor (HGF), the substance discovered by the 1986 Nobel Laureate Stanley Cohen. Other pharmaceutical specialities of KabiVitrum include intravenous nutrition solutions and a range of blood products. (Source: SIP, Stockholm, May 1987)

Antibody test for Alzheimer's faces ambiguity in practice

Severe memory loss after the age of 60 is virtually the only clue, short of brain biopsy, that a physician can go on in diagnosing an aged patient's dementia as Alzheimer's disease (AD). Now, an antibody-based diagnostic test is about to be clinically tried here and in Western Europe, by Immuno-Products Industries, Inc., of Middlesex, N.J.

Instead of brain biopsy, the experimental immuno-assay pinpoints an apparently AD-specific antigen in cerebrospinal fluid (CSF). Samples of CSF from 50 to 75 suspected AD cases, plus normal matched controls, will come to Immuno-Products for in-house testing during the summer. The company also expects their European distributors will reach 20 to 25 reference laboratories in Belgium, Britain, the German Federal Republic, Greece, Italy and Spain, to put the test into commercial use.

With the data thus obtained, Immuno-Products will then go to the U.S. Food and Drug Administration for approval of its diagnostic device, which is an ELISA sandwich assay. But to sidestep the patent monopoly on monoclonal sandwich assays held by Hybritech, Inc., San Diego, the AD system sandwiches the enzyme between a monoclonal and a polyclonal antibody.

The critical antigen against which the antibodies react in the test was discovered by researchers at the New York State Office of Mental Retardation and Developmental Disabilities, led by Khalid Iqbal, head of chemical neuropathology. This protein is found in the brain cells of AD patients, but not in those of people suffering most other forms of dementia, and those rare exceptions can be ruled out clinically. Under the microscope, degenerating AD brain neurons display peculiar tangles of paired helical filaments, and plaques of degenerating nerve tissue. Iqbal and his team surmise that the telltale antigen consists of protein with a defect in phosphorylation. This "tau antigen" shows up in CSF - routinely drawn from neurological patients - which makes the new test possible.

The institute has patents pending on the CSF assay in the USA and abroad, and has licensed it to Senetek PLC, Mountain View, Calif., which in turn designated Immuno-Products to format and test the clinical test.

An estimated four million Americans suffer some form of senile dementia, half to three-quarters of them diagnosed as Alzheimer's. This population-wide prevalence of about 0.75 per cent rises to 20 per cent after age 80.

Iqbal's prime scientific competitor in the hunt for an AD-specific clinical marker is Peter Davies,

professor of pathology and neuroscience at Albert Einstein College of Medicine, New York. He has discovered a different antigen, which is "elevated 15 to 30 times ... in Alzheimer patients" over normal brain cells. Davies cautions that, "The real problem we all have in developing a diagnostic test is to confirm its accuracy by direct examination of brain tissue." Clinical diagnosis, he adds, "is accurate 70 per cent to 90 per cent of the time", but the only way to verify the antibody test would be by brain biopsy - which few patients are willing to undergo - or to wait an average of nine years till the individual dies, and autopsy is possible. (Source: McGraw-Hill's Biotechnology Newswatch, 18 May 1987)

Cloned human skin cells being marketed

Clonetics, a small biotechnology firm, is marketing cloned human skin cells, which have potential in medical research and in testing chemical and environmental agents. Previously, scientists had the choice of culturing normal human skin cells or relying on live animals, abnormal human cells and animal cells. Licensed by the University of Colorado (Boulder), Clonetics produces normal human epidermal keratinocytes in a serum-free medium that has similar nutrients to those in the human body. Live skin cells can reproduce to 100 million cells within 10 days. (Extracted from Industrial Chemistry, January 1987)

Interferon in treatment of MS

Intrathecal human beta-interferon can help reduce incidence of flare-ups in multiple sclerosis, according to L. Jacobs of Millard Fillmore Hospital (Buffalo, NY). The treatment remains investigational, and intrathecal delivery may not be the best dosing regimen. The two-year trial involved 34 patients receiving 1 million units of beta interferon weekly by lumbar puncture for four weeks and then monthly for five months. A 35-patient control group had lumbar punctures at the outset and conclusion of the study and false lumbar punctures in the intervening period, with no interferon injection. Patients on interferon had 0.76 events/year after treatment, vs. 1.79 events/year before treatment. The placebo group had 1.48 events/year vs 1.98 events/year before the sham treatment. The effect was still noted 18 months after treatment had stopped. Better interferon delivery methods might make the improvement even more dramatic. Alpha interferon may be beneficial for patients with early, mild relapsing MS. (Extracted from Medical World, 9 February 1987)

Novo scientists claim insulin drug advance

Scientists at Novo Industri in Denmark are claiming to have developed in collaboration with York University, UK, a new series of insulin molecules that will offer a more effective and convenient means to control blood sugar. But research is still at an early stage and commercially-available products are at least five years away.

Using computer aided molecular modelling techniques, scientists at the Danish concern have developed insulin molecules that can overcome the natural barrier of insulin delivery without affecting potency or immunogeneticity. Results from the first human trials confirm that these properties have been conferred upon the molecules.

Key properties possessed by the new series include rapid activity and solubility. One set of molecules are absorbed much faster from the subcutaneous tissue after injection. This will mean, according to the company, that peak insulin serum levels will be attained within 15 to 30 minutes, about three times faster than conventional treatment and closer to the natural secretion of healthy patients in response to meals.

Novo's long acting insulin preparations, however, are soluble and should be easier to administer, the company claims. After injection the insulin molecule crystallizes, producing a protracted and very reproducible absorption profile. This series will mimic normal basal insulin levels with less variation than current prolonged acting crystalline preparations. In addition, the company plans to use this series with its Novopen delivery system. Novo believes that the new molecules could fill a very important gap in the insulin therapy market.

Novo has submitted patent applications for both the products and the manufacturing technologies, and the company is now planning to pursue new therapeutic strategies with the molecules, as well as using the combined computer and gene splicing techniques to develop other therapeutic molecules. (European Chemical News, 15 June 1987)

Parkinson's protection?

Low doses of a chemical known as MPTP cause brain damage and movement disorders that closely match Parkinson's disease in both humans and monkeys. Robert J. D'Amato of Johns Hopkins University in Baltimore and his colleagues now report that conventional doses of the antimalarial drug chloroquine partially protect monkeys from MPTP-induced symptoms.

The investigators propose that chloroquine interferes with the binding of a poisonous MPTP by-product - MP^+ - to cells that produce the neurotransmitter dopamine in a small area of the brain known as the substantia nigra. In a previous report, D'Amato and his co-workers suggested that MPP^+ sticks only to dopamine cells containing the pigment neuromelanin. Nerve terminals that channel MPP^+ out of neuromelanin-bearing dopamine cells in other brain structures are scarce around the substantia nigra.

The proposed neuromelanin connection, while not endorsed by all MPTP researchers, is supported by the new data. (Source: Science News, Vol. 131, 6 June 1987)

Synthetic drugs to detect melanomas

Victor J. Hruby, of the University of Arizona in Tucson has synthesised "alpha-melanocyte stimulating hormone" (αMSH), a drug that causes melanocytes in the skin to secrete dark pigment. He sees its first uses coming in the treatment of melanomas (skin tumours) and other skin diseases, but an eventual enormous market as a cosmetic.

Hruby has been investigating alternatives to natural peptides for several years, looking for those that control a specific behaviour without causing side effects. His original interest in MSH was as an early-warning system for melanomas - skin tumours that are hard to detect in their early stages and which often kill. If the melanomas can be induced to secrete large amounts of pigment, it will be easier for doctors to spot them when they are still small.

MSH now shows even greater promise, however, as a way to prevent skin cancers before they start. MSH, in all the animal tests which Hruby and his colleagues have carried out so far, has proved to be long-lived, nontoxic and to affect only the site where it is applied (site specific). Specificity is important when dealing with peptides because so many hormones

act on several body systems, and some affect the brain. Alpha-MSH, though, appears to act only in the skin, and does not, Hruby says, seem to cross the blood-brain barrier. Human clinical trials should begin soon.

Tests on animals have also shown that MSH remains active for days in the body. Finally, Hruby says that MSH, even in huge amounts, showed no carcinogenic activity in standard toxicity tests. Curiously, MSH does not, Hruby says, seem to be the body's main pathway for tanning. Many different factors seem to control the secretion of melanin in normal skin.

The drug can be given orally or intravenously, or applied to the skin as a cream. If clinical trials proceed according to plan, Hruby hopes that MSH creams will be on the market in "three to six years". (Source: New Scientist, 28 May 1987)

Liposomal cancer drug enters clinical trials

The first cancer drug encapsulated in a liposome - a sphere made from phospholipids, the same material as cell membranes - has entered clinical trials. Ciba-Geigy has encapsulated muramyltripeptide-phosphatidyl ethanolamine (MTP-PE) for treating patients with several types of cancer, including Kaposi's sarcoma. Liposomes allow administration of higher concentrations of MTP-PE, which accumulates in phagocytic cells in the lung, spleen, liver and bone marrow. The accumulation activates these cells, stimulating the body's natural immune response to tumour cells. (Source: Chemical Week, 20 May 1987)

Mab to human IL-1

Genzyme has now launched a monoclonal antibody to human interleukin-1. The development of this Mab is the first step in developing a test for research purposes. This will complement the existing test for interleukin-2, InterTest 2. (Source: European Chemical News, 20 April 1987)

New pharmaceuticals facility

Genzyme Fine Chemicals is to push ahead with its plans to build a pharmaceuticals facility in the UK.

Civil construction, to start immediately, will be done by Chemical and Thermal, a subsidiary of Bywater. The utilities will be built by Hands Engineering and consultancy assistance has been provided by GEC. The facilities will be built to meet both US Food and Drug Administration and UK Department of Health and Social Security standards.

The new plant will produce bulk pharmaceuticals for Europe and the US as well as high value drugs and intermediates using proprietary chiral enzymatic synthesis techniques.

These enzyme techniques will allow for the production of optically active isomers of key drugs such as betablockers. In addition the company, in collaboration with the Massachusetts Institute of Technology (MIT), has developed a methodology for the synthesis of phospholipids for liposome drug delivery systems. Currently, the cost of obtaining well defined phospholipids from natural sources is about $70/gram. Genzyme is on the verge of improving this by a factor of 10.

Two key areas in the company's R&D programme are the development of hyaluronic acid derivatives and glycoprotein remodelling.

Currently, hyaluronic acid is manufactured at the Middlesex, Kent facility in the UK and then shipped to Cambridge, Massachusetts, for the production of finished materials. The company has five derivatives in areas including ophthalmic, orthopaedic and soft tissue implants. Products are likely to be in the marketplace by late 1988.

Using the technology in-house Genzyme is planning to bring two therapeutic products to the market itself. The company has enzyme therapies for both Gaucher's disease and Fabry's disease. In each case the company has remodelled the sugar residues of missing enzymes which can improve serum lifetime. (Extracted from European Chemical News, 13 April 1987)

Interleukin-2 treatment response

Interleukin-2 (IL-2) developers will have received a boost from research findings published in the 9 April edition of the New England Journal of Medicine. Two research teams have confirmed that therapies using IL-2 may be useful in the treatment of certain types of cancers.

Researchers at the US National Cancer Institute report a total of 48 responses - eight complete, 28 partial and 12 minor - among 146 patients treated with a variety of doses and schedules of IL-2 and lymphokine-activated killer (Lak) cells. With IL-2 alone, seven responses - one complete, five partial and one minor - were reported from among 46 patients.

In a second study, Biotherapeutics, in collaboration with the Biological Therapy Institute confirms the findings of the National Cancer Institute. A team led by William West found that using a constant infusion protocol for administering IL-2 reduced tumours in 13 patients from a clinical population of 40 by >0 per cent. In addition to responses in renal cancer and melanoma, confirming earlier studies, partial responses were observed in Hodgkin's disease, non-Hodgkin's lymphoma, lung cancer, ovarian cancer and parotid cancer.

In addition to the clinical responses reported in the article, the authors described a new method for activating lymphocytes in a semi-closed system of tissue culture bags. This method gave equivalent to superior lymphocyte activation and a lower risk of contamination to the patient. The procedure also proved to be much more time and cost efficient than previously reported methods. Both research teams were using IL-2 supplied by Cetus.

But while both research teams are optimistic about the preliminary clinical studies, caution is still necessary. The toxicity of the treatments is not inconsiderable and there is also the hint that Lak cells may be a necessary part of the treatment. These cells are killer cells generated in the laboratory by stimulating white blood cells with IL-2.

One significant modification currently being investigated is the substitution of Lak cells with tumour infiltrating lymphocytes (TIL). Animal studies suggest that these cells may have a better anticancer effect while cutting down toxicity. (Source: European Chemical News, 20 April 1987 and Company news Release, 9 April 1987)

IL-2 now broadly available

The United States Food and Drug Administration (FDA) has approved the dissemination of interleukin-2 (IL-2) clinical studies to the 38 National Cancer Institute (NCI) comprehensive cancer centres under a

modified Group C designation. This new status was recommended by the Oncologic Drug Advisory Board of the FDA and will focus on renal cell carcinoma and melanoma.

Physicians associated with Biotherapeutics Incorporated will also be conducting interleukin-2 and lymphokine-activated killer cell (IL-2/LAK) clinical studies on a wide range of cancers. These studies are being conducted in Franklin and Memphis, Tennessee and in San Diego and Newport Beach, California. Biotherapeutics plans to establish an international network of laboratories that will support the clinical activities of physicians utilizing biotherapies for individual cancer patients. (Source: Company News Release, 8 May 1987)

Human testing of breast cancer treatment begins

The first tests of an immunotoxin (a monoclonal antibody combined with a toxin) against breast cancer in human patients were started by Cetus Corp. in May. The idea is that the monoclonal antibody should target and bind to specific cancer cells, which the toxin would then destroy. The Fox Chase Cancer Center in Philadelphia is the first medical centre to use Cetus' immunotoxin against breast cancer. Details from: Cetus Corp., 1400 Fifty-Third Street, Emeryville, CA 94608, USA or on (415) 420-3300. (Source: Biotechnology Bulletin, Vol. 6, No. 5, June 1987)

GM-CSF in Phase I trials

Immunex will test a new human protein that could boost the body's defenses against cancer. The Phase I, or safety, tests of the drug GM-CSF are to begin at the University of Texas. Phase I tests will also set dosage levels. Multicentre clinical trials are to begin in the US and FRG with Behringwerke. Immunex has produced enough of the substance for both Phase I and Phase II, which is designed to test its effectiveness. GM-CSF (granulocyte-macrophage colony stimulating factor) is one of a new class of proteins that promote the production and growth of blood cells to fight infection. The drug is thought to stimulate growth of granulocytes, or white blood cells, as well as macrophages, or 'killer' cells. These two cell types attack microbes as well as tumour cells. Scientists hope the substance will ultimately be helpful in treating a number of diseases. University of Texas researchers hope the drug, if effective, might be used before or after chemotherapy to allow a patient to receive more of a potent anti-tumour agent. (Extracted from Wall Street Journal, 26 January 1987)

Cancer earlier warning systems

Two groups of researchers have found chemical signals in blood that they think might work as early signs of cancer. One was found by Dr. Eric Fossell at the Beth Israel Hospital in Boston. He and his colleagues noticed that lipoproteins (combinations of fats and proteins) appear to be slightly different in cancer patients.

