OCCASION

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

DISCLAIMER

FAIR USE POLICY

CONTACT

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

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

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

The *Genetic Engineering and Biotechnology Monitor* proposes to accept industry-related advertisements from companies interested in reaching planners and policy-makers as well as entrepreneurs and members of the scientific community in some sixty developing countries throughout the world and inform them about their products and services.

The *Monitor* is published four times a year and distributed free of charge to individuals and institutions on an approved mailing list which includes at the moment 1300 entries. The *Monitor* has been published since 1982 and has built up a sound reputation both in developed and developing countries.

Our activities in the field of advertising are directed towards helping to finance the preparation, publication and mailing of the *Monitor*, which will continue to be distributed free of charge.

Advertisements will be printed in black and white and in English only. Prices in Austrian Schillings or the equivalent in $US will be AS 5,000 for a full page; for half page advertisements, AS 3,700; and for a quarter page, AS 2,500. Requests for placing of advertisements, accompanied by a layout, illustrations and text, should be submitted to the Editor, *Genetic Engineering and Biotechnology Monitor*, at the address below.

CONTENTS

CONTENTS (continued)

CONTENTS (continued)

CONTENTS (continued)

A. POLICY NEWS

UNIDO News

Workshop on protein structure and engineering

Researchers from around the world gathered in Trieste, Italy, in late March to learn more about protein structures and applications to problems of food and health. Entitled "From Protein Structure to Protein Engineering", they attended a workshop (21-25 March) being conducted as part of the International Centre for Genetic Engineering and Biotechnology's (ICGEB) initial programme at its component in Trieste, organized by the United Nations Industrial Development Organization (UNIDO).

The aim is to present basic aspects and recent results that connect protein structure, dynamics, function and engineering. Together with these topics, the series of 14 lectures will also cover genetics and protein design.

Following the workshop, a forum of scientists - consisting of ICGEB staff, members of its Panel of Scientific Advisers (PSA), Directors of affiliated centres and scientists from ICGEB member countries - will meet to elaborate the Centre's R&D activities, including input to the preparation of a five-year work programme, as well as to find ways to promote exchange of information among ICGEB and its member countries. (Source: Press Release, 21 March 1988)

India signs agreement to fund ICGEB work

Third world health and agriculture received a major boost with the signing of an agreement between the Government of India and UNIDO to enable implementation of the interim programme of the International Centre for Genetic Engineering and Biotechnology (ICGEB).

Covering the period from now until the end of 1989, funding will go towards research, facilities and operations at the New Delhi component of ICGEB, based in its provisional premises at the National Institute of Immunology and Jawaharlal Nehru University. The Indian Government will be supplying the equivalent of some $1,500,000, in rupees and dollars.

Research projects will focus on genetic engineering as applied to plants and human and animal health of importance to developing countries. The aim is to provide a foundation for research in these areas after the interim period.

During the current programme, the New Delhi component will have a research team of six senior scientists, 18 junior scientists, 10 post-doctorates (funded by the Italian Government), as well as 24 technicians, support scientists and research fellows. (Source: Press Release, 25 March 1988)

UN and other organizations' news

WHO's campaign against AIDS

A former secretary of the Medical Research Council in Britain will spearhead a world-wide scientific assault on AIDS. Sir James Gowans will chair a committee of researchers who will formulate the first phase of a new campaign against the disease by the World Health Organization in Geneva.

The Organization wants Gowans and his committee to draft a report by the beginning of 1989 on the most important scientific aspects of AIDS. WHO wants the committee to put forward a series of suggestions on diagnostic tests, treatment and drugs, and the development of vaccines.

The preparation of the report is the first phase of the WHO's new attack on the disease. Between February and May of 1988, scientists involved in AIDS research from all parts of the world will have the chance of giving their views on the suggestions made by Gowans and his committee.

The Organization established its Special Programme on AIDS with Jonathan Mann as the Director, last February. The Organization estimates that there are between five million and 10 million people throughout the world infected with the human immunodeficiency virus, which leads to AIDS. There are more than 600,000 cases of AIDS reported to WHO, and WHO estimates that the number could be 10 times greater in five years' time. (Extracted from New Scientist, 5 November 1987)

Vetting for pesticides trade

The UN Food and Agriculture Organization (FAO) has resolved to include the principle of prior informed consent in its international code on the use and distribution of pesticides by 1989.

This amendment may help curb the sale to Third World countries of pesticides that are banned or severely restricted in their country of manufacture.

Exporters would have to ensure that their own governments explain to prospective importing governments the reasons for domestic bans or restrictions on use of a pesticide. The importing government must approve the transaction before it proceeds. (Source: New Scientist, 3 December 1987)

The Bogève Declaration - Towards a people-oriented biotechnology

Twenty-eight participants from 19 countries met at La Soleillette, Bogève, France, 7-12 March 1987, for the 1987 Dag Hammarskjöld Seminar on "The Socioeconomic Impact of New Biotechnologies on Basic Health and Agriculture in the Third World". The seminar was organized and sponsored by the Dag Hammarskjöld Foundation, Uppsala, Sweden, and the Rural Advancement Fund International (RAFI), Pittsboro, USA, and Brandon, Canada, in co-operation with the International Organization of Consumers Unions (IOCU), Penang, Malaysia, the International Coalition for Development Action (ICDA), Brussels, Belgium, and the United Nations Non-Governmental Liaison Service (NGLS) in Geneva.

The Declaration reads as follows:

We, the seminar participants, met in Bogève, France, to discuss the impact of new biotechnologies on health and agriculture in the third world, where the vast majority of the world's people live. In discussing the nature of the new biotechnologies, and their significance for humanity, recognize that:

Biotechnology is a global issue. It cannot be assigned such attributes as positive, negative, or neutral. Like any other technology, it is

inextricably linked to the society in which it is created and used, and will be as socially just or unjust as its milieu. Therefore, we conclude that in today's world this most powerful new technology is more likely to serve the interests of the rich and powerful than the needs of the poor and powerless.

We fully recognize the potential of biotechnology to improve the quality of life of humanity. But it is important to emphasize the risks and hazards associated with biotechnology, including serious and possibly irreversible health, safety, environmental and socio-economic consequences, as well as the use of such technology in biological warfare.

In agriculture, for instance, while biotechnology may promise to increase production and reduce costs, it is more likely to accentuate inequalities in the farm population, aggravate the problem of genetic erosion and uniformity, undermine life-support systems, increase the vulnerability and dependence of farmers and further concentrate the power of transnational agribusiness.

In health, for instance, biotechnology promises more effective diagnostic tools and new ways of preventing and curing diseases. However, the pharmaceutical industry is more likely to focus on the most profitable commercial opportunities and divert attention from basic health requirements.

In view of the above, we make the following recommendations:

At the citizen level:

- That we accept a major role in the development of public discussion and policy related to biotechnology;
- That we monitor industry activities in this field;
- That we commit ourselves to taking action in this field with the relevant UN bodies including FAO, GATT, ILO, UNCTAD, UNEP, UNIDO, WHO and WIPO;
- That we agree to carry our concerns back to the networks with whom we are engaged, such as Health Action International (HAI), International Baby Food Action Network (IBFAN), Pesticide Action Network (PAN) and Seeds Action Network (SAN) in order to facilitate co-operation;
- That we seek to promote appropriate technologies that are socially just and ecologically sustainable, including regenerative agriculture, alternative crop protection strategies, preventive medicine, recycling of resources and wastes etc.

At the national level:

- That a dialogue be established to determine the real needs of society and the main requirements for a national biotechnology strategy based on these needs;
- That the socio-economic and environmental implications of such a strategy be fully considered;
- That the regulatory requirements for the safe testing and introduction of the technology be established and stringently enforced;
- That the control over the technology be assigned to the public sector and that the monopolization of the technology by private interests be resisted.

At the international level:

- That, as at the national level, a wider-ranging international discussion of the impact of biotechnologies be encouraged and begun as soon as possible, noting particularly the initiatives begun in UNIDO/ICGEB (The International Centre for Genetic Engineering and Biotechnology), UNCSTD/ATAS (The Advance Technology Alert System) and other international bodies;
- That third world governments take measures to develop appropriate biotechnologies and further explore the opportunities for South-South co-operation in all aspects of the development and use of biotechnology, in particular with regard to the utilization of genetic raw materials;
- That the evolution of research and development of biotechnology be closely monitored so that the interests and rights of the third world are kept foremost in institutions working on these issues;
- That changes in existing intellectual property rights discussed in WIPO, which deny the rights of the third world, be closely monitored and that a major revision of the Paris Convention be encouraged in order to safeguard the interests of the third world.

In conclusion we wish to reaffirm that a rational biotechnology policy must be geared to meet the real needs of the majority of the world's people and the creation of more equitable and self-reliant societies while working in harmony with the environment.

For more information, contact:

International Organization of Consumers Unions (IOCU), Regional Office for Asia and the Pacific, P.O. Box 1045, 10830 PENANG, Malaysia (Attention: Dr. Martin Abraham) or Rural Advancement Fund International (RAFI), P.O. Box 1029, PITTSBORO, NC 27312, USA (Attention: Ms. Hope Shand).

Regulatory issues

OECD to set rules for international science

Science ministers from the 24 member states of the Organization for Economic Co-operation and Development (OECD) have agreed to try to establish a set of guidelines covering all aspects of international relations in science. The guidelines will include, for example, the extent to which each country should contribute to the world's basic research effort and the conditions under which foreign research workers are permitted to attend scientific meetings.

The agreement was reached at the prompting of the Reagan Administration. It took the form of a request to the OECD secretariat to prepare "proposals for a general framework of common principles for international co-operation in science and technology".

At a separate meeting in Geneva, the United States also proposed that a new initiative should be launched within the framework of GATT (General Agreement on Tariffs and Trade) to tighten up on the policing of intellectual property protection, for example by agreeing on common norms covering the way in which intellectual property legislation is written and applied.

Proposals for an international agreement on the principles under which scientific research is conducted within OECD countries were put to the Paris ministerial meeting by William R. Graham, director of the Office of Science and Technology Policy and science adviser to President Reagan. Such an agreement, he told the meeting, could help dispel the "grey clouds of protectionism" growing in various quarters. The goal, he said, should be "to collect common principles, assumptions, and beliefs in a precise form which is reasonably comprehensive and complete, and could be taken as accepted principles in bilateral discussions".

Although Graham told the OECD meeting that he felt it would be possible to start drawing up international guidelines immediately, there was reluctance on the part of some other nations represented. Some of the smaller nations with less-developed research bases, for example, expressed the fear that principles they were being asked to endorse might restrict their access to technology-related scientific advances in the larger countries, particularly the United States.

Others argued that the principles the United States chose to apply to its national research efforts, such as leaving most initiatives to the private sector, were inappropriate in countries where substantial government involvement is still required to build up a significant scientific and technological capability.

After a lengthy drafting session, a final communiqué was approved listing three necessary factors for international relations in science and technology: an equitable contribution from all countries in supporting basic research and maintaining up-to-date research facilities; an open system of publication of the results of fundamental research; and an equitable contribution of all countries to the training of the next generation of scientists and engineers.

Firms should enjoy greater access to world markets to ensure the rapid diffusion of new technology. And there should also be an "open circulation of technologies, subject to universal protection of intellectual property rights for firms and organizations which have invested in the development of technology".