The researchers studied blood from 331 people - some of whom had cancer - and found that with an accuracy of over 90 per cent their technique differentiated between blood from cancer patients and that from other people. Interestingly, it confused pregnant women with cancer patients. This makes some sense because babies and tumours are both lumps of fast-dividing cells. It will be a while before the technique can be widely used. More tests on animals and people are needed; so is a machine to do the analysis. A machine costing $400,000 could carry out about 3,000 tests a week.

The other technique is about to come on the market. Dr. Samuel Bogoch of Boston University reasoned that the things to look for were not the products of the tumour, but the antibodies that the body makes in response to those products. These would not be so scarce when the tumour was small. In the 1960s, while studying a different subject in brain tissue, he and his colleagues found a substance they called malignin that seemed to be produced by tumours and that raised an antibody response. Some years later, Dr. Bogoch returned to this anti-malignin antibody and founded a company called Oncolab to exploit its potential in testing for tumours.

Further research showed that the antibody is specific and that it is made in large quantities by a person's body when malignin levels are still too low to be detectable. Moreover, it seems to work for tumours other than those on the brain. Oncolab will market the anti-malignin test from June; it will cost about $125 to test somebody's blood. Up to 19 months before a cancer can be detected clinically, this test will reveal its presence. (Extracted from The Economist, 30 May 1987)

New blood products laboratory

A new $55-million plasma-processing laboratory recently opened will see England and Wales self-sufficient in Factor VIII, the product used to treat haemophiliacs, by 1989. A new high-temperature process will inactivate hepatitis non-A, non-B and AIDS viruses.

For the first time in the United Kingdom, this drive to produce Factor VIII is expected to lead to surplus production of other plasma products which could be sold. As the Blood Products Laboratory obtains all its plasma from voluntary donations, it stresses that it will not be exploited for commercial purposes.

The new laboratory at Elstree, which is part of the National Health Service, will make all of its products from plasma, the fluid that remains once the blood cells have been removed from whole blood. The manufacture of the pure heat-treated Factor VIII, which is called 8Y, includes filtering to remove bacteria, freeze-drying and then heating the freeze-dried preparation to 80°C for 72 hours. Tests on haemophiliacs who received 8Y for 20 months suggest that this type of Factor VIII does not transmit viral infections. (Source: Nature, Vol. 327, 14 May 1987 and New Scientist, 30 April 1987)

Haemophiliac drug

Baxter Travenol Laboratories says that its Hyland Therapeutic unit has begun the first human clinical trials on genetically engineered Factor VIII, the clotting agent missing from the blood of most haemophiliacs. Unlike Factor VIII concentrate currently in use, genetically engineered Factor VIII would not be limited by the availability of human plasma and will be completely free from blood-borne viruses, including AIDS and all forms of hepatitus. (Source: Chemical Marketing Reporter, 6 April 1987)

Allelix, DDI pharmaceuticals to collaborate on genetically-engineered human superoxide dismutase (hSOD)

Allelix Inc. of Toronto, Canada has announced the signing of an agreement between its Biochemicals Division and DDI Pharmaceuticals Inc. (NASDAQ National Market System - DDIX) to collaborate on the research and development of genetically-engineered micro-organisms to produce the enzyme human superoxide dismutase (hSOD).

Under this Agreement, DDI Pharmaceuticals will fund and work with Allelix Biochemicals to develop genetically-engineered micro-organisms that can produce large quantities of bSOD at low cost. This collaboration will combine Allelix's expertise in state-of-the-art genetically-engineered production systems with DDI's in-depth SOD know-how.

Superoxide dismutase (SOD) is a naturally occurring enzyme found in all life forms that use oxygen. It eliminates superoxide, a potentially harmful form of oxygen created by the body's cells. Dosage from bovine SOD (bSOD), developed by DDI, is currently used in certain European countries to treat osteoarthritis and other conditions. SOD is also being investigated for use in heart attacks and organ transplants.

DDI Pharmaceuticals, of Mountain View, CA, is the pioneering developer of pharmaceutical forms of SOD. DDI's licensees market bSOD in the FRG, Austria, Switzerland, Spain, Italy and six other countries. Since 1981, when bSOD was first marketed by DDI's licensees in Europe, bSOD has been administered in almost a million multi-injection courses of treatment for osteoarthritis and other conditions.

Allelix Biochemicals is a division of Allelix Inc., (Canada) which is owned by three Canadian organizations: Canada Development Corporation, John Labatt Ltd. and the Ontario Development Corporation. Allelix Biochemicals is engaged in the development and discovery of therapeutic drugs. These products and related proprietary technologies are being commercialized primarily through collaborative or licensing agreements with companies in specific markets. For further information, contact Dr. Man-chiu Yang, Commercial Manager, Allelix Biochemicals, (416) 677-0831. (Source: Company News Release, 4 May 1987)

New hepatitis B vaccine tested

Researchers in France are testing a new vaccine for protection against hepatitis B on 3,000 volunteers. The trial will end this summer. Health authorities in France could approve the vaccine before the end of this year so that it can go on sale early next year.

The researchers, from the Pasteur Institute in Paris, make the vaccine by inserting genes that code for the outer envelope proteins of the hepatitis B virus into cells from the ovaries of Chinese hamsters.

The hamster cells multiply in culture and secrete these viral proteins into the culture medium. By tagging a chemical marker onto the proteins, the researchers can "harvest" the envelope proteins and include them in a vaccine.

Pierre Tiollais, the head of the institute's Genetic Recombination and Expression Unit, reckons that the vaccine may prove cheaper than existing genetically engineered vaccines against the disease.

If the French health authorities approve the vaccine for general use, Pasteur Vaccins, a company affiliated to the institute, will sell it under the name Hevac-B at the beginning of next year. Frank Pruliere, the company's marketing director, estimates that Hevac-B could work out 30 per cent cheaper than existing vaccines, placing it within financial reach of the countries most in need of it.

The Pasteur Institute says that the genes that are introduced into the hamster cells code for two types of viral protein, the S protein and the pre-S protein. This combination of proteins in a vaccine, the institute says, produces better immunity in a person than vaccines based on just one of the two proteins. Some vaccine experts contest this claim, so the trials could well resolve the dispute.

Already, the institute has tested the vaccine on chimpanzees. It says that the results were "very good".

In September last year, Merck Sharp and Dohme launched a genetically engineered vaccine in Germany. In November, Smith Kline Biologicals of Belgium received marketing approval to sell its gene-spliced vaccine, called Engerix-B, in Belgium.

The vaccine is also on sale in Czechoslovakia, Honduras, Saudi Arabia, Venezuela and in Yemen as well as Singapore, the only country in Asia - where hepatitis-B is a serious problem - to have approved the vaccine so far. (Extracted from New Scientist, 30 April 1987)

Biotechnological hepatitis serum

A "third generation" hepatitis-B vaccine using genetic and protein engineering methods has been developed by Takeda Chemical Industries Ltd. The new vaccine is an antigen called P31, a protein made up of 281 amino acids. It is larger than conventional P25 type antigens and can remove the effects of the hepatitis virus while conventional products only neutralize the effects. The gene structure of the new vaccine has been changed by means of protein engineering to make it chemically more stable. Clinical trials are planned to start in July 1987. (Source: Biotechnica '87 Hannover Journal No. 3)

Drug companies press on with AIDS drugs and vaccines

Pharmaceutical majors continue to search for AIDS treatments. Merck has just joined forces with Repligen to develop and market a vaccine against the disease while the US unit of Hoffmann-La Roche has won the exclusive right to develop dideoxycytidine (DDC) from the US National Cancer Institute.

Currently, the US Food and Drug Administration is reviewing 16 drugs targeted for use against the AIDS virus (HIV) under investigational new drug applications. These drugs come from three different classes: antivirals; immunomodulators and; biologicals like the interferons and interleukins.

Merck and Repligen claim that their project is well under way and expect to apply for approval to conduct clinical tests later this year.

Hoffmann-La Roche has pulled off a small coup winning the rights for DDC. Like Wellcome's AIDS treatment Retrovir, the compound is a nucleotide analogue which is thought to block a key enzyme in the replication of the virus. The drug is, however, still in the early phases of clinical study and there have been suggestions that side effects may, however, limit the drug's use.

DDC is one of the drugs currently being looked at by the FDA. Immunomodulators being investigated are thymopentin (Ortho Pharmaceutical), thymostimulins (Serono Laboratories), methionine-encephaline (National Jewish Hospital) and isoprinosine (Newport Pharmaceuticals).

Antivirals include DDC, ansamycin (Adria Laboratories), ribavirin (Viratek and ICN Pharmaceuticals), HPA-23 (Rhône-Poulenc), AL 721 (Matrix Laboratories) and Foscarnet (sponsored by the National Institute of Allergy and Infectious Diseases).

Alpha interferon (Hoffmann-La Roche), gamma interferon (Genentech), Imreg-1 (Imreg), interleukin-2 (Hoffmann-La Roche), IL-IV (Sandoz and Alpha Therapeutics) and poly Ic12U (NBH Research) are the biologicals under review. Du Pont has recently acquired a minority stake in the latter company and rights to its potential AIDS drug. (Source: European Chemical News, 8 June 1987)

Hope for an AIDS drug

Last week, researchers at Hahnemann University (Philadelphia) reported positive results from a pilot study in which 10 patients suffering from AIDS were treated with the experimental nontoxic drug, Ampligen. The drug, manufactured by HBH Research (Rockville, Md.), is a synthetic ribonucleic acid that induces interferon production in the body. The Hahnemann report says the study showed that Ampligen both strengthened the body's natural immune system and suppressed the AIDS virus in patients with AIDS-related complex and lymphadenopathy syndrome. The findings, say the researchers, suggest that Ampligen may provide effective treatment in the early stages of the disease and may form a foundation for different types of combination regimens for patients with advanced disease. (Source: Chemical Week, 10 June 1987)

Antibody boost

Clinical trials of a new drug that stimulates immunity are under way in the USSR. The Soviet Pharmacological Committee has authorized the use of the drug, called myelopid, for the treatment of secondary immune deficiency, chronic infections and post-surgical complications, in 15 clinics.

Ram Petrov, director of the Institute of Immunology, and his colleague Augusta Mikhailova, identified a substance in the bone marrow of animals and humans which stimulates production of antibodies. They found that this is one of a group of proteins made in the marrow, the so-called myelopeptides.

When the researchers tested the substance on immune-deficient rats, it doubled their life span. Petrov believes that the protein works in two ways, by stimulating the B lymphocytes, cells that produce antibodies, and by "switching off" T lymphocytes, which can suppress antibody production.

The institute has set up a small production unit for myelopid, where marrow is cultured, the proteins separated out and then sterilised and dried for use in the clinics. The researchers are now working to decipher the structure of the proteins so that they can synthesise them. Petrov and Mikhailova believe that other members of the myelopeptide group may be useful in the control of pain and to treat some forms of anaemia. (Source: New Scientist, 9 April 1987)

Using drug combinations in the battle against AIDS

Combinations of AIDS drugs may prove more effective in treating the human immunodeficiency virus (HIV) than any single drug used alone. Among the combinations that showed increased activity in laboratory tests were azidothymidine (AZT) with other dideoxynucleosides, such as dideoxycytidine (DDC), and tumour necrosis factor alpha with gamma interferon. Castanospermine, a plant-derived alkaloid that inhibits formation of the viral envelope, is currently being evaluated in combination with unspecified "other anti-HIV agents" for possible synergistic effects by researchers at Harvard. National Cancer Institute researcher David Broder reported that DDC, which is in the first stage of testing, "may have less bone marrow suppressive effects" than AZT. Broder said that large-scale clinical trials of AZT given to asymptomatic persons testing positive for HIV will begin in July. (Source: Chemical Week, 10 June 1987)

Antiviral drug to be Phase I tested

Burroughs-Wellcome will jointly launch a test of antiviral drugs in 'healthy' carriers of AIDS. The test will combine the anti-AIDS drug azidothymidine (AZT) with the anti-herpes drug acyclovir against the AIDS virus in patients who are infected but thus far free of symptoms. The test is designed to find an agent that can prevent the development of AIDS, which occurs in 20-30 per cent of patients who test positive for the disease antibodies. The experiment will be backed by Burroughs-Wellcome - which makes both of the drugs being tested - the US Centers for Disease Control, the University of California and the San Francisco Health Department. The effort represents the first practical step towards a chemical preventive against AIDS for the estimated 1.5-2 million Americans now infected with the virus. The study will initially involve 20 men in Phase I, or safety, study expected to start in Spring 1987. (Extracted from Wall Street Journal, 9 February 1987)

New AIDS test method

A new fast diagnostic method for AIDS which requires only five minutes has been developed at the Tokyo Medical College. The three conventional methods used to diagnose AIDS require 30 minutes to two hours of waiting for test results. The new latex agglutination method uses specially treated particles of latex to react with serum in the blood of carriers of the AIDS virus. The agent containing the particles remains opaque when it reacts with normal serum but agglutinates through the antibody-antigen reaction when the blood is infected with the AIDS virus. (Source: Biotechnics'87 Hannover Journal No.3)

Japanese HIV test brings quick results

A Japanese company has developed a diagnostic kit for infection with human immunodeficiency virus (HIV) that it claims is quicker, cheaper and more reliable than the existing standard tests. The new test's simplicity may make it particularly useful for screening in developing countries, such as in Africa.

Last October, in response to the problem, Japan's Ministry of Health and Welfare ordered health authorities to screen all blood donations for antibodies to HIV. Now, the Japanese company Fujirebio has developed a diagnostic test kit that should speed up the process of screening donated blood.