The proposals on intellectual property put to the Geneva meeting would represent a significant move beyond current international conventions covering the mutual recognition of patents and copyright, such as those administered by the World Intellectual Property Organization. The United States argued that adopting measures such as the extension of international dispute procedures to the protection of intellectual property would help curb practices estimated to cost the pharmaceutical, electronics and automobile industries up to $60 billion a year.

Under the US proposals, retaliation could be taken against any country that failed to comply with the recommendations, under a dispute procedure set up within the framework of the GATT agreements. Such retaliation could include the withdrawal of tariff concessions enjoyed by the offending country. (Extracted from Science, Vol. 238, p.741, D. Dickson, 6 November 1987, Copyright 1987 by the AAAS)

Europe negotiates gene regulation

There is little disagreement in Europe that the development of acceptable safety guidelines for releasing genetically altered micro-organisms into the environment is currently the biggest outstanding issue in the regulation of biotechnology. But there is major disagreement over how this should be done, given the wide variation in the public perception of the risks involved.

Europe's biotechnology companies in particular argue that the mosaic of regulatory régimes they currently face places them at a serious disadvantage with respect to US and Japanese competitors. They like to quote the views expressed in the United States in 1986 to a group of visiting European officials that, because Europe is unable to create the right regulatory and commercial framework for the successful development of biotechnology, the United States' only real competitor is Japan.

At present, European countries fall into three categories on the regulation of the deliberate release of genetically engineered organisms into the environment. The first are the "yes, but" countries - those that have said they approve of such practices in principle, but have designed a carefully controlled approval process in which each project is assessed by a range of government agencies before being given the go-ahead.

The United Kingdom has perhaps advanced the most in this direction. A subcommittee of the Advisory Committee on Genetic Manipulation has already given approval to several experiments, the first being those conducted by David Bishop in Oxford, without generating any significant public opposition. The subcommittee includes representatives of industry, local authorities, and several government departments, as well as two "card-carrying ecologists". France also has a panel, created by the National Institute of Agricultural Research (INRA) to give approval to experiments, and a similar procedure is under consideration in the Netherlands.

A very different strategy has been adopted by the second group of countries, the "no, but" European nations. Here the philosophy is to impose a general ban on all deliberate release experiments, on the grounds that more information is needed on the likely hazards, but to allow for exemptions in individual circumstances.

Denmark has gone furthest in this direction, with a law passed almost unanimously last year in the Danish Parliament forbidding all such experiments unless explicit permission has been given by the Minister of the Environment. The Federal Republic of Germany's view is close to the Danish position. The Government is currently working out how to react to the proposals of a parliamentary committee, published at the end of 1986, that there should be a five-year moratorium on deliberate release, with exceptions possible in specific cases.

In between are the remaining seven member States of the European Economic Community (EEC), which have not yet introduced any regulations at all. Although some of these, such as Greece and Portugal, are unlikely to carry out major experiments in the near future, others - in particular Italy - have much more developed biotechnology industries.

The task of trying to create a coherent picture out of this uneven patchwork falls to the EEC Commission which is currently drafting a directive, outlining a common procedure for approving the deliberate release of genetically altered micro-organisms to be followed by all EEC countries. If accepted by their two joint political bodies, the Council of Ministers and the European Parliament, the directive would eventually become binding on all member States - and could therefore require individual countries, such as Denmark, to change legislation currently on the statute book.

Under the terms of the current draft of the directive, all applications for controlled release into the environment would be initially evaluated by what are referred to as the "competent national authorities" (such as Britain's Advisory Committee) using a commonly agreed upon set of procedures. These would be based primarily on proposals offered last year in a report published by OECD.

After this evaluation, applications for large-scale releases would be passed to the Commission for final approval. In the case of small-scale release, which would include most research experiments, the Commission would merely require that it be notified.

In general, Europe's biotechnology companies are enthusiastic about the idea of a single, harmonized set of regulations, particularly since the procedures currently being considered are close to those already proposed by its own lobbying organization, the European Biotechnology Co-ordination Group.

In their current form, however, several aspects of the Commission's proposals, which are scheduled for publication for public comment early next year, remain highly controversial. One is the fact that, once an application for a large-scale release has been submitted for approval to the EEC, it will then be passed to the other 11 member States. These will then have time (the current suggestion is 60 days) to file an objection.

In theory, this could make it possible for authorities in one country to try to veto a planned experiment in a neighbouring country; in practice, EEC officials envisage a review procedure involving both government representatives and independent scientists designed to resolve any disagreements that emerge, but many companies are unhappy about the delays that could result.

Even more controversial is the question of whether some countries should be allowed to step out of line and impose harsher restrictions than others. Would Denmark, for example, be permitted to maintain its ban? In general, the biotechnology community is adamant that no deviations from a European norm should be allowed - including the mutual recognition of the conclusions of risk-assessment studies.

However, the argument that harmonization is necessary for guaranteeing maximum safety is strongly contested by many environmental groups.

The biotechnology companies accept the idea that more rigorous risk-assessment techniques are needed. But they are concerned that excessive caution could itself prove harmful. (Extracted from Science, Vol. 238, p.18-19, D. Dickson, 2 October 1987, Copyright 1987 by the AAAS)

UK seeks to extend genetic manipulation regulations

Officials at the UK Health and Safety Commission are proposing changes to the rules regulating genetic manipulation that will extend the requirement for notification and risk assessment. The HSC intends to extend the scope of the current regulations which are covered by non-mandatory schemes.

The Commission is planning to make notification of the use of gene-spliced organisms compulsory, particularly those in large scale and industrial usage. It also intends to make compulsory the notification of planned release of gene-spliced organisms into the environment.