The conventional method of testing for HIV is the enzyme-linked immunosorbent assay (ELISA) developed by Abbott.

Fujirebio's test is much simpler. It produces definitive results with a single assay, and these results correlate well with those produced by immunofluorescence, the standard method for confirming the result of the first test. A further advantage is that the new kit produces results within two hours of incubation, compared with ELISA's three-and-a-half. It is also cheaper. Finally, someone can read the results with the naked eye.

The new test relies on particles of gelatin coated with viral antigens. The operator adds dyed samples of serum to wells containing these particles. If the serum contains any antibodies to HIV, the particles clump together, so that the dye diffuses distinctively through the well.

Fujirebio sells the test under the name Serodia-HIV in Japan and has adapted the method into a test for HTLV-I, the retrovirus that causes adult T cell leukaemia. This disease is quite common in Japan.

The same company plans to introduce a semi-automated system for reading its tests, aimed at improving the efficiency of screening. The operator places the tray of samples into an automatic reader. This machine takes two seconds to read each well. The automatic reader passes the results to a computer which stores the data. (Extracted from New Scientist. 25 June 1987)

A test to distinguish HIV-1 from HIV-2

As the number of related human retroviruses increases, the need for a simple test that will accurately distinguish one from another also increases. Erling Norrby of the Karolinska Institute in Stockholm and his colleagues have developed a new type of test that can distinguish between infection by the human immunodeficiency virus-1 (HIV-1 and its relative HIV-2.

Whereas current AIDS tests use whole proteins from HIV-1 to detect antibodies to the virus in infected individuals, the new method, called "site-directed serology," detects the antibodies by means of a short synthetic peptide corresponding to a segment of a viral protein. The peptide segment used, Norrby says, has to be a good elicitor of antibody production, and also conserved among the many variants of HIV-1 or HIV-2. A peptide that fits this description and the one chosen by Norrby and his colleagues, who include Richard Lerner of the Research Institute of Scripps Clinic in La Jolla, California, is from the outer segment of the viral transmembrane protein.

These new generation tests, which are under development in several laboratories in addition to those of Norrby and Lerner, should have a number of advantages over the original AIDS virus tests, especially in developing countries where medical facilities may be limited. The need for a specific HIV-2 test is greatest in West Africa, where the virus is endemic.

Tests based on site-directed serology are both sensitive and specific because they detect a single antigenic site of a particular virus. Moreover, Norrby says, the materials used are more stable than those in the current tests. But perhaps the greatest advantage of the newer tests is that they can be completed in one step. Current tests require two. With the new methods, Norrby says, "The screening test gives you the final answer." (Source: Science, Vol. 236, 19 June 1987)

AIDS vaccines poised for trials

Several potential vaccines against AIDS are beginning to show promise in American laboratories. At least three research teams are poised to begin tests on humans. However, scientists cannot agree on the best regime for testing a vaccine.

Gerald Quinnan, chief of vaccine development at the US's Food and Drug Administration (FDA), said he was certain that trials to test a vaccine on people would begin this year. Allan Goldstein of George Washington University has asked the administration for permission to begin such trials, and has two dozen subjects lined up. Two other as yet unidentified research groups have also asked to start tests on humans.

Most scientists agree that it will not be easy to prove that a vaccine is safe and effective. Because the human immunodeficiency virus (HIV) mutates over time, and even the nature of the disease that it causes differs from place to place, one vaccine might not be effective against all strains. So far, experimental vaccines have varied in their effectiveness against different strains of the virus in laboratory tests.

Most of the vaccines make use of one of the proteins found on the surface, or envelope, of HIV. When introduced into a healthy individual, the protein causes a person's immune system to respond by producing antibodies. The antibodies neutralise the protein and, presumably, would do the same to the whole virus should the person come in contact with it. Other candidate vaccines rely on another virus such as vaccinia or adenovirus, to carry the viral gene that produces the protein - often by inserting this gene into the DNA of the carrier virus. No one has yet prescribed a genetically engineered vaccine - for any disease - for humans, and extra precautions to test the safety of such a vaccine will be needed.

There is still uncertainty over how much danger even a piece of the virus poses to an uninfected person. Goldstein has avoided the problem by creating a synthetic protein that closely matches a protein in the core of HIV, but is not identical to it. When administered to animals, the synthetic protein induces antibodies that neutralise the virus. Unfortunately, scientists believe that genes coding for the core of HIV mutate as frequently as those coding for proteins in the virus's envelope.

One unresolved problem is the question of how safe and effective the vaccine has to be in tests on animals before proceeding to tests on humans. Some primates produce antibodies against HIV vaccines, but these animals are not immunologically identical to humans. (Source: New Scientist, 2 April 1987)

New drug to treat AIDS symptoms

A large international trial of a promising new drug to treat the symptoms of AIDS is about to begin after a lengthy, and so far unexplained, delay. An American company, Praxis Pharmaceuticals, owns all world rights to the drug, which is called AL721. Doctors in seven centres, including London, Tel Aviv and New York, will test it on 300 to 400 patients.

The news of the trial comes at a time when many patients with AIDS, particularly in the US, are becoming increasingly impatient with the medical establishment's failure to speed up investigations into novel treatments.

AL721 is a mixture of natural lipids (fats) made from the yolks of hens' eggs. The "AL" stands for active lipid; the "721" represents the ratio of the three different lipids that the drug contains. It is a yellow oily liquid, which patients can take either in orange juice or spread on bread. Scientists do not know exactly how it works. One theory is that AL721 removes cholesterol from the membrane around the virus. This prevents the virus from infecting white blood cells and so damaging the immune system.

The reason for the hold-up appears to have been that the American firm that holds the rights for AL721, a small company called Praxis Pharmaceuticals, has had difficulties in manufacturing the drug.

Brian Whittle Associates, a British pharmaceuticals firm, will probably import and package the drug for the part of the [illegible] based in London.

Scientists at the Weizmann Institute of Science near Tel Aviv in Israel discovered AL721 first. They developed the drug because it could remove cholesterol from cell membranes. Cholesterol builds up in cell membranes during old age, reducing the activity of the membrane. Doctors have given AL721 to elderly people in order to improve their immune systems through the drug's effect on cell membranes.

The institute sold the rights to manufacture the drug to Praxis in the early 1980s, when scientists were beginning to realise that AL721 could help to fight viral infections. Meir Shinitzky, a biophysicist at the Weizmann Institute, says that American researchers at the University of Virginia discovered in 1978 that some viruses need large amounts of cholesterol in their membranes in order to infect cells. When the researchers extracted cholesterol from the viral membrane, the virus stopped being infective. If they replaced the cholesterol, the infectivity returned.

Shinitzky says that human immunodeficiency virus (HIV), which causes AIDS, derives its membrane from that of the T4 lymphocyte, the type of white blood cell that virus infects. The viral membrane contains a high level of cholesterol. The theory is that once the viral membrane has lost its cholesterol, its density changes. Proteins that normally project from the surface of the virus sink into the membrane, which then conceals receptor sites that are important in binding to the T4 lymphocyte.

Shinitzky and his colleagues, Yehuda Shoenick and Zvi Bentwich, first recognised that AL721 could be effective against infection with HIV after Praxis had given them permission to use AL721 to treat patients with cancer. "During this trial, there was one AIDS patient with lymphoma. AL721 had a remarkable effect on this patient," says Shinitzky.

When the multicentre trial begins, one of the centres will be Tel Aviv. Shinitzky says he does not know why the trial has been delayed. "I feel very upset about it," he said. "On the one hand they [Praxis] have this treasure in their hands; on the other, they don't know what to do with it."

Doctors at St. Luke's Roosevelt Hospital in New York have also used AL721 to treat patients infected with HIV. Arthur Englard, Michael Grieco and Michael Lange carried out a small trial in June, July and August last year on eight people. All of these people had persistently swollen lymph glands, a condition called persistent generalised lymphadenopathy, as a result of infection with HIV. In five out of seven patients, he said, there was a "dramatic decrease" in the numbers of HIV found in their blood. In some, there was no evidence of viral activity - as indicated by levels of a viral enzyme - after two months on the drug. The patients' immune systems improved as well, he said. In addition, there appeared to be no side effects to the treatment.

Englard says that he has had difficulty in obtaining supplies of AL721. The patients in the trial had come off the drug in September. In all cases, the virus reappeared in their blood. The doctors could not start treating the patients again immediately because AL721 was not available. Two months ago, however, they obtained fresh supplies and the patients were able to start taking AL721 again. (Source: New Scientist, 21 May 1987)

An AIDS test gets FDA approval

The US Food and Drug Administration has approved commercial sales of Western Blot tests for detecting antibodies to the AIDS virus, to be manufactured by Biotech Research Laboratories (Rockville, Md.) and distributed by Du Pont. The tests, currently used only in a research setting, are needed to confirm positive results from enzyme-linked immunosorbent assays (ELISA), which are the standard AIDS tests now manufactured by at least seven companies. The new test standardizes and simplifies the Western Blot procedure so blood bank personnel can use it themselves. (Source: Chemical Week, 6 May 1987)

British Bio-technology develops pseudovirus

British Bio-technology Limited has revealed details of what could be a breakthrough in vaccine technology. In collaboration with a team of molecular biologists at Oxford University, researchers at British Bio-technology have developed an artificial virus - dubbed a pseudovirus - that mimics natural viruses. This development, the firm believes, will lead to safe and effective vaccines against AIDS and other diseases.

Using techniques of total gene synthesis a construct is built that contains multiple copies of external and internal antigens of the virus to stimulate antibody production. Such genes can then be fused to those coding for virus particles.

The resulting pseudovirus is strongly antigenic but totally harmless since it contains none of the replicating machinery of the natural virus and hence cannot cause the disease.

The company plans to continue feasibility studies for production as well as scale-up and process development.

British Bio-technology has now filed a series of patent applications for the technology in the UK and the US to consolidate the original applications from the Oxford team. (Extracted from European Chemical News, 27 April 1987)

Livestock applications

Biotechnology to be used in Japanese fishing industry

Scientists are using biotechnology and other methods to develop new and more valuable types of fish. Other nations have grown increasingly reluctant to give Japanese fishermen unrestricted access to their waters. In 1986 the USSR reduced Japan's allotment from 600,000 million tons per year to 150,000 million tons per year, and the US has demanded rights to all salmon spawned in US rivers. Japan's distant-water catch reached a peak of 3.7 million tons in 1974 but has since fallen to 2 million tons per year. It must now rely more on its own waters and on fish farms. Fish farms alone provide 10 per cent of Japan's total catch.

The Ministry of Agriculture & Forestry began to support "biotechnology fish" projects in 1985 and is currently providing fishery laboratories with Yen 27 million/year in loans and Yen 28 million/year in grants. One technology being studied is gynogenesis, in which trout sperm are exposed to ultra violet light to denature the chromosomes. Eggs fertilised with the sperm are then chilled nearly to freezing point so that they later develop only with the mother's chromosomes and produce all female offspring. Another path being explored is the production of sterile fish by chilling the eggs immediately after sterilization. Since sterile fish do not use energy for egg production, they simply keep growing bigger. Sterile salmon grow twice as big as normal. Most of Japan's special fish projects are being run by university or government laboratories, but some private companies are also becoming

involved. Kyowa Hakko Kogyo may introduce a growth hormone for salmon in a few years. Nisshin Oil Mills is using cell fusion technology to produce algae that are 350 times more efficient in raising brine shrimp. None of the new bioengineered fish have been released into open waters. The Ministry of Agriculture is working out guidelines to cover this area.

A fish gene library will be set up by the Japanese Fisheries Agency. The genes will be stored for possible study for gene recombination work. Genetic research on fish and shellfish lags behind that done in agriculture and pharmaceuticals. Some researchers have already produced growth hormone for salmon and eels via biotechnological methods. (Extracted from Asian Wall Street Journal, 16 February 1987)

Biotechnology project aids fish farming

Igene Biotechnology, Columbia, Md., and the New York Aquarium will evaluate genetically selected yeast as a feed supplement in tank farming of salmon and shrimp. The yeast contains a gene for biosynthesis of astaxanthin, a carotenoid pigment responsible for the pink flesh colour and characteristic taste of ocean-living salmon and shrimp. Tank raising of the animals can result in flesh that is an unappealing white with a mealy taste. Norwegian fish farmers use pigment-rich krill or shrimp and crayfish waste as feed supplements, which have a mineral content high enough that it causes problems in formulation, or they use synthetic pigments not approved by the US FDA. Igene scientists developed the yeast by genetic selection and mutation techniques. The project also will evaluate effects of yeast nutrients on rates of animal growth. (Source: Chemical and Engineering News, 11 May 1987)

Vaccine against Newcastle disease

A new vaccine against a virulent chicken disease has been developed in Australia. It could give about 60 per cent of traditionally reared chickens in South East Asia immunity from Newcastle disease. The Malaysian Government is expected to be the first to grant approval to the vaccine, developed by scientists at the University of Queensland. Burma, Sri Lanka, Indonesia and Thailand are all close to a decision. (Source: European Chemical News, 11 May 1987)

Leaner meat from a new pig vaccine

A vaccine that immunises male pigs against their own pheromones - hormones that attract female pigs - and thus neutralises their sex drive has been developed at Michigan State University's (East Lansing) Department of Food Science and Human Nutrition. The vaccine is intended as a substitute for the common practice of castrating male pigs to make them more docile. However, castration, besides removing pheromones, also eliminates such hormones as testosterone and estrogen, which are believed to affect metabolism by increasing muscle production at the expense of fat production. For example, pigs that are not castrated produce lean meat up to 30 per cent more efficiently. The Michigan State vaccine - which consists of bovine serum albumin coupled with pig pheromone - could therefore mean cheaper, higher-quality meat in the future, says Michigan State. The university has applied for a patent on the vaccine. (Source: Chemical Week, 22 April 1987)

New US protein facility planned

After successful testing on the pilot-plant scale, International Minerals and Chemicals has decided to construct a commercial facility for the production of porcine somatotropin (PST), a pig growth hormone. The $50 million plant, to be sited at Terre Haute, Indiana, is to be built by Stearns Catalytic.

International Minerals and Chemicals expects to become a leader in the promising animal healthcare biotechnology market and expects its new plant to be profitable within the first year. The company licensed the original fermentation technology from Biogen a couple of years ago and the Massachusetts-based firm will receive royalties.

Completion of the facility in the summer of 1989 is expected to coincide with the necessary US Food and Drug Administration approvals. PST, a protein that improves the lean weight and rate of weight gain while reducing the cost of swine feed, is the first product that the company expects to launch. Other products include kitasamycin and lypococllin which will require further new production facilities. (Source: European Chemical News, 11 May 1987)

Agricultural applications

A joint venture to develop biofungicides

Biopesticides maker Ecogen (Langhorne, Pa.) and ML Technology Ventures (MLTV), a branch of Merrill Lynch, are teaming up to develop strains of Pseudomonas, a bacterium with potential to control soil-borne fungal diseases in cotton, wheat and vegetables. Under the pact, MLTV will provide $4 million during the next three years to Ecogen, which will develop selected strains of the bacterium and formulate and test products using the strains. The Pseudomonas strains covered by the agreement were selected from naturally occurring strains for their ability to control plant fungal diseases, specifically those caused by Pythium, Rhizoctonia and the so-called "take all" fungus, all of which kill plants. Ecogen has been conducting field trials with several strains for three years. (Source: Chemical Week, 20 May 1987)

Fungal test launched

Agri-Diagnostics Associates, the joint venture between DNA Plant Technology and Koppers, has started marketing its monoclonal antibody test kits for turf grass fungal detection in the UK. The kits allow for same day on-site detection of pythium blight, dollar spot or brown patch, three highly destructive fungal diseases, before visible symptoms appear.

Initially, the joint venture is targeting 900 golf courses - about 8 per cent of the national golf market - and plans to increase this later in the year. The company is also planning a trial use programme targeted at professional lawn care operators and diagnostic centres in lawn and garden retail outlets.

Agri-Diagnostics is also conducting extensive field trials of a kit for the detection of a major fungal disease affecting several commercially important crops. This programme is proceeding under the terms of a research and product development agreement with Ciba-Geigy, the Swiss chemicals major. (Source: European Chemical News, 8 June 1987)

New technique developed to introduce genes into maize

A new technique has been developed to introduce genes into maize, according to researchers at the Friedrich Miescher Institute (Basel) and the John Innes Institute (Norwich, UK). The bacterium, Agrobacterium tumefaciens, normally produces crown gall disease only in dicots, but the researchers have used it to inject viral DNA into grass plants. Maize streak virus produces a characteristic streaked appearance in maize, so it is easy to detect its presence. When Agrobacterium containing the viral DNA was used to attack maize seedlings, the plants became infected, indicating that the bacterium was indeed transmitting the virus into the plant. Researchers will now have to see if the bacterium can be used to

introduce useful genes into maize. (Extracted from New Scientist, 19 February 1987)

Cuphea possible for commercial development

The oilseed cuphea might be developed for commercial use, according to the US Department of Agriculture. The crop's potential was recognized in 1960, but research did not begin until the late 1970s. There are some 260 species of cuphea, and W. Roath of the US Department of Agriculture says commercial growing might begin in the late 1990s. (Soybeans took 30-40 years of research before they were commercially grown.) Cuphea oil might replace palm kernel or coconut oils, which are used in soaps, detergents and other non-food products. Problems to be overcome include the fact that cuphea seeds fall to the ground easily, they may take several years to germinate, and the plants ripen unevenly, making harvesting difficult. Sticky seed hairs might clog harvesting equipment. Research is being done at the US Department of Agriculture, Oregon State University and by the soap and detergent industry. (Extracted from Chemical Marketing Reporter, 2 March 1987)

Genetically-designed seeds

Biotechnology firms are developing genetically-designed seeds for use with specific herbicides. According to Experience (Minneapolis, MN), an agribusiness consulting firm, farmers will have to revise their seed and herbicide buying practices by the 1990s because of the new seeds. Although weed control will be improved, the trend will pose problems for those farm chemical and seed producers unable or unwilling to package an advanced seed-weed control package. Crops most likely to be affected first include tobacco, corn, cotton, soybeans and tomatoes. (Extracted from Industry Week, 26 January 1987)

Genes to be used as insecticide

Malarial mosquitoes and crop-eating caterpillars are the twin targets of two genetic-engineering developments announced last month by Plant Genetic Systems NV (PGS) (Belgium). Both involve cloning genes from the insecticidal bacterium Bacillus thuringiensis.

PGS has entered into a collaborative agreement with Ecogen Inc. of Langhorne, Pa. to develop insect-resistant lettuce using recombinant DNA technology. Ecogen will produce and supply cloned genes from B. thuringiensis that code for proteins toxic to caterpillars that eat and destroy commercial agricultural crops such as corn and leafy green vegetables. PGS will use its own vector-system technology to express the genes in plants for stable reproduction.

In a separate development, PGS scientists say they have discovered a way to control malaria through vector control, as opposed to vaccination or medicine, by altering the food source on which malaria-infected mosquito larvae feed.

Working with scientists at the universities of Bangkok and Michigan, PGS laboratories in Ghent, Belgium, isolated and characterized a protein from B. thuringiensis that selectively kills mosquito larv . Scientists here subsequently isolated the gene coding this mosquitocidal protein and expressed it in blue-green algae. These unicellular organisms, found in fresh-water biotopes across the globe, form a major food supply for mosquito larvae. PGS's genetically transformed algae synthesise the toxic protein and stably pass it on to later generations. However, problems remain before a viable commercial product emerges. Blue-green algae strains vary according to the region and each must be adapted to fit different environmental conditions across the tropical world where malaria is found.

It is too early to assess costs, until trials have moved into the field later this year. (Extracted from McGraw-Hill's Biotechnology Newswatch, 1 June 1987)

New vegetable

The Kirin Brewery Co. and Tokita Seed Co. in Japan have successfully produced a new vegetable called "Semposai" by interbreeding cabbage and Komatsuna, a type of Chinese cabbage. Another hybrid vegetable called "Nichakuran" has been successfully produced by Takii and Co. by fusing cells from Hakusai, another type of Chinese cabbage, and red cabbage called Aka Kanran. (Source: Biotechnica '87 Hannover Journal No. 3)

Rice hybrid by cell fusion

The Plantech Research Institute established jointly by Mitsubishi Chemical Industries Ltd. and Mitsubishi Corp. has produced a rice-millet plant hybrid by electric cell fusion techniques. The regenerated plant has over 100 chromosomes (more than the combined total) and shows high photosynthetic activity other than rice and major crops in Japan. (Source: Biotechnica '87 Hannover Journal No. 3)

New plant research centre

Twyford International, the horticultural plant breeding company, has announced plans to build a £6 million plant biotechnology research centre at Cambridge Science Park. The company set up a molecular biology unit at its laboratories in Somerset last year, and will now expand this on the planned site.

The new laboratory represents a growing interest in agricultural crops and recombinant methods for introducing disease resistance. Among other things, molecular biologists at the company are now looking at the potato in an attempt to engineer varieties resistant to viruses. (Source: Chemistry and Industry, 1 June 1987)

Biological control of agricultural pests

Biological control of agricultural pests and diseases is an area of rapidly developing technology, though one that is only at the doorstep of widespread use. Some of the research at the Institute of Horticultural Research, formerly the Glasshouse Crops Research Institute, was outlined by Dr. Jim Lynch.

In one project, a virus preparation is being developed which is suitable for control of the codling moth, a fruit-tree pest. The granulosis virus eliminates the pest without harming its natural predators. This contrasts with the normal chemical treatment with deltamethrin, which also kills the insects that feed naturally on the moth.

Another line of investigation is aimed at controlling the mushroom sciarid fly. This insect is the major pest on mushrooms, which are Britain's biggest glasshouse crop. The new approach involves infecting the flies with nematodes. When these have entered the flies, bacteria inside the nematode gut are released and these produce a toxin that kills the fly. The nematodes are applied by mixing them with the peat on which the mushrooms are grown.

Rhizoctonia disease on lettuce is a problem that could be tackled by one strain of fungus being developed at the Institute. The fungus, Trichoderma

viridi, produces volatile toxins - pyrones - and enzymes that degrade cell walls. The investigators have found that one strain of the fungus reduced the weight loss in infected lettuce giving satisfactory control of the disease.

These developments, while promising in field trials, still await the test of economic viability as measured by their commercial success in the market-place.

Nevertheless, the Agricultural Genetics Compa. is supporting the development of control by nematodes and granulosis virus. The commercial products from this research could be available in two to three years.

At Rothamsted Experimental Station, in Hertfordshire, researchers have also turned to a fungus to help to control pests - this time nematodes in the soil.

Brian Kerry is concentrating his efforts on Verticillium chlamydosporium, a fungus that attacks a variety of nematodes including cereal, potato and beetroot cyst nematodes and root-knot nematodes. These worms attack the plants' roots and stunt their growth.

Verticillium grows well in the laboratory on a number of media. The fungus is harvested, dried, made into granules and added to the soil. There, the fungus extends its thread-like mycelium and attacks the nematodes, either the eggs before they hatch or the adult females before they can form root cysts.

At the moment Kerry has to apply more than a ton of the fungal preparation per hectare of land in order to control the nematodes. This, he says, is impractical for those farmers who need to treat large areas. He aims to reduce the dose to 25 kilograms per hectare by selecting strains of the fungus that are most deadly to the nematodes.

Although the fungal preparation is not likely to be available commercially for some time, it promises to be an effective alternative to chemical pesticides. Nematocides are expensive and highly toxic. In the US many of these pesticides are being withdrawn because they pollute ground water. (Source: Chemistry and Industry, 4 May 1987 and New Scientist, 30 April 1987)

A shotgun approach to genetic engineering

Scientists at the Cornell University have built a .22 calibre gun that fires millions of tiny metal pellets coated with DNA into plants at 1,000 mph. The pellets are so small they don't even bruise the plant tissue. In one experiment, the biologists fired bacterial and viral genes into onions, and the genes caused the plants to begin producing the foreign proteins. Similar results were obtained with corn and eggplant cells, and another Cornell researcher is using the device on rice. The biologists want to try the technique on animal cells next. (Extracted from Business Week, 1 June 1987)

Guayule resin a good wood protectant

Resin from the guayule plant, which has been studied for several years as a source of natural rubber, is showing good potential as an effective protective agent against various marine and terrestrial wood destroyers, according to John D. Bultman, a chemist at the Naval Research Laboratory. Working in collaboration with Firestone Tire & Rubber, the Gila River Indian Community, in Arizona, and the universities of Arizona and Mississippi State, Bultman is conducting an evaluation of the nonrubber-producing extractive component of the guayule plant to determine its wood protectant characteristics. Only 10 per cent of the extractives can be used to produce rubber. Bultman carried out his tests by impregnating pine sapwood with resin obtained from plants grown in the Gila River Indian Community guayule fields. (Source: Chemical and Engineering News, 4 May 1987, p.18)

'Ancient microbe' increases yield in the paddy fields

Researchers in the United States have discovered a bacterium in the paddy fields of Thailand that could force microbiologists to redesign the microbial evolutionary tree. Moreover, the bacterium fixes atmospheric nitrogen at a remarkable speed and has potential as a powerful natural fertiliser.

Heliobacillus mobilis is a photosynthetic bacterium that lives in the soil. It has features that relate it to two different groups of bacteria, which suggests that it is a direct descendent of an ancient bacterium from which evolved a range of modern bacteria.

Howard Gest, Jeffrey Favinger and Peggy Beer-Romero, from the University of Indiana at Bloomington, established the relationship between Heliobacillus mobilis and other bacteria by examining the structures of certain key molecules. They found that the bacterium's chlorophyll is more closely related to that of cyanobacteria and green plants than to that of other photosynthetic bacteria.

When the researchers looked at the amino acid sequences of ribosomal RNA, however, they found that it was more closely related to certain types of non-photosynthetic bacteria. This result surprised Gest and his colleagues because it links Heliobacillus mobilis with a group of bacteria known as the Gram-positives, so-called because of the way their cell walls take up dyes. Cyanobacteria are Gram-negative, and are molecularly distinct from Gram-positives.

This makes Heliobacillus mobilis the first photosynthetic Gram-positive bacterium to be identified.

The structure of the chlorophyll molecule suggests that the bacterium is a forerunner of the cyanobacteria, which, in turn, are supposed to have given rise to the photosynthetic elements of green plants.

Heliobacillus mobilis is more than a taxonomic puzzle. It is an important source of nitrogen for rice plants in the Thai fields where it was first found. Rice growers might be able to exploit this feature. Heliobacillus is potentially an excellent fertiliser. It fixes nitrogen 10 times faster than cyanobacteria and reproduces many times faster. To take advantage of the bacterium's abilities, farmers would need to enrich the soil with nutrients that encourage the bacteria to grow. Organic acids, such as butyrate, malate and succinate, specifically encourage heliobacteria, but other organisms in the soil cannot use them.

Such a programme would not help Thailand, where farmers grow rice continuously and the heliobacterial flora is well established. But it could improve production in South America, where the value of rice fluctuates and production stops and starts. (Source: New Scientist, 7 May 1987)

Hybrid cotton

A small Californian company, called Seeds of Tomorrow, has apparently invented a cheap, hybrid variety of cotton. Its fast-growing hybrid could change the shape of the world's cotton industry.

Cotton has proved difficult to hybridise. Although different varieties of cotton will breed happily together, getting them to do so is expensive as they must be pollinated by hand. It takes around ten man-hours to produce one lb of seed. Hand-pollination puts the price of seed beyond the reach of farmers.

Seeds of Tomorrow believes it has found the answer: second-generation hybrids. Some pioneering work was done on these second-generation seeds, known as F2s, in the 1950s. This early work was abandoned because the researchers reckoned that too much hybrid vigour dwindled away between the generations. According to Seeds of Tomorrow, the loss of vigour depends on which parents you put together, and how you breed them.

Through many trials, and some error, the company has obtained F2 seeds that retain most of their extra growing power, and which grow in three-quarters, or less, of the time that the standard cotton seed takes.

Fast-growing cotton can also be grown in areas where the summer is too short for ordinary cotton. Seeds of Tomorrow reckons that its hybrid could push the cottonbelt 150 miles north. This possibility has interested the Russians: the Soviet Academy of Sciences is now testing the seed in Uzbekistan. (Extracted from The Economist, 6 June 1987)

Food production and processing

BHA a genotoxin?

A recent study at BIBRA, the UK industrial toxicology research association has shown that butylated hydroxyanisole (BHA) can damage DNA in animal cells in vitro.