Other changes proposed in the HSC's consultative document include the requirement to notify the Health and Safety Executive of planned experiments with risk assessments and the establishment of safety committees to oversee genetic manipulation.

It is also envisaged that new regulations will close two loopholes in the current legislation. The new rules will cover the transfer of all foreign DNA into cells such as micro-injection and the deliberate release of genetically-altered material from offshore installations.

While the regulations will be designed to tighten up the existing rules in some areas there will be relaxation intended to cut red tape. Those areas defined as low risk will not require full details of experiments although all laboratories will be required to conduct their activities according to best known practices.

The proposals have been developed by the Health and Safety Commission after discussions with the Advisory Committee on Genetic Manipulation. The Commission claims that its plans have been well received by industry.

Once the comments from interested parties have been reviewed the Commission will draw up a final version of its proposals for new regulations and present them to the Government in the spring of 1988. While the process will depend largely on the parliamentary timetable, the Commission is confident that the rules will become law by next summer.

If the proposals become law, then scientists who defy them will face the heaviest fines - up to £2,000 - for releasing organisms in the open without permission.

The Advisory Committee on Genetic Manipulation (ACGM), which advises the Commission on matters relating to gene-spliced organisms, judges these experiments to carry the greatest risks because the impact on the environment and on human health of loosed organisms is difficult to predict. The UK Department of Trade and Industry is hoping to interest companies in jointly funded experiments to assess the risk of deliberately releasing genetically manipulated plants or microbes. If experiments of sufficient interest to a number of companies can be identified, the Department's Biotechnology Unit is prepared to pay half of their cost.

Roy Dietz, head of the unit, anticipates that such experiments will be carried out under contract at independent laboratories, such as those of the Agricultural and Food Research Council or Natural Environment Research Council that already have experience in deliberate release experiments. A major aim of the "Planned Release of Selected and Manipulated Organisms" initiative, he says, is to hasten the evolution of a framework for deliberate release, which is being constructed on a case-by-case basis by the Advisory Group on Genetic Manipulation. (Sources: European Chemical News, 12 October 1987, New Scientist, 1 October 1987 and Nature, Vol. 329, 1 October 1987)

The NAS report on 'deliberate release'

In August the National Academy of Sciences (NAS) released an important report on planned introductions (also known as deliberate releases) of genetically engineered organisms into the environment. The report offers the eminently reasonable view that "there is adequate knowledge of the scientific principles, as

well as sufficient experience with rDNA-engineered organisms, to guide the safe and prudent use of such organisms outside research laboratories".

The most important of the NAS panel's conclusions and recommendations are:

- There is no evidence of unique hazards associated with deliberate release - either in the use of rDNA techniques or in the movement of genes between unrelated organisms.

- The risks associated with the introduction of rDNA-engineered organisms are the same in kind as the risks associated with the introduction of organisms modified by other methods.

- A regulatory process must consider previous experience in the regulation of rDNA and the regulation (or its absence) of organisms modified by traditional techniques.

- The assessment of risks associated with introducing rDNA organisms into the environment should be based on the nature of the organism; based on the environment into which the organism is to be introduced; and independent of the method of engineering per se.

- There must be established confidence (or risk) categories, in order not to hinder testing of low-risk organisms because of a justifiably cautious approach to high-risk organisms, such as vertebrate pathogens or noxious weeds.

- A classification scheme for confidence categories should rely on the nature of biological function affected or introduced by genetic engineering; the environment from which the host organism was taken; the ecological characteristics of the rDNA organism; the characteristics of the recipient environment; and the scale and frequency of the introduction.

The NAS report's recommendation to focus risk assessment on product rather than process echoes the federal Government's regulatory framework. Also, the report's recommendation for establishing risk categories is redolent of the National Institutes of Health (NIH) Guidelines' specifications for exempting certain classes of field trials from government review. In practice, any investigator contemplating a field trial should first compare the particulars of his own experiment with the relevant assessment criteria stated by the federal regulations. This will allow him to determine whether he needs government approval prior to conducting the experiment.

Both the NAS report and the current federal regulatory scheme iterate the important principle that there are categories of products that do not require special governmental scrutiny or restriction. These products entail negligible or trivial risk in a small-scale field trial. They can be defined broadly (as in "all well-characterized non-pathogens") or more specifically (as in "Pseudomonas syringae, Bacillus thuringiensis, Rhizobium, and Thiobacillus ferrooxidans", manipulated in a way that constitutes self-cloning).

The simple, unassailably logical precepts of the NAS report provide clear perspectives on field trials of recombinant DNA-manipulated organisms. They could, if adopted in toto, introduce a high level of rationality and enlightenment into societal oversight of the testing of genetically engineered organisms.

There are several areas of the world where this would be especially welcome. In Japan, guidelines that are in effect (Ministry of International Trade and Industry, and Ministry of Health and Welfare) or proposed (Ministry of Agriculture, Forestry, and Fisheries) are process-based; that is, the regulatory requirements for rDNA-manipulated organisms are much more stringent than those for similar organisms that are engineered by older, less precise techniques. Similarly, the proposed community-wide directive for the European Economic Community, if adopted, will establish a draconian two-tiered scheme applicable only to rDNA-manipulated organisms. (Extracted from Bio/Technology, Vol. 5, October 1987)

Indo-US vaccine pact disputed

A co-operative Indo-US vaccine development programme has been the subject of a sharp exchange of criticism in the Indian press and rebuttal by the Indian Government. A main contention of the critics, denied by the Government, is that US drug companies intend to use the agreement to make India a testing ground for bioengineered vaccines, thereby bypassing stringent US regulations on vaccine field trials on humans.

Target of the critics is a memorandum of understanding for a vaccine action programme signed on 9 July 1987 by the two countries. The agreement calls for US spending of $7.6 million over five years. India will spend $2 million in its own funds.

Under the agreement, collaborative efforts are to be directed at high-priority vaccines "which can be developed or adapted to the Indian situation". Cholera, typhoid fever, rotavirus, hepatitis, dysentery, rabies, pertussis, pneumococcal pneumonia, and malaria are described in project documents as "priority areas".

Critics charge that the agreement called for a patent accord that would impose strong, US-style patent protection on patentable results produced in India under the programme, replacing India's existing patent provisions which provide less protection to developers. The critics had also complained about the weakness of the agreement's provisions for safeguards on the introduction of genetically engineered organisms into the environment.

The Indian Government responded in detail to a number of the critics' points in a "clarifying" statement on 19 August 1987. The statement said, for example, that no vaccine developed elsewhere will be tested in India unless it has been cleared for testing in the country in which it was developed.

Indian-US co-operation in health R&D has a long history, but has been subject periodically to hostile comment in India in incidents usually reflecting Indian suspiciousness toward US intentions. At this point, categorical answers to the current questions about US motives are unavailable. The memorandum of understanding provides only a framework for activities under the agreement. Still to be negotiated are appendices that will govern two of the most sensitive issues - protection of subjects in field trials of vaccines and provisions on patents, copyrights, and other intellectual property. (Extracted from Science, Vol. 236, J. Walsh, p.19, 2 October 1987. Copyright 1987 by AAS)

Social issues

US physicians issue ethics guidelines for AIDS

The American Medical Association recently took the unusual step of issuing explicit ethical guidelines concerning patients infected with the virus that causes acquired immune deficiency syndrome (AIDS).

This is the first time AMA has issued ethical guidance in response to a single disease. AMA has no legal ability to enforce these guidelines, but as the largest and most influential medical organization in the US, its ethical guidelines are the most widely used code of ethics.

The AMA's Council on Ethical & Judicial Affairs, which wrote the guidance, says that physicians cannot refuse to treat people infected with the AIDS virus. Further, the Council recommends that physicians infected with the AIDS virus refrain from activity "that creates a risk of transmission of the disease to others".

If the latter recommendation is accepted by the medical profession, surgeons infected with the AIDS virus will likely have to refrain from operating on patients. During surgery there is always a risk that these surgeons could transmit the virus to the patient.

If no risk exists, AMA rules, a physician need not disclose his or her medical condition to patients. Such disclosure would "serve no rational purpose," the association declares.

According to the AMA guidance, a physician is morally obligated to respect the privacy and confidentiality rights of AIDS patients or those individuals infected with the virus. However, a physician must dissuade AIDS-infected individuals from engaging in activities that can transmit the virus. If persuasion fails, AMA says physicians have an obligation to notify public officials who can take measures to protect third parties. If this, too, fails, then physicians "may have a common law duty to warn endangered third parties".

State licensing boards are also beginning to take action. The New Jersey State Board of Medical Examiners recently told physicians in the state that they "may not categorically refuse to treat a patient who has AIDS or AIDS-related complex or [who tests positive for the AIDS virus] when [they] possess the skill and experience to treat the condition presented." Under certain conditions, a physician may apply for an exemption, which the licensing board will grant under unspecified "extenuating circumstances". Even if permitted not to treat AIDS-infected patients, the physician must make other arrangements for proper care of the patient.

The New Jersey licensing board has yet to receive a complaint regarding refusal of treatment. "We remain confident that our licensees are appropriately shouldering their responsibilities," the board concludes. (Abstracted with permission from Chemical and Engineering News, 30 November 1987. Copyright (1987) American Chemical Society)

Miscellaneous

ATCC offers fungi isolated from diesel fuel

The American Type Culture Collection (ATCC) is making available 12 strains of fungi isolated from diesel fuel in New Zealand. They were identified during a study of diesel fuel blockages and fuel gauge failures in navy ships and buses. Details from: Sales and Marketing Department, ATCC, 12301 Parklawn Drive, Rockville, Maryland 20852, USA or on (301) 881-2600. (Source: Biotechnology Bulletin, Vol. 6, No. 9, October 1987)

New plant biotechnology research centre

The Plant Gene Expression Center, a research facility that will seek to identify agriculturally important plant genes and understand how they function, has been dedicated in Albany, Calif.

The centre is a joint venture of the US Department of Agriculture's Agricultural Research Service; the University of California, Berkeley; and the California Agricultural Experiment Station. Its dedication marks completion of construction of new laboratories at USDA's Western Regional Research Center and recruitment of a scientific staff of about 70.

Among the projects being pursued at the centre are development of methods for inserting genes into cereal crops. Techniques include electroporation (in which an electrical charge is used to create pores in cell membranes through which DNA can pass), micro-injection, and the use of high-velocity micro-projectiles coated with DNA.

Also being investigated are the sources of the high rate of somoclonal variation in plant cells growing in cell culture. Somoclonal variation introduces unwanted variations in genetically engineered plants. The centre's researchers are studying genes involved in plant development, flowering, fruit ripening, plant senescence, disease resistance, and photosynthesis. (Abstracted with permission from Chemical and Engineering News, 30 November 1987. Copyright (1987) American Chemical Society)

Perspectives for biotechnology in the Caribbean

A Seminar/Workshop on Perspectives for Biotechnology in the Caribbean Subregion held in Port of Spain, Trinidad and Tobago, 25-27 February 1988 brought together some 34 participants representing 18 institutions both public sector and private sector from 10 countries. The objectives of the seminar/workshop included establishment of subregional priorities in biotechnology, examination of sources and mechanisms of funding projects and the setting up of a Caribbean Biotechnology Network that would also link into other regional and international networks.