The result could prove to be a weakness in the theory that BHA, a widely used food antioxidant, found carcinogenic to rat forestomachs, is not a potential human carcinogen because it acts not by direct attack on the chromosomes, but by somehow causing mutation via an indirect mechanism. According to this theory, BHA would only produce cancer where it comes directly into contact at relatively high concentrations with forestomach tissue. Humans, of course, have no forestomach.

However, Dr. Barry Phillips, a genetic toxicologist at BIBRA, has found that BHA can directly damage chromosomes in a study conducted on Chinese hamster ovary cells in vitro. On the basis of this result, the UK Government's Committee on Mutagenicity has concluded that the work should be repeated "as a matter of urgency".

The repeat studies are being performed by industry, under the co-ordination of Dr. Phil Coppen, at May & Baker, a leading UK manufacturer of BHA.

The study could help to determine the mechanism by which BHA causes the forestomach tumours in rats. Phillips suggested that his study supports the theory that BHA metabolism in rats produces active oxygen species, such as peroxide ions, that can damage DNA. (Extracted from Chemistry and Industry, 4 May 1987)

Chemical applications

New role for Mabs

Monoclonal antibodies may be about to assume a new role as chemical catalysts. The Research Institute of Scripps Clinic and the University of California (Berkeley) have designed antibodies that do the work of an enzyme. Recent advances have generated antibodies that specifically bind to just about any molecule. Researchers hope that catalytic groups normally not found in antibodies can be linked with the binding sites of antibodies, creating unique and powerful semisynthetic catalytic antibodies. A major long-term goal is to design antibodies to act as highly specific proteolytic enzymes to have the potential to selectively cleave a single peptide bond anywhere in a protein. This would greatly facilitate the study of protein chemistry. P. Schultz et al of the University of California (Berkeley) are working on using antibodies to catalyze various reactions, including macrocycle ring closure, the formation of an amide bond and certain oxidation reactions. The Scripps group is using antibodies carefully elicited from mice to catalyze the hydrolysis of carboxylic esters. (Extracted from Industrial Chemistry, March 1987)

Energy and environmental applications

An aerobic waste treatment research plant

As part of its pollution control research strategy, the UK Science and Engineering Research Council (SERC) has funded the construction of a transportable anaerobic plant for the treatment of organic waste. The plant, currently sited at the Bird's Eye Walls factory at Gloucester, will be used by industry, universities and polytechnics for research in this field. There is growing use of anaerobic treatment for industrial wastewater, particularly in the food and drink sector. But the best designs and operational procedures are not always fully developed and results in the laboratory have not always been translated into equivalent performance in scaled-up plants. Unilever Research and Bird's Eye Walls are contributing towards the management of the project and SERC is providing research grants for an initial programme involving five academic institutions: the Polytechnic of Wales; the University of Birmingham; Cranfield Institute of Technology; Imperial College of Science and Technology; and the University of Newcastle upon Tyne. (Extracted from Biotechnology Bulletin, Vol. 0, No. 4, May 1987)

Bacteria eats nuclear waste

The Finnish Imatra Power Company (IVO) and Industrial Power Company (TVO) have been successfully experimenting at Loviisa Nuclear Power Station with a type of nuclear waste compost where the low-active service waste decomposes into small volume. IVO believes that this technique will halve the need for final burial space for service waste. In the test facility, the volume of the test batch is reduced down to only a few percent of the original. The technique consists of a waste shredder, mixing tank, biogas developer, and a clarifier and collector for the precipitate. (Source: Biotechnica '87 Hannover Journal No. 3)

Bacterial blends clean up cyanides

British scientists are developing a cheap, foolproof method to detoxify wastes containing cyanide bound into organic molecules. The method relies on bacteria that convert the cyanides which are in the form of nitriles into less harmful byproducts such as carbon dioxide and ammonia.

Normally, chemical companies dispose of nitriles - byproducts from the manufacture of some plastics - by destroying them with heat or chemicals, but this is expensive. Otherwise, they bury the wastes out of harm's way in deep wells or dispose of them at sea. Burying and sea disposal, however, do not destroy the toxic materials. Nitriles are potentially as dangerous as inorganic cyanides. They disrupt ecosystems and interfere with respiration in mammals and plants.

Chris Knowles and Jerry Wyatt from the University of Kent's department of biology are developing "custom blends" of bacteria that destroy nitriles more cheaply and cleanly than conventional treatments. They tackle waste that was thought to be beyond the powers of bacterial degradation in orthodox sewage works.

Knowles and Wyatt have a "library" of some 100 bacteria that can be blended in different combinations to treat different nitrile wastes. They hope to develop similar "libraries" of different bacteria to treat other complex industrial effluents.

The bacteria contain enzymes that convert the toxic wastes into harmless materials. Ordinary sewage works that rely on bacteria in sludge to detoxify waste can be overwhelmed by the effluent from many chemical processes such as the production of acrylonitrile. This is a starting material from which polyacrylamides are made to be turned into a variety of plastics for foams and clothing textiles for example.

The team at Kent believes that the system, already licensed to a chemical company in the US, is the first that tackles organic cyanides, or nitriles, by biological action. (Source: New Scientist, 21 May 1987)

'Magic' microbes eat the dirt

Microbes that feast on toxic chemicals are helping to decontaminate a derelict gasworks site in Blackburn, Lancashire, to make it fit for redevelopment.

The Greenbank gasworks site - which covers 10 hectares - used to be peppered with cyanides, phenols, oil tars and heavy metals.

Biotreatment, a Welsh company based in Cardiff, is getting rid of most of the contaminants with microbes that convert them into harmless chemicals such as water, nitrogen, oxygen and carbon dioxide.

Biotreatment isolated the microbes from samples of soil at the site, but only in tiny amounts. By breeding them in the laboratory and blending them into cocktails, company scientists generated enough bacteria to decontaminate the site in weeks instead of centuries.

The microbial brews are being used in conjunction with conventional techniques to decontaminate the site. In all, Biotreatment is cleaning up 40,000 cubic metres of soil, 14,000 of them by conventional means. The soil contaminated with heavy metals is too toxic to sustain the microbes and is being buried in sealed landfills or treated chemically.

The remaining 26,000 cubic metres are being purged by the microbes. Workers on site pile the contaminated soil into mounds which are sprayed with solutions containing the bacteria. Site workers then add nutrients to the soil to help sustain the microbes and to increase the activity of those already in the soil.

The work, which began in October last year, is proceeding faster than expected. It will work out cheaper than conventional techniques. (Source: New Scientist, 5 March 1987)

Defending the environment

Genetic engineers are modifying micro-organisms to attack industrial pollutants such as cadmium and PCBs, thereby creating a vast new business to treat indoor air, waste and sludge.

The US Environmental Protection Agency (EPA), is co-ordinating three projects to genetically engineer more efficient bacteria to work on specific pollutants. According to spokesman Fred Bishop, the EPA is sponsoring a University of Washington research team for development of cadmium binding proteins. This work is expected to be finished within a year.

A second project is looking for a gene to de-halogenate toxic compounds such as PCBs. When located, this gene will be put into facultative organisms rather than anaerobic ones, according to Bishop, "to give them a better chance of survival".

A third project is aimed at the selection of more appropriate, naturally occurring organisms to manage specific waste problems in existing artificial marsh treatment systems.

One company on this new frontier, Biological Water Purification Inc. (BWP) of New Jersey, has been in the business for 14 years, and holds 14 patents for two of the most promising processes developed to date - the Root Zone Method (RZM) and the Max Planck Method. Both were developed under the aegis of the Max Planck Institute in FRG. BWP already has 20 operational Max Planck units using bulrushes and phragmites in lined basins.

The two methods differ in that RZM uses a much drier atmosphere than does the Max Planck Method. With RZM, fluids for treatment run through the underground root systems, whereas the Max Planck system incorporates the plants in ponds.

NASA has been experimenting for several years with commercial systems that exploit the properties of the rhizosphere. It also produces systems ranging from single-home units to major installations for 40,000 to 50,000 people. Another NASA development is the use of plants to purify and condition indoor air. Lessons from Skylab are being applied to reduce inner-space pollution with cheap, "benign" technology based on plant life.

NASA has identified 53 organic chemicals in buildings, ranging from acetone, benzene and styrene, to toluene, xylene and formaldehyde. To further complicate matters, new buildings are practically airtight, and high-rise ventilation rates have been decreased to minimize heating and cooling costs. These factors cause what has been described as "sick building syndrom", - one of the new diseases of the twentieth century.

In the 1970s, NASA scientists at the National Space Technology Laboratories (NSTL) started looking at natural biological processes to run life-support systems. For bioregeneration of air and water, they concentrated on using higher plants and the micro-organisms surrounding their roots.

One simple system uses a common spider plant, with room air pumped through activated charcoal surrounding its roots. Both roots and leaves absorb gases other than carbon dioxide. Common houseplants such as the spider plant, Chinese evergreen, syngonium, peace lily, golden pothos, peperomia and banana plant can significantly reduce formaldehyde and carbon monoxide in the atmosphere.

Larger systems using window planters have also been used. Equipped with a pump and registers, these are sufficient for the average house, according to NASA. A large plant atrium sitting atop a building or factory can act as a very simple and cheap-to-maintain air-conditioning system, and returns oxygen as well as fresh air into the building below. Such atriums also enhance a structure's beauty and value.

A fuller utilization of "plant power" could combine the air and waste treatment properties of plants while integrating utilitarian gardens and atriums into buildings. Of course, such extensive use of glassed-in greenery will have significant heating properties as well as "ventilation" attributes. (Source: Canadian Research Biotechnology Canada, April 1987)

Extraction industry applications

In search of a living bath-plug

The oil industry is vexed by a problem known as coning, which can occur wherever the oil lies just above the water table. Because the briny water is much less viscous than the oil, anything more than gentle extraction pressure can cause the water under the well to push through the oil layer and form a cone ten feet across and stretching up to the pipe. When this happens, the pump draws water along with the oil. Maintaining low extraction pressure, or treating the oil at the surface to remove water both mean higher costs.

The threat to production caused by coning varies from well to well and depends on the type of rock at the bottom of the well.

The answer is to put a waterproof plug between the oil and the water - if you can do it. Oil companies have tried cement and polyacrylic to make plugs. But these materials are expensive and cannot penetrate certain types of rock to reach the place where they can do good. Bacteria might do the job better.

All well-fed bacteria are coated in a layer of carbohydrate called a glycocalyx. This thick layer of sugar allows bacteria to coalesce, forming a "biofilm". The waterproof biofilm serves both a protective and an anchoring function, and is generally deplored. Because bacteria in biofilms have some resistance to chemicals they tend to lurk in pipelines, catheters, plastic medical devices and river bottoms and to reject attempts to dislodge them. These usually anti-social characteristics are promising ones for waterproof plugs to prevent cones, but pumping normal bacteria down will not work.

This is where Dr. W. Costerton of the University of Calgary, Canada thinks a piece of academic microbiology might come in useful. About five years ago, microbiologists noticed that water samples from the deep sea contained no bacteria when examined under their light microscopes, but that when nutrients were added to the water visible bacteria would suddenly appear. Electron microscopes confirmed that some bacteria were indeed present in the deep-water samples, but they had starved themselves to a size of about one-fifth of a millionth of a metre long, below the resolution of a light microscope. When nutrients were added, the bacteria would resume activity and swell in volume by 500-fold.

Starved ultra-micro bacteria from the deep sea contain almost nothing except their genes. They have no glycocalyx, and so do not stick together. Yet, when nutrients are added, they grow, multiply and produce a thick glycocalyx. Dr. Costerton and his group reasoned that if ultra-micro cells could exist in the deep sea, they could probably exist in deep ground water as well and be used to prevent coning.

If his reasoning is right, owners of coning-infected oil wells will sometime in the future inject ultra-micro cells that can readily penetrate even tight rock formation. After the bacteria are introduced the oilmen will pump down pulp and paper waste products to feed them. The bacteria will then swell and clump, forming a plug that Dr. Costerton reckons could measure 30 feet in diameter. Because the plug is directly under the well, it will delay coning and allow for a more vigorous extraction of the oil. (Source: The Economist, 16 May 1987)

Industrial microbiology

Enzymes become tough enough for industry

Financed by a co-operative grant from the British Biotechnology Directorate and from ICI, Chris Lowe and his colleagues have developed hardy synthetic coenzymes from molecules originally intended for use as textile dyes.

Lowe and his colleagues tagged the dye molecules to chemical groupings that perform the function of coenzymes. The hybrid molecules proved tough enough to partner the enzymes as catalysts in industrial processes. They have now secured a patent for the procedure.

The team believes that the synthetic coenzymes will lead to a wider application of enzymes in industry. (Extracted from New Scientist, 21 May 1987)

Counting up the bacteria

The time taken to count the number of bacteria in clinical, environmental and food samples could be reduced from up to 72 hours to just a few minutes, if a test method being developed by a UK government-sponsored research consortium comes to fruition. A programme to improve on existing technology for measuring the adenosine triphosphate (ATP) in bacteria has been set up by the Department of Trade and Industry's Biotechnology Unit, which will pay for half of the research costs. Industrial sponsors will pay the other half.

The method, which involves reacting luciferase and its cofactor luciferin with the ATP and measuring the light produced, has been used in certain industrial and medical applications for some time. However, its widespread use has been hampered by lack of suitable photometers and by expensive and insufficiently pure supplies of the enzyme and co-factor.

The research consortium, led by the textile research association WIRA Technology Group, aims to improve the sensitivity of the test and overcome problems with protocols for certain applications.

The first phase of research will be aimed at challenge testing of manufactured commodities such as textiles and electronics components. In these tests, materials are sprayed with bacteria and incubated in order to find out if they will support microbial growth and could thus deteriorate.

The group will then look at the rapid assessment of surface hygiene. This could be used in hospitals where catering hygiene is now subject to the law following the removal of Crown immunity. It could also be used to assess the performance of cleaning contractors.

The search for a UK producer of very pure luciferase is 'a long-term aim' of the consortium. The consortium's other members are the Water Research Centre, Thames Water Authority, and Nottingham University. Two other ATP technology research consortia will be established shortly to look at applications in the food industry and medicine. (Source: Chemistry and Industry, 4 May 1987)

Industrial equipment

Sensors available now

Enzyme electrodes - especially those using glucose oxidase or urease - have been available for some time. New Brunswick (Bartlesville, OK) is marketing a Clark dissolved oxygen electrode that can be used with interchangeable immobilized enzymes to construct sensors for different analytes. Each enzyme is immobilized in a gel matrix and attached to the tip of the electrode. The substrate concentration is directly proportional to the decrease in oxygen in the enzyme matrix as sensed by the oxygen electrode. The company provides a gel starter kit with alcohol, glucose, lactic acid, and lactose sensors. "Blank" gel matrix allows the scientist to create other sensors at will.