Participants reviewed various programmes of work in the region including work on micropropagation and tissue culture, genetics of Rhizobia, yeast microbiology, genetic improvements of potato, aroid root crops and ornamentals, interferon, vaccine and antisera production and revision of patent legislation.

In discussing priorities in biotechnology for the subregion in the context of existing work programmes and available resources, areas identified and agreed upon included:

Micropropagation and tissue culture
Integrated pest management
Nitrogen fixation
Germplasm conservation
Antisera and diagnostics
Enzymology
Sugar industry fermentations.

It was also agreed that a Subregional Caribbean Biotechnology Network be set up initially on a pilot basis to focus on promoting co-operation through

pooling resources, dissemination of information, exchange of personnel, joint training and research efforts.

The network is to be set up initially on a three-year basis (1988-1991) and will have its secretariat located at:

Caribbean Industrial Research Institute
Tunapuna Post Office
Trinidad and Tobago

Telephone: 809 662 7161 to 5 or 809 663 4161
Telex: 24438 CARIRI WG
Telefax: 809 663 4180.

The Chairman of the network is Dr. Desmond A. Ali.

The recommendation of this seminar/workshop were later considered by the Caribbean Community Ministers responsible for Science and Technology when they had the First Meeting in Trinidad and Tobago, 9-10 March 1988. Ministers endorsed the recommendations of the Biotechnology seminar/workshop and agreed that this was a high priority area in their Action Programme that must be accorded fullest support.

Many angles to competitive analysis

Performing competitive analysis is always difficult, but it is a particularly daunting task to forecast winners in biotechnology. Timing, luck, R&D breakthroughs, commercial partners, and financing have a whole lot more to do with ultimate success than one would like to think, according to Steven Burrill at the Bio/Technology seminar on "Assessing Competitive Strength", held at the end of September 1987.

Burrill, who is chairman of the national high technology group at Arthur Young (San Francisco, CA), believes financial staying power is the key to corporate success in this emerging industry. Such resources allow a firm to do research and product development, attract and retain key people, build appropriate facilities, buy time in the face of regulatory delays, fight for patent rights, and integrate vertically if so desired.

Wall Street also has trouble analysing competitive position, according to PaineWebber (New York, NY) vice-president Linda Miller. Complicating factors include:

- The tangling interrelationships in biotechnology;
- The requirement for multidisciplinary, synergistic talents within companies;
- The unclear strength (and value) of patent positions; and
- The increasingly global nature of biotechnology, which means that large, international concerns must be factored into the competitive equation.

When Miller analyses competitive position, she looks first to technological strength, then to business strategy and operational skills, and finally to product portfolio and financing strategy.

George Rathmann, president of Amgen (Thousand Oaks, CA), stressed the interrelationship between science and business.

As if analysing competitive strength in biotechnology were not hard enough, there are also a few "wild cards" that the seminar's panelists believe make things even tougher. These include the role of public perception, whether the courts will enforce the rulings of the Patent and Trademark Office, any reallocation of turf between the various offices of the Food and Drug Administration, the real value of strategic partnerships, product liability questions, and the eventual impact of second-generation products.

Amgen's Rathmann suggested that companies choose projects whose commercial feasibility can be determined relatively quickly.

KEY ASPECTS ON WHICH TO EVALUATE BIOTECHNOLOGY COMPANIES AS THEY MATURE

0-2 years	2-6 years	6-8 years	8-10 years
Extent of financing	Mezzanine financing	PLA/NDA	Market franchise
Investor quality	Corporate partners	Product intro	Product innovations
Venture	IND filing	Revenues	↑R&D expense
Corporate	Patent application	Profits	Internal cash generation
R&D expense	Cash vs. burn rate	Direct marketing	
BOD/SAB/MGMT	Product utility	Product pipeline	
Experience	Leadership	↑R&D expense	
Track record	↑R&D expense		
Performance	Resource allocation		

Data from George Rathmann, Amgen. Key: BOD = board of directors; SAB = scientific advisory board; MGMT = management; IND = investigational new drug; PLA = product license application; NDA = new drug application.

(Extracted from Bio/Technology, Vol. 5, November 1987)

An analysis of partnerships

Many of the world's major corporations began their involvement in biotechnology around 1980 by forming partnerships or strategic alliances with small biotechnology firms. This has been particularly true for corporations in Japan, although Japan has not generated a new biotechnology industry consisting of start-up companies. Japan's entry in biotechnology has, however, been spearheaded by its large, established corporations. In so doing, these companies have formed marketing agreements, licensing arrangements, research contracts, and other types of joint ventures with the world's biotechnology firms, especially with those in the United States.

Figure 1 indicates the number of relationships formed between Japanese and US companies each year.

Table 1 lists the partnerships formed between Japanese corporations and US biotechnology companies. Also listed are a broad range of US biotechnology companies, including those generally deemed to be the most successful.

U.S.-JAPANESE CORPORATE COLLABORATIONS IN BIOTECHNOLOGY

Japanese Company	Japanese Company Focus	U.S. Partner (Products, Year)
Ajinomoto	amino acids, food products, pharm.	Searle (aspartame, 82)
Banyu	pharm	Merck (pharmaceuticals, 83)
C. Itoh	trading company, manufacturer's rep.	Bioreactor Technology (bioreactors, 86); Repligen (proteins, 83)
Chiyoda	engineering, construction, bioreactors	Stearns Catalytic (production technology, 86)
Chugai	pharm., diagnostics	Genetics Institute (erythropoietin, 84)
Daiichi Seiyaku	pharm	Genentech (G-IF, 83) Genetic Systems Corp (diagnostics, 86)
Daikyo Oil Company	energy	Cyanotech (N/A, 86)
Dainabot	diagnostics	Immuno Nuclear (diagnostics, 83)
Dainippon Ink & Chem.	edible algae, sweeteners, pharm., pest.	Diagnostic Products (diagnostics, 86)
Dainippon	pharm	Abbott (IF assay, 82), Searle (N/A, 82)
Essex Nippon		Schering Plough (A-IF, 82)
Fujirebio	pharm., diagnostics, enzymes	Integrated Genetics (DNA probes, 84)
Fujisawa	pharm	Biogen (TPA, 82) Genentech (lymphotoxin, 84) Lymphomed (pharmaceuticals, 84)
Fujizoki	pharm., reagents, plasma products	Biotech Research Labs (MAB, 82), Hana Biologics (diagnostics, 82), Techniclone (diagnostics, 82)
Funakoshi	pharm	Molecular Biosystems (microspheres, 84), Ventrex (MAB, 84)
Green Cross	pharm., plasma products, diagnostics, chemicals	Alpha Therapeutics (IF, 78), Biogen (vaccines, 81) Bristol-Myers (N/A); Collaborative Research (urokinase, B-IF, 81-83), Genex (HSA, 82), Hybritech (MAB, 82), Interferon Sciences (IF, 82)
Iatron Laboratories	diagnostics and clinical test reagents	Synbiotics (veterinary, 84)
Japan Scientific Inst	instrumentation	Applied Biosystems (reagents, 85)
Kamura		Calgene (herbicide tolerant rapeseed, 85)
Kanto		Enzo Biochem (enzymes, 81)
Kirin Brewery	beer, soft drinks, carcinostatic agents	Amgen (erythropoietin, 84), Plant Genetics (synthetic seeds, 84)
Kurary	pharm., diagnostics, chemicals	Calgene (agriculture chemicals, 85), Xenogen (diagnostics, 83)
Kyowa Hakko Kogyo	pharm., biomass, energy, fermentation	Human Antibody Tech (diagnostics, 84), Genentech (TPA, 85), Native Plants Int'l (N/A, 86)
Meiji Seika Kaisha	pharm., enzymes, foods, beverages	Biogen (antibiotics, 82), Enzo Biochem (HCG test, 82), Searle (B-IF, 82)
Mitsubishi Chemical	medical diagnostic equip., pharm., agriculture, energy, bioreactors	Battelle (N/A, 84), Genentech (vaccines, TPA, HSA, 82-85), Hybritech (anti-IgE kit, 81), Ingene (sweeteners, 86)
Mitsui Toatsu Chem	energy, foods, chemicals, agriculture, pharm., amino acids, diagnostics	Endotronics (instrumentation, 84), Genex (urokinase, 82), Occidental Petroleum (rice, 86), Xenogen (feed additives, 83)
Mochida		Searle (B-IF, 82)
Nagase & Co.	enzymes, hormones, diagnostics	Genzyme (amylase, 86)
Nippon Chemical Ind	chemicals	Endotronics (HGH, 84)
Nippon Lederle K.K.	pharm	Collagen (dyderm implant, 85)
Nippon Mining	metals, chemicals, petroleum	SRI International (N/A, 85)
Nissho Iwai	pharm., licensing representative	University Genetics (N/A, 83)
Oriental Yeast	pharm	Atlantic Antibodies (antisera, 84), Gibco (N/A, 83)
Otsuka	pharm., blood agents	Dow Chemical (N/A, 81)
Sankyo	pharm., blood agents	DuPont (drugs, 82)
Sekisui		Cetus (MAB, diagnostics, 85)
Shin Meiwa Ind		Queue Systems (bioreactor and bioseparation products, 84)
Shionogi	pharm., insecticides	Biogen (HSA, IL-2, 82-83), Eli Lilly (insulin, 81), Merck (hepatitis vaccine, 85), Molecular Genetics (animal drugs, 85)
Showa Denko	pharm., chemicals, amino acids	Diamond Shamrock (veterinary products, 83)
Snow Brand Milk	pharm., foods	Innovax Labs (N/A, 83)
Sumitomo	chemicals, pharm., agriculture, biomass conversion	Am. Type Culture Collection (genes and cells, 86)
Suntory	alcoholic beverages, pharm	Biogen (colony stim. factor, 85), Native Plants, Int'l (foods, 84)
Takeda	pharm., vitamins	Biogen (TNF, 83), Schering Plough (IF, 83) Abbott (diagnostics, 82), Genentech (B-IF, 82), Liposome Technology (N/A, 86)
Teijin	pharm., chemicals	Biogen (factor VIII, 82), Hybritech (MAB, 82), Zymogenetics (blood factors, 84)
Toray Industries	pharm., feed additives	Bioassay Systems (IF assay, 82), Centacor (diagnostics, 83), Genentech (IF, 81)
Toray-Fuji Bionics		Bioassay Systems (viral diagnostics, 86)
Toyo Jozo	pharm., food, agriculture, chemicals	Schering Plough (antibiotics, 85)
Toyo Soda	sweeteners, foods, pharm., bioreactors	Hybritech (diagnostics, 84), Ungene Laboratories (immunization technology, 85)
Toyobo	enzymes	Integrated Genetics (TPA, 83)
Yamanouchi	pharm., chemicals, foods	Biogen (anti-inflammatory compounds, 82), Eli Lilly (pharmaceuticals, 83), Genex (TPA, 82), Schering Plough (IF, 84)
Yoshitomi	pharm	Genex (IL-2, 83)

TABLE 1. Japanese corporate partnerships with U.S. biotechnology companies. Japanese corporations are listed with their primary industry focus and the partnerships they formed with U.S. biotechnology firms. The product involved and the year the partnership was formed are indicated in parentheses, where available. Key to abbreviations: IF (interferon); A-IF (alpha interferon); B-IF (beta-interferon); G-IF (gamma-interferon); HCG (human chorionic gonadotropin); HGH (human growth hormone); HSA (human serum albumin); IL-2 (interleukin-2); MAB (monoclonal antibodies); MAF (macrophage activating factor); TPA (tissue plasminogen activator); TNF (tumor necrosis factor); pharm. (pharmaceuticals); N/A (not available).