Another, more conventional, sensor now available monitors culture biomass by its fluorescence. NAD(P)H (reduced nicotinamide adenine dinucleotide phosphate) is an important metabolic intermediate present in all living cells. This pyridine dinucleotide fluoresces when illuminated at about 340 nm; its oxidized form, NAD(P) does not. Therefore a measure of the culture's fluorescence indicates the metabolic activity of the cells, and the biomass. Indirectly, these measurements indicate any limitations in oxygen or nutrients. BioChem Technology (Malvern, PA) and Ingold (Urdorf, Switzerland) both offer such a probe. Both probes are in situ sterilizable; both allow continuous measurement. BioChem Technology's fluorometer is miniaturized within a probe that is inserted into a culture vessel at a 90° angle; Ingold's uses head-on measuring. Both probes contain an ultraviolet light source, a detector for the emitted fluorescent light, and optical filters. BioChem Technology's sensor cannot be used alone, however. Because the NAD(P)H concentration is sensitive to metabolic parameters such as substrate concentration and oxygen supply, factors that influence metabolism can influence fluorescence without any change in cell concentration. Thus, it might be wise to simultaneously monitor dissolved oxygen concentration for accurate biomass measurements. (Extracted from Biotechnology, Vol. 5, May 1987)

E. PATENTS AND INTELLECTUAL PROPERTY ISSUES

US biotechnology patent law may be reformed

The Industrial Biotechnology Association (IBA) and the Association of Biotechnology Companies (ABC), both in Washington D.C., are urging US Congress to strengthen and extend US patent law. The two key areas are patent term restoration for agricultural products and extending process patent protection to products manufactured abroad.

More than half of all US biotechnology patents now being granted cover production processes rather than the products themselves, but a loophole in current US law extends no protection to holders of such process patents when the products are manufactured abroad and then imported. Thus, for example, a patented process can be used with impunity outside the US to make a particular product, which then may be sold below a fair market price when imported.

The biotechnology community also is seeking patent term restoration for agricultural products, many of which are subject to extended pre-market regulatory review. The aim is to lengthen the period of actual patent protection by making up for the time lag after a patent issues but before the product is approved for sale. Such reform was instituted in 1984 for human pharmaceutical products.

There are several bills pending in the House of Representatives and the Senate that address these issues. Process patent reform may be incorporated into the Omnibus Trade Bill (HR.1155 and S.539) now under consideration. Provisions for extending the patent lifetime of agricultural products have been linked as amendments to the Federal Insecticide Fungicide and Rodenticide Act.

Some reforms for harmonizing procedural differences between US and other patent agencies, including Canada, Europe and Japan, are also being considered.

Meanwhile, the past several years have seen considerable expansion in the activity of PTO's biotechnology group. Efforts are now under way at PTO to clarify if and when applicants for patents must deposit micro-organisms or cell lines. Many inventors routinely deposit strains in centralized facilities, such as those provided in Rockville, MD, by the American Type Culture Collection. However, some companies resist doing so, arguing that written descriptions of experimental processes are sufficient to describe their work nor "those skilled in the art", thus fulfilling patent law stipulations. Some researchers also argue that legal requirements are satisfied if, for example, monoclonal antibodies are supplied even though the cell line from which they derive is withheld. PTO currently disagrees and will soon publish proposed rules on such issues, bringing an opportunity for industry to comment.

A US Senate judiciary sub-committee has approved legislation that would better protect US chemical, drug and biotechnology companies who obtain patents to safeguard their manufacturing processes.

A compromise bill would improve US intellectual property rights by broadening the legal options available to American companies. The owner of a US process patent would be able to sue in a Federal court if another company or individual imports or sells in the US a product made through this process patent.

Under current law, manufacturers from countries without process patent laws can sell products in the US that were manufactured through American processes.

The bill, which was approved unanimously, is scheduled to go before the full judiciary committee for a vote. The House has already passed a similar measure. (Extracted from Bio/Technology, Vol. 5, June 1987 and Chemical Marketing Reporter, 18 May 1987)

Animals ruled patentable

In April, the US Patent and Trademark Office (PTO) ruled that animals may be patented, thereby extending this protection to virtually anything biological.

The PTO decision revolves around a procedure for making oysters polyploid, which was described in a 1984 patent application from Standish K. Allen, Jonathan A. Chaitow, and Sandra L. Downing of the University of Washington (Seattle). It was rejected originally as "obvious" and also because animals were considered unpatentable. However, PTO's Board of Patent Appeals and Interferences - taking into account the Supreme Court's 1980 ruling on Diamond v. Chakraberty which pertained to micro-organisms and PTO's 1985 decision on Ex parte Hibberd which extended patent protection to plants - said that because other "man-made" life forms are "non-naturally occurring" they too are eligible for patent protection. The patent application still was rejected, however, as the appeals board agreed that the would-be inventors' claim to polyploid oysters - which are better tasting than the diploid variety - was obviously based on a previous method of making these oysters. This

rejection will be appealed in the courts. The decision specifically excludes patenting humans, but it still raises some intriguing possibilities. (Source: Bio/Technology, Vol. 5, June 1987)

Biotechnology patents

A British court is soon to decide whether Genentech, the acknowledged leader in biotechnology, can retain exclusive marketing rights in Britain for its leading research product, a heart drug known as TPA. It is a test case of whether biotechnology patents are worth the paper they are written on.

Some 6,000 such patents have been filed. Biotechnology companies depend on them to recoup the costs of developing a new drug. Human insulin, the first genetically engineered drug (approved for sale in 1982), cost about $100 million and 1,000 man-years on its way to market.

Biotechnology firms are particularly sensitive about protecting their patents because, unlike established pharmaceutical firms, many are racing to make essentially the same products. About 20 of them, for instance, are developing TPA. All want a share of a market that analysts expect to grow to $800 million a year within 10 years in America alone - despite a serious setback earlier this month when a committee at America's Food and Drug Administration refused to approve Genentech's drug.

Several legal battles are already raging over the ownership of biotechnology products. One of the fiercest centres on the human growth hormone (HGH), used to combat dwarfism.

A further problem emerges from the broad patents pioneering firms applied for in the early days of biotechnology research to cover themselves against all possible technological breakthroughs. These shut out competitors which is why firms are prepared to take on expensive legal fights to defend (or overturn) them. In December 1986, the European Patent Office revoked a patent issued to Biogen in 1984. Rival companies had objected that it was so broad that it covered all products that might be produced by a genetically engineered E. Coli.

In theory, a patent is only awarded if the discovery of the product was not obvious. A main issue for the courts to decide is whether companies can patent products that are replicas of substances found in nature. At the end of last year, a federal appeal court in America upheld a patent on a diagnostic test used to detect pregnancy and cancers. Monoclonal Antibodies, a biotechnology firm, disputed the patent (awarded to Hybritech, a subsidiary of Eli Lilly) on the grounds that Hybritech's test relied on the application of a known biotechnology technique to a standard diagnostic test.

The court found in favour of Hybritech on the grounds that the commercial success of its kits demonstrated that the invention was not that obvious. High legal costs deterred Monoclonal Antibodies from pursuing its case to the Supreme Court. Hybritech is now fighting a similar battle with Abbott Laboratories, a big drugs firm. (Source: The Economist, 27 June 1987)

Cytogen receives antibody linker patent

Cytogen, a Princeton, N.J.-based biotechnology company, last week received a patent for its antibody linker technology. The patent covers novel methods for site-specific attachment of drugs or isotopes to antibody molecules. The linkers leave unimpaired the antibody's ability to target and bind to antigens such as those expressed by tumours, blood clots and other disease states. The patent also covers systems using the firm's linker technology that can release drugs from an antibody after it binds to an antigen so that adjacent tumour cells not expressing the same antigen are also destroyed. Unlike conventional approaches, this second generation technology is expected to ensure total effectiveness of the antibody as a targeting vehicle for treating and diagnosing disease. Furthermore, the patent is both specific regarding Cytogen's core technology and broad-based in that it is not product or market limiting. (Source: Chemical & Engineering News, 15 June 1987)

European patent application of IL-2 analogues

The European Patent Office in Munich, FRG, is about to grant Cetus its patent application for genetically engineered pharmaceutical and veterinary preparations of interleukin-2 analogues. Once the patent is published other companies and parties will have nine months to object. The company's Proleukin IL-2 is currently in clinical trials in both the US and Europe for anti-cancer indications. (Extracted from European Chemical News, 23 March 1987)

Recombinant A-interferon product patent sought

Interferon Sciences Inc., a subsidiary of National Patent Development Corporation, has asked the Food and Drug Administration for approval to market "Alferon" gel, a recombinant alpha interferon product used to treat genital herpes, the first product resulting from the company's research agreement with Busch Biotech Inc., a subsidiary of Anheuser-Busch Company.

Under the agreement, ISI will supply Busch Biotech with a yeast strain that has been genetically altered to produce alpha interferon, produced by humans as part of the body's immune system. Busch Biotech will then grow the yeast at its research plant in St. Louis, using fermentation technology acquired from Busch Industrial Products Corporation, a major producer of baker's yeast. By inserting the interferon gene into a yeast cell, large-scale commercial quantities of interferon can be produced.

An ISI official says this is the first time that topical alpha interferon has been demonstrated in a double-blind placebo-controlled trial. With FDA approval, the product will be used to relieve the pain and shorten the duration of viral shedding from recurrent herpes lesions. (Source: Chemical Marketing Reporter, 11 May 1987)

Corn process patent granted

Sungene Technologies Corporation has been granted a patent (US serial number 06/6389/ for a new regeneration process to develop improved corn strains from tissue culture. The company says its process will be widely applicable to commercial lines used to produce hybrids for the $1.5 billion per year hybrid seed corn market.

Sungene claims that this is the first patent of its kind to be awarded to a biotechnology company for tissue regeneration of corn. In the past, commercial hybrid corn seed lines had resisted improvement through tissue culture techniques. Sungene's process, which involves the plant growth hormones dicamba and chloramben, has resulted in improvement of even

previously resistant lines, including B-73, the most widely used type for hybrid development.

Improvements in hybrid seed types resulting from the process were first observed in 1983. Subsequent field testing in 1984 and 1985 showed them to be genetically stable over several generations.

Sungene is completing negotiations with a major international seed marketing company to introduce its first seed products to the hybrid corn market, on a commercial basis. (Source: Chemical Marketing Reporter, 25 May 1987)

Max Planck Institute proposes new biotechnology patent rules

European patent law has not been able to keep up with the rapid development of biotechnology or its research results which are ready for practical utilization. Therefore, attempts are being made on a national and international level to implement suitable reforms which would bring the patent law in line with this development. The Max Planck Institute for Foreign and International Patent, Copyright and Antitrust Law in Munich plays an important part in these efforts.

In general, the reform proposals aim at expanding and facilitating patent protection which is currently still restricted in the biotechnology area. One proposal, for instance, would make it possible in all countries to receive patent protection for micro-organisms and similar results of microbiology research (but also for microbiology inventions (new plant varieties and animal species)), if the general requirements (novelty, level of invention, commercial feasibility, and sufficient disclosure) have been met. In addition to a possible description, the deposition of micro-organism which has been recognized for patent protection so far should be sufficient disclosure for obtaining a product patent. Patent protection is supposed to extend to animal breeding as well - an area which has been neglected completely up to now. After elimination of the double protection prohibition, the area of plant breeding should be able to choose between protection of plant varieties and patent protection or to claim both types of protection. Finally, the Max Planck Institute suggests an innovation grace period of one year which is intended primarily to allow the research scientist to report on his research results in writing or orally during this period without thereby excluding subsequent patent protection.

Professor Friedrich-Karl Beier, managing director of the Max Planck Institute for Foreign and International Patent, Copyright, and Antitrust Law, and Dr. Joseph Straus, scientific section head at the Institute, based the reform proposals on their comparative legal studies regarding patent protection for biotechnology inventions in various countries, particularly the United States and Japan. (Extracted from Neue Zuercher Zeitung, 3 December 1985)

F. BIO-INFORMATICS

SERC Directory of Bio-research

The fourth edition of the Directory of Research in Biotechnology has been published by the UK Science and Engineering Research Council's Biotechnology Directorate. It provides details of all the research supported by the Directorate as of 1 October 1986. Of the 135 programmes described in the Directory, 32 are Club projects jointly sponsored by groups of companies, and an additional 18 are Co-operative Research Grants with individual firms. Of the 157 studentships listed, 67 are CASE awards jointly supervised by industrial partners.

The Directorate has identified a number of priority areas, which account for nearly 95 per cent of its funding. These areas are: process engineering in biotechnology; bioconversions; animal cell biotechnology; plant cell culture; whole plant biotechnology; host-vector systems; biosensors and bioelectronics; and protein engineering. Details from: Mrs. Audrey Williams, SERC Biotechnology Directorate, Polaris House, North Star Avenue, Swindon, Wilts SN2 1ET or on 0793-26222, ext. 2310.

Genetic Technology Sourcebook

Company profiles, research projects and corporate sponsors are all features of the Genetic Technology Sourcebook: A Guide to R&D Activity, just published by Technical Insights, Inc. Fifty nine companies active in biotechnology and over 170 corporate sponsors are identified. The 400 page report costs $637 ($672 outside North America). Details from: Marketing Director, Technical Insights, Inc., P.O. Box 1304, Fort Lee, NJ 07024, USA or on (201) 568 4744.

Genetic Engineering and Biotechnology Yearbook, 1986-1987

Anyone looking for short profiles of leading biotechnology companies around the world should obtain a copy of Elsevier's 1,230-page Genetic Engineering and Biotechnology Yearbook 1986-1987, published in late 1986. The first, 640-page volume focuses on US companies, the second on the rest of the world. Although there is no overview comparing the work that the companies are doing, the profiles do provide a useful introduction to the market areas in which the companies are operating - and each contains an address and telephone number for follow-up. Details from: Elsevier Science Publishers, BV, Sara Burgerhartstraase 25, P.O. Box 211, 1000 AE Amsterdam, The Netherlands.

Feeding the world

Gene Banks and World Food (by Donald Plucknett et al, Princeton UP. 247 pages, £23.40) discusses the pros and cons of in situ and ex situ conservation. Seed banks, cryopreservation techniques and tissue culture, problems with recalcitrant seeds, genetic drift in seedbanks and somatic variation in tissue culture are discussed, as well as providing a brief introduction to the limitations and use of genetic engineering.

The authors gratefully acknowledge the enormous contribution of plant collectors of the past in the collection and distribution of new crops and crop varieties.

This is a well-produced book, free from prejudice, written by acknowledged leaders in the field of genetic conservation. The authors have deliberately avoided unnecessary scientific jargon yet provided a text that is easily understood by both a scientific and lay reader.

ICDA focuses on biotechnology: should third world ignore patents?

Convinced that biotechnology will have a profound impact on agriculture, health and the environment, critics of current and emerging styles of development are beginning to think about the implications of biotechnology in the third world. In New Hope or False Promise? Biotechnology and the Third World, Henk Hobbelink of the International Coalition for Development Action (ICDA) poses some difficult questions for biotechnologists.

Dedicated to building a more just and equitable international order, ICDA has long campaigned against the international seeds business, stressing the

dangers of monopolistic control of genetic resources - and warning of a narrowing of the international food base. One conclusion: third world countries should ignore patents, appropriating the biotechnologies they need. Details of the 72-page booklet, price $5.00 (incl. postage and packaging) from: International Coalition for Development Action (ICDA), Apartado 23398, 08080 Barcelona, Spain or on 34 (3) 215-8949.

New study on European immunoassay instrument market

Chemically induced light will be one of European medicine's fastest-growing tools, according to a new Frost & Sullivan study of the European clinical immunoassay instrument market. Luminescence (LIA) equipment will nearly quadruple by 1991, the report predicts, leading a strong swing away from the use of radioisotopes in testing.

The European immunoassay area is growing faster than other clinical laboratory market sectors. Immunodiagnostic reagents are expected to top $1.4 billion in European sales at the turn of the decade, and, while the equipment market is much smaller, "it is equally dynamic, with a continuing flow of new instrumentation being launched". The national instrumentation markets in France, Italy, the UK and the FRG are examined in depth, with sales in these countries representing more than three-quarters of total European sales, or almost $75 million. Details of the report (£862), price $2,600, from Customer Service, Frost & Sullivan Ltd, Sullivan House, 4 Grosvenor Gardens, London SW1W ODH or on 01-730-3438. In the US, talk to Frost & Sullivan Inc. on (212) 233-1080.

OTA study optimistic on biotechnology

An overwhelming majority of Americans (80 per cent) expect developments in science and technology will benefit them and their families, according to a new survey by the US Office of Technology Assessment. Two-thirds say they think that genetic engineering will enhance life for all. 71 per cent say there will be risks and 52 per cent believe that genetically-engineered products are "somewhat likely" to be dangerous to people and the environment.

The survey found people willing to accept some risks to the environment. If there were no direct risks to humans and very remote risks to the environment, a majority said they would approve environmental applications of recombinant organisms. Eighty-two per cent favoured small-scale testing of such organisms; 67 per cent said they would favour (53 per cent) or not care about (14 per cent) small-scale testing in their own communities. Details of New Developments in Biotechnology: Public Perceptions of Biotechnology (GPO stock no. 052-003-01068-2, price $5.50) from: US Government Printing Office (GPO), Superintendent of Documents, Washington, Washington, DC 20402, USA or on (202) 783-3238.

Arthur Young launches first British industry-wide survey of biotechnology

A new annual survey of the UK biotechnology industry has been launched by the international accounting and consultancy firm, Arthur Young, in collaboration with the Association for the Advancement of British Biotechnology (AABB). Questionnaires will be sent to a variety of companies, including product manufacturers, contract researchers and suppliers.

A similar study published in the USA last year (Biotech 86: At the Crossroad) concluded that, while operating losses predominate in this R&D intensive industry, "the biotech industry will survive and prosper as a unique entity, distinct from allied industries but open to joint ventures with them". Details of the survey and the US report, priced at $25, from: Nick Fascicha, Arthur Young, Wells Buildings, Fetter Lane, London EC4A 1NH.

Genetic engineering achievements

The Commonwealth Scientific and Industrial Research Organization (CSIRO) has published a book detailing Australian achievements in genetic engineering. The book emphasizes that genetic engineering is an adjunct to, not a substitute for, conventional plant and animal breeding. Achievements listed in the book include:

- The introduction of a seed protein high in sulphur amino acids to lucerne, to improve the wool yield of sheep feeding on the crop;
- The production of faster growing, leaner, larger sheep using single cell embryo microinjection of preferred genes; and
- Overcoming instability in cheesemaking with virus-resistant bacterial cultures.

Information by: CSIRO Headquarters, P.O. Box 225, Dickson, A.C.T. 2602, Australia.

Software Directory for Molecular Biologists: A Complete Guide to the Selection of Computer Software for the Management and Analysis of Molecular Sequences. By Christopher J. Rawlings. Macmillan, London/Stockton, New York: 1986. pp. 412. £40, $80.

Its nomenclature and glossary cover the field, and explain the relevant computer terminology including that used in the software employed for sequence analysis; it outlines the use of word-processing packages, data-management systems, terminal emulation and even spread-sheets. More than 75 per cent of the contents is taken up by the well-cross-referenced directory of software, with 60 per cent of the references being from the special computer issues of Nucleic Acids Research.

For those knowing the field, the book will be very helpful as a single source of reference. However, it does not address the problem of unrefereed publications, as no real opinions are given about the value of the packages described.

Molecular electronics: Beyond the Silicon Chip, 2nd Edition, Revised

This is the ninth in Technical Insights Inc.'s Emerging Technologies series and is a state-of-the-art report on this emerging science, with particular emphasis on the ways in which it will bring about changes in the field of computers.

This extensively revised and updated report goes far beyond the speculative concerns of its first edition to present an in-depth overview of the emerging field. It outlines the progress of recent research results, provides a directory of important research groups and forecasts upcoming events. This report first surveys the present status of biotechnology in general, and explains how bioelectronics and its subdivisions - organic semiconductors, biosensors, and molecular electronics - are evolving within it. Included is a primer on computer and silicon chip technology that demonstrates the limitations of silicon devices, and introduces the advantages of molecular ones.

The report covers the potential applications of molecular electronics that are now motivating some of the world's leading corporations - to conduct intensive

research on these devices. There is information on advances in the areas of computer speed and power, gate spacing and circuit density, heat reduction in computers, prosthetic implants, biosensors, pattern recognition, robotics, artificial intelligence and the reliability of computers. The report also describes which synthetic chemical materials are being used for molecular-scale electronics. There are analyses of work being done on electrically conducting polymers, such as polyacetylene, charge transfer salts and phthalocyanines. It examines the methods for synthesizing and designing molecular electronic devices (MEDs). Included are evaluations of lithographic and vapour deposition techniques, chemical synthesis involving Merrifield and surface modification techniques and the biotechnical synthesis of computer ultra-circuits and assembly. In addition, there is coverage of subassembly methods, signal transport methods, periodic tunnelling, soliton switching, plus advances in molecular electronic materials, molecular microlasers, soliton amplification and switches with memory.

The second edition features a new Delphi survey on the future of molecular electronic technology. The Delphi survey has also been extended to provide information on the potential market for molecular electronic computers. (148 pp; ISBN: 0-914993-21-6) Price: US$390 for US readers, US$425 outside the USA. Further information available from Technical Insights, Inc., JBMG87, P.O. Box 1304, Ft. Lee, NJ 07024, USA.

A report on new developments in biosensor technology

Biosensor technology is catching up rapidly with today's level of computer technology. That combination will result in a host of technical opportunities... - from new ways to monitor industrial effluent to new ways of tracking a patient's progress back to health.

Many of the emerging products and systems can be spotted in a study - Biosensors: Today's Technology, Tomorrow's Products, from Technical Insights, Inc.

This report is the first published survey of current biosensor research, present and future applications, and expected developments. It covers efforts of leading research groups and delves into specific market areas for biosensors.

A Delphi survey that gives experts first hand views of the significance of current trends, when to expect specific developments (such as the artificial pancreas), and what problems need to be solved before such developments are fully realised is included. The report indicates 89 top biosensor research groups around the world, describing their work and giving the address, phone number, researchers' names and person to contact for each group.

The report also lists and describes over 200 recent patents in biosensor technology and reveals available, state-of-the-art biosensor devices from the United States, Japan, FRG, France, Sweden, Denmark, UK, Italy, Switzerland and Hungary. Price: $440 for US readers, US$475 elsewhere. Further information from Technical Insights, Inc., Dept. JBMG87, P.O. Box 1304, Ft. Lee, NJ 07024, USA.

Canadian Biotechnology Sourcebook, 1986

The declared objective of the Canadian Biotechnology Sourcebook [MOSST] is to provide comparative information on private-sector activities in the field. It is essentially a directory of commercial organizations involved in biotechnology research, development and/or manufacturing. It also contains an analysis of relative efforts in the various sectors.

This sourcebook was based on a 1985 mail survey. Some organizations declined to participate, so coverage may not be complete. For more current information, it is suggested that the organizations be contacted directly.

There are 110 organizations listed in the 1986 sourcebook, out of the 200 contacted. To be included, an organization had to be commercially involved in biotechnology research, development or manufacturing. Further information available from Dr. David Shindler, Biotechnology Unit, Ministry of State for Science and Technology, Ottawa, Ontario K1A 1A1. Tel. (613) 990-6322 or Telex 053-4123.

Genetic Engineering Techniques

This publication (from the seminar held in November 1986) examines the way in which Gene Cloning Technology has continued to develop. Published by IBC Technical Services Ltd., Byfleet, Surrey, UK. Price: £40.

New French-language publications:

Vocabulaire des Biotechnologies includes over 700 definitions. Price: 95 Fr.

Les Biotechnologies dans le monde gives the development and strategies for biotechnology development in eighteen countries. Price: 370 Fr.

Conférence International de Biofthique covers the principal questions of bioethics. Price: 280 Fr.

Further information available from the Centre d'Etude de Systèmes et des Technologies Avancées (CESTA), 1, rue Descartes, 75005 Paris, France.

New journals

The Oncology Information Service, based at Leeds University, publishes a monthly bulletin on AIDS and retroviruses. It lists relevant published papers, mostly within two to four weeks of first appearance. The service scans 1,300 major biomedical journals and usually provides an abstract of the article. Further details are available from: Oncology Information Service, Medical and Dental Library, University of Leeds, Leeds LS2 9TJ.

Soviet biotechnology

A new, bi-monthly journal, Soviet Biotechnology, published under the auspices of the USSR Ministry of Medical and Microbiological Industry, is now available. Details from: Edward M. Michael, Vice-President, Marketing, Allerton Press Inc., 150 Fifth Avenue, New York, NY 10011, USA. Subscription price is $385.00, with $35 charged for subscriptions from outside North America. Next year, the company plans to publish the Chinese Journal of Biotechnology.

Common Property Resource Digest

The Common Property Resource Digest is the work of the US Department of Agricultural and Applied Economics, 332 Classroom Office Building, 1994 Buford Avenue, University of Minnesota, St. Paul, MN 55108. In the hope of creating a network of people who work in common property or common pool resources, the Digest's editor, Edward D. Lotterman, put out a call for articles in the first edition. He identified seven areas of particular interest.

1. Sustaining and preserving existing ecosystems.

2. Fragile lands and other fragile resources.

3. Biological and genetic diversity.

4. Cultural and social diversity.

5. Effects of population growth on biological and social systems.

6. Effects of technological change on biological and social systems.

7. Inducing appropriate technological and institutional innovation.

Apios Tribune

Apios Tribune is dedicated to promoting information that will help develop Apios americana as a food crop.

For a copy of Apios Tribune, write to: William F. Blackmon or Berthal D. Reynolds, Department of Plant Pathology and Crop Physiology, Louisiana Agricultural Experiment Station, 302 Life Sciences Building, Louisiana State University, Baton Rouge, LA 70803.

"Take-home" biotechnology

The Open University (Milton Keynes, UK) has designed a biotechnology course, published last summer, that combines a variety of texts with video presentations. The programme, which examines the impact of biotechnology from a European perspective across a variety of industrial sectors, is designed for senior and middle managers in industry, investors, production engineers and research scientists. It is also viewed as a resource for secondary school and more advanced teachers, as well as for company training.

The core of the "Biotechnology Pack" consists of two volumes called Laboratory to Marketplace. These, in turn, comprise six "blocks":

- Biology made business;
- The pharmaceutical industry;
- The chemical and food processing industries;
- Agriculture;
- Energy and environment; and
- Biotechnology and society.

Augmenting the blocks are four case studies - on high fructose syrup, single-cell protein, nitrogen fixation, and ethanol. The written portion of the course also includes three other books:

- Module I: Biology, which further delves into biotechnology's biological underpinnings;
- Module II: Process Technology; and
- Source Book, which includes a glossary and bibliography.

What makes the Open University's effort unique is its combination of written and video material. The six 25-minute videotapes are:

1. Profile of a Start-up (on Biogen);
2. Interferon: The First Four Minute Mile;
3. A Problem of Scale;
4. Muddy Field to Business Field (which looks at ways to improve potato crops);
5. Biotechnology UK (contrasting Celltech and the Agricultural Genetics Co.); and
6. Gentlemen Place Your Bets (a discussion group).

Norman Cohen, chairman of the biotechnology course team, reports that even without a strong marketing effort the University received some 700 enquiries about the course - 500 of these from industry - while it was being prepared.

The biotechnology study pack costs £119; the six videos are available for £115 each, or £299 for the set. To order, write to the Learning Materials Sales Office, Centre for Continuing Education, the Open University, P.O. Box 188, Milton Keynes MK7 6DH, UK.

ATCC data on line

Databases run by the American Type Culture Collection are now available for online search, via the CODATA Network on Dialcom. Details from: Bioinformatics Department, American Type Culture Collection, 12301 Parklawn Drive, Rockville, MD 20852, USA or on (301) 881-2600.

UK introduces on-line micro-organism database

Searching key facts relating to micro-organisms is an increasingly important aspect of biotechnology research. Apart from the drudgery involved, the task can be haphazard.

Now the UK Government is providing a means of obtaining such information from remote computer terminals. Known as MiCIS, an acronym for Microbial Culture Information Service, the new service enables subscribers to search its databank rapidly for information on micro-organisms, or to pinpoint organisms with certain properties.

MiCIS is offered by the Laboratory of the Government Chemist, an arm of the UK's Department of Trade & Industry. It incorporates data on more than 30,000 microbial strains isolated, characterised, and stored largely by Britain's nine national culture collections located in various parts of the country. It could be the forerunner of a Europe-wide computer database system designed along similar lines, and eventually of a global service.