Figure 2 represents an analysis of these actions by year. In all categories, the peak years were 1982 to 1984, with decreases in these numbers for more recent years.

Table 2 summarizes Japanese/European joint actions.

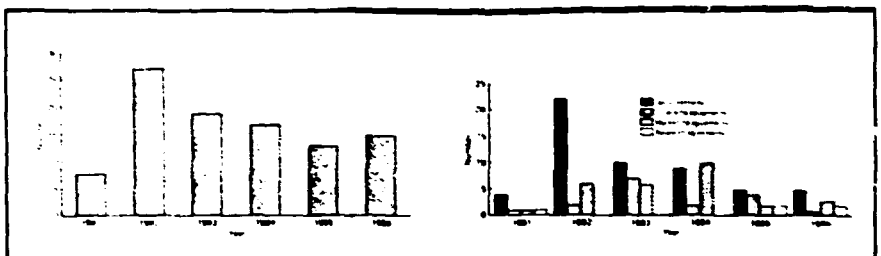

FIGURE 1: Total U.S.-Japan external agreements listed by year. FIGURE 2: U.S.-Japan external agreements listed by year and type of agreement

JAPANESE-EUROPEAN CORPORATE COLLABORATIONS IN BIOTECHNOLOGY

Japanese Company	European Partner	European Country	Products	Year
Ajinomoto	Hoffmann-LaRoche	Switzerland	IL-2	84
Ajinomoto	Orsan	France	amino acids, lysine	84
Chugai	Amersham	U.K.	NBA	83
Eisai	Sandoz	Switzerland	cardiovascular drugs	82
Green Cross	French Com. of Atomic Energy	France	MAB	85
Immuno	Institut Pasteur Production	France	diagnostics	84
Kodama Ltd	Novo Industri A/S	Denmark	insulin	85
Mitsubishi	Biocarb AB	Sweden	carbohydrates	86
Sankyo	Celltech	U.K.	TPA, calcitonin, MAF, TNF	84
Shionogi	Biogen	Switzerland	G-IF	82
Sumitomo	Burroughs-Wellcome	U.K.	IF, TPA	82
Sumitomo	Celltech	U.K.	MAB	82
Sumitomo	Kabi Vitrum	Sweden	growth factor	84
Takara-shuzo	Amersham	U.K.	enzyme reagents	82
Takeda	Hoffmann-LaRoche	Switzerland	MAB, A-IF, antibiotics	84
Takeda	Burrough-Wellcome	U.K.	lymphoblast IF	82
Toya Soda	Dutch State Mines	Netherlands	copertama	85
Toyobo	BASF	West Germany	TPA	85
Yamanouchi	Nordisk Gentofte	Denmark	HGM	86
Yamasa Shoyu	Celltech	U.K.	B-IF	84

TABLE 2. Japanese corporate partnerships with European biotechnology companies. Key to abbrevations: See for Table 1

DEALS BETWEEN JAPANESE AND OUTSIDE CONCERNS ANNOUNCED IN 1987

Japanese Company	Outside Concern	Comments
Ajinomoto	Centocor	Ajinomoto to distribute Panorex anti-pancreatic cancer monoclonal in Far East
Asahi Glass KK	Queens University (U.K.)	Asahi licenses rights to an atrial natriuretic factor from Queens
Calbee Potato Inc	Plant Genetics Inc. (PGI)	Calbee licenses PGI's No-Spud® potato production technology
Cosmo Bio	Sumitomo Medical	Cosmo will distribute Sumitomo's monoclonal antibodies in Japan
Daiichi Seiyaku	Connaught Laboratories (Canada)	Establish a joint venture called C-D Vac to manufacture and market Connaught's vaccines in Japan
Dainihon Jochugiku	Agrocetus	Dainihon licenses chemical termiticide
Dainippon Pharmaceutical	Genentech	Dainippon licenses its tumor necrosis factor patent rights covering Austria, F.R.G., Italy, Spain, and Switzerland to Genentech
Kurary	Immunomedics	Kurary acquires exclusive Japanese marketing rights to Immunomedics' diagnostics
Kyowa Medex (subsidiary of Kyowa Hakko Kogyo)	Murex Corp.	Development and marketing of AIDS diagnostic
Kyowa Hakko Kogyo	Phillips Petroleum	Joint research on mass production of the salmon growth hormone protein
Maruzen Corp.	Michigan Biotechnology Institute (MBI)	Maruzen will represent MBI in Japan
Mitsubishi Chemical	Genentech	5 year deal under which Genentech will market future Mitsubishi biotech products in U.S. and Canada, while Mitsubishi will market certain Genentech products in Japan
Mitsubishi Corp.	Applied biotechnology	Mitsubishi will represent Applied in Japan
Mitsubishi Yuka Laboratory of Medical Science	Analytical Biosystems	Mitsubishi Yuka to evaluate an in vitro chemosensitivity assay to test anti-cancer drugs
Mitsui Petrochemical Industries Ltd	Allelix (Canada)	Development of Allelix's plant cell fermentation process for manufacturing therapeutics; the anti-cancer drugs vincristine and vinblastine will be first
Nagase	Cetus Corp	Nagase to market Cetus' HLA-typing DNA probe test
Nippon Oil	Genex Corp.	Nippon licenses Genex's manufacturing technology for vitamin B12 cyanocobalamin
Nippon Steel	Calgene	Product development agreement for engineering a novel vegetable oil
Nitteh Sangyo