The task of maintaining the data base will never really reach completion. New data will be added as they become known, existing information will be continually updated, and information areas will be broadened as the system develops.

As part of its preparation to begin the service, the Laboratory of the Government Chemist has been issuing a quarterly newsletter since October 1985 that contains facts about the system and the culture collections providing the data. There also is related information of general interest. Data include the source of each micro-organism, alternative names, morphology, culture conditions, patent position, and industrial uses. Genetic information is not yet included, but may become so. Subscription to the service, which is open to all, costs £200 per year plus £60 per hour of computer time.

Many West European and other countries are in various stages of computerising data from their microbial culture collections. In most cases, the catalogue is limited to the names of the organisms in the collection, their file number, who isolated them, and how they may be acquired. Nevertheless, moves are under way that will allow searches of data to be made transnationally. Within the European Economic Community, for instance, the Microbial Information

Network Europe, or MINE, will be such a system. It is being developed as part of EEC's Biotechnology Action Programme.

MINE will be a computerized catalogue of culture collection holdings linked initially through nodes in Belgium, Federal Republic of Germany, the Netherlands, and the UK. France and Portugal will likely join, and it may be extended to include the other countries of the community. Unlike MiCIS, MINE will not include full strain data. Instead, it will direct users to where collections of interest are located.

On-line databank

BIKE (Biotechnologie Informationsknoten für Europa), produced by Gesellschaft für Biotechnologische Forschung (Braunschweig, FRG), contains information on European biotechnology. Included are addresses of research and technology institutions, technology transfer facilities, state collections, consultants, products, and publications. A spin-off, the Biotechnology Year and Address Book, was published in March.

New protein data base for Europe

On-line support for researchers using protein sequence data should soon be offered by the Max Planck Institute for Biochemistry at Martinsreid, just outside Munich, FRG. A new data base called MIPS (Martinsreid Institute for Protein Sequence data) will serve as the European partner to the Protein Identification Resource (PIR) offered by the National Biomedical Research Foundation (NBRF) in the United States.

The data base will address a key problem of accessibility for European researchers. A computer programme offering a data base and sequence analysis has proven popular among the scientists at Martinsreid, who have accessed it more than 10,000 times within the past year.

In addition to improving accessibility, the staff of MIPS will also push for speedier processing of protein sequences submitted for publication. The current lag time of 12-18 months between discovery of a sequence and its appearance in a data base will be shortened by three months or more.

MIPS has already received support from the European Economic Community (EEC) and is expected to receive a grant of DM 6.6 million within the next six months. Private companies such as Boehringer have also expressed an interest.

The MIPS databank will be housed in a minicomputer hooked up to two front-end processors. As with PIR, the data and software used will be released into the public domin without user fees.

Eventually, MIPS will offer several spinoffs from the main sequence databank, including listings of protein fragments and artificial and natural mutants. Both of these aims are already within reach. A long-term goal is to offer a database that reveals the known biological activity and function of a protein when given the structure.

The group at Martinsreid is not the only one interested in improving on the status quo in protein databases. Amos Bairoch at the Geneva University Medical Center has created a database called SWISSPROT which is an adaptation of the NBRF database.

Los Alamos scientists to set up computerised AIDS data bank

The speed with which the AIDS virus mutates, coupled with the rate at which scientists are uncovering new facts about its gene sequence and proteins, is making it extremely difficult for even committed AIDS researchers to keep up with the latest developments. Now the US National Institute of Allergy and Infectious Diseases (NIAID) has awarded a three-year grant to Dr. Gerald Myers of the Theoretical Division at the Los Alamos National Laboratory, New Mexico, which should result in the launch of a new computerised AIDS data base early in 1988. Quarterly updates of the latest data will be made available to qualified investigators.

Howard Hughes Human Gene Mapping Library will assist nucleic acid sequencing

The Howard Hughes Medical Institute's human Gene Mapping Library consists of a number of loosely interconnected databases. Five are of particular interest to those working in human genetics. These are: LIT (literature citations and abstracts), MAP (mapped genes), PROBE (information on probes), RFLP (restriction fragment length polymorphisms), and CONTACT (investigators who have probes).

These databases are of different sizes and at different states of completeness. MAP is small (1,504 entries) but complete. LIT is large (5,616 references) and quite comprehensive, though not complete. RFLP (372 entries) has records for all RFLPs published in the latest New Haven Human Gene Mapping Library Chromosome Plots (HGM-8/July 1986), and for many published since. PROBE is quite incomplete despite 2,100 entries, and is reported to be in need of improvement. CONTACT contains the names, addresses and phone numbers (where available) of 1,364 contacts for probes or additional information.

Additional databases providing other types of information about DNA segments will be added later.

C. MEETINGS

4-9 October 1987
9th International Enzyme Engineering Conference, Santa Barbara, USA. Details: Engineering Foundation, 345 East 47th Street, New York, NY 10017, USA

5-7 October 1987
The Molecular Biology of Human Disease: An Asian Perspective, Singapore. Details: Diana Berger, Conference Co-ordinator, Nature Publishing Co., 65 Bleecker Street, New York, NY 10012, 212/477-9600. Science Council of Singapore, 1, Science Park Drive #03, The Fleming, Singapore Science Park, Singapore 0511, 7797066

5-9 October 1987
International Symposium on Biotechnology and the Food Industry, Budapest, Hungary. Details: Hungarian Scientific Society for Food Industry, (MÉTE) POB. 5, H-1361 Budapest, Hungary

13-16 October 1987
Symposium on Molecular Biology of Brain and Endocrine Peptiderie Systems, Montreal, Canada. Details: Dr. Michel Chrétien, 110 Pine Avenue west, Montreal, Canada H2W 1R7. Phone: (514)842-1461, ext. 229, Telex: 055-60398 CKIN ATL (MW974)M

14-16 October 1987
5th Symposium and Workshop on Ion-Chromatography, St. Moritz, Switzerland. Details: Workshop Office IAHAC, M. Frei-Häusler, Postfach 40, CH-4123, Allschwil 2, Switzerland

19-21 October 1987
Biotechnology in Agriculture, Food Processing and Dietetics, Naples, Italy. Details: Consorzio per il Trasferimento delle Biotecnologie, Fondazione Giovanni Lorenzini, Via Monte Napoleone 23, I-20121 Milano, Italy

19-23 October 1987
EUCHEM Conference: Biotechnology in Chemistry, Biocatalysis and Bioprocess Engineering, Schloss Elmau, FRG. Details: GDCh-Geschäftsstelle, Abt. Tagungen, Postfach 900 440, D-6000 Frankfurt 90, FRG

25-28 October 1987
Congress on Cytokine Research and Congress on Growth Factors, Philadelphia, USA. Details: Esther Bicoway, Mary Ann Liebert Inc., 1651 Third Avenue, New York, NY 10128, USA

27-30 October 1987
Pollution of the Marine Environment, Venice, Italy. Details: Janet Glover, Conference Associates Acops, 27A Hedway Street, London SW1P 2BD, UK. Telephone 01-222 9493. Telefax 01-222 4246. Telex 934346 COMPAS G.

2-4 November 1987
7th International Symposium on HPLC of Proteins, Peptides and Polynucleotides, Washington, DC, USA. Details: Shirley E. Schlessinger, Symp. Manager, 400, East Randolph, Chicago, IL-60601, USA

2-4 November 1987
National Symposium on Agricultural Bioethics, Ames, Iowa, USA. Details: Michael Warren, Technology and Social Change Program, 318B Curtiss, Iowa State University, Ames, IA 50011, USA

4-6 November 1987
5th International Symposium on Rapid Methods and Automation in Microbiology and Immunology, Florence, Italy. Details: A. Turano, Instituto de Microbiologia, Universita di Brescia, POB 317, I-25100 Brescia, Italy

9-12 November 1987
International Conference on Bioreactors and Biotransformations, Gleneagles, Scotland, UK. Details: Elspath Gibson, NEL, East Kilbride, Glasgow G75 0QU, Scotland, UK

25 November - 3 December 1987
MIKROBIOPHOR-87. International Exhibition: Equipment and Methods in Microbial Production, Moscow, USSR. Details: EXPOCENTR, Sokolnitscheskijwal, 1 a, Moscow, 107 113, USSR

3-4 December 1987
Symposium on Extremophiles in Biotechnology, London, UK. Details: Society of Chemical Industry, 14/15, Belgrave Square, London SW1X 8PS, UK

4-5 December 1987
International Symposium on Lectins and Glycoconjugates. Structure, Function, Clinical Application, Göttingen, FRG. Details: Ms. Janice Francis, Zentrum Innere Medizin, Abt Hämatologie/Onkologie, Robert-Koch-Strasse 40, D-3400 Göttingen, FR Germany, Tel: (0551) 396047.

5-10 December 1987
Course on Frontiers in Molecular Biology, Cairo, Egypt. Details: Dr. G. Bernardi, Laboratoire de Génétique Moléculaire, Institut Jacques Monod, 2 Place Jussieu, 75005 Paris, and to Dr. M. Kamel, National Research Center-NRC, Tahrir Street, Dokki, Cairo, Egypt.

8-10 December 1987
Research Symposium on Hyperlipidaemia and Atherosclerosis. The Corn Exchange, Cambridge, UK. Details: Networks (N1), 19 Chaucer Road, Cambridge, CB2 2EB, Telephone 0223-61342 or 022026-3746 or Organising committee: P.M.E. Groot, D.A.A. Owen, M. Sreeharan, K.E. Suckling, Smith Kline & French Research Limited, The Frythe, Welwyn, Herts., UK Tel.: 0707-32511

9-11 December 1987
Conference on Innovations in Protein Therapeutics: From Research to the Clinic. Walt Disney World Resort, Lake Buena Vista, Florida, USA. Details: M.L. Nucci, ENZON Inc., 300 C Corporate Court, South Plainfield, NJ, 07080, USA.

10-11 December 1987
Biotechnology and the Food Industry, Kensington, Exhibition Centre, London, UK. Details: Margaret Johnston, Conference Secretariat, Society of Chemical Industry. Telephone 01-235 3681. Exhibition details from Richard Bull, Press Officer, Exhibitions Division, National Exhibition Centre, Birmingham, UK. Telephone 021-780 4171.

12-17 December 1987
Course on Biotin Labelling and Detection of Nucleic Acids. Cairo, Egypt. Details: Dr. G. Bernardi, Laboratoire de Génétique Moléculaire, Institut Jacques Monod, 2 Place Jussieu, 75005 Paris, France, and to Dr. M. Kamel, National Research Center-NRC, Tahrir Street, Dokki, Cairo, Egypt.

13-22 December 1987
Advanced Course on Plant Genetic Transformation and Gene Expression. University of Leicester, UK. Details: Mrs. Kate Penny, Continuing Education Unit, University of Leicester, Leicester LE1 7RH; or tel.: (0533) 522464.

UCLA SYMPOSIA on Molecular & Cellular Biology

For information and registration form contact: UCLA SYMPOSIA, 103 Molecular Biology Institute, Los Angeles, CA 90024, USA (213) 206-6292

1988 Programmes

17-23 January 1988
Biological and Molecular Aspects of Atrial Peptides, Steamboat Springs, Colorado, USA

24-30 January 1988
Oxy-Radicals in Molecular Biology and Pathology, Park City, Utah, USA

24-30 January 1988
Growth Factors and their Receptors: Genetic Control and Rational Applications, Keystone, Colorado, USA

24-30 January 1988
Growth Inhibitory and Cytotoxic Polypeptides, Keystone, Colorado, USA

24-31 January 1988
Mechanisms and Consequences of DNA Damage Processing, Taos, New Mexico, USA

30 January - 6 February 1988
Technological Advances in Vaccine Development, Park City, Utah, USA

31 January - 7 February 1988
B Cell Development, Taos, New Mexico, USA

6-12 February 1988
Gene Transfer and Gene Therapy, Tamarron, Colorado, USA

6-12 February 1988
Molecular Biology of the Eye: Genes, Vision & Ocular Disease, Santa Fe, New Mexico, USA

28 February - 6 March 1988
Cell Biology of Viral Entry, Replication and Pathogenesis, Taos, New Mexico, USA

6-12 March 1988
Bone Marrow Transplantation: Current Controversies, Tamarron, Colorado, USA

26 March - 2 April 1988
The Molecular Basis of Plant Development,
Steamboat Springs, Colorado, USA

3-10 April 1988
Cellular and Molecular Biology of Muscle Development,
Steamboat Springs, Colorado, USA

4-10 April 1988
Molecular Biology of RNA, Keystone, Colorado, USA

4-10 April 1988
DNA-Protein Interactions in Transcription,
Keystone,
Colorado, USA

10-16 April 1988
Stress-Induced Proteins, Keystone, Colorado, USA

10-17 April 1988
Molecular Biology of Stress, Keystone, Colorado, USA

17-23 April 1988
Molecular and Cellular Mechanisms of Human
Hypersensitivity and Autoimmunity, Keystone,
Colorado, USA

17-23 April 1988
Cell Activation and Signal Initiation,
Keystone,
Colorado, USA

23-30 April 1988
Human Tumor Antigens and Specific Tumor Therapy,
Keystone, Colorado, USA

23-30 April 1988
Action and Therapeutic Applications of Biologicals in
Cancer and AIDS, Keystone, Colorado, USA

25-30 July 1988
International Symposium on Mucus and Related Topics.
University of Manchester, UK. Details:
Dr. E. Chantler, Department of Obstetrics and
Gynaecology, University Hospital of South Manchester,
Hall Lane, West Didsbury, Manchester M20 8LR,
United Kingdom

11-13 September 19[illegible]
2nd Symposium on Current Problems in Testing and
Evaluation of Experimental and Clinical Effects of
Immunomodulators. Košice, CSSR. Details: University
of P.J. Šafárik, Medical Faculty, Department of
Pharmacology, c/o Prof. A. Micák, M.D., D.Sc.,
2nd Symposium on Immunomodulators, Tr.SNP, 1.,
04066 Košice, Czechoslovakia

25-29 September 1988
4th International Congress on Computer Applications in
Fermentation Technology. University of Cambridge,
UK. Details: Sponsors and Organizers, The Conference
Department, The Society of Chemical Industry,
14-15 Belgrave Square, London SW1, UK.

UNITED NATIONS INDUSTRIAL DEVELOPMENT ORGANIZATION

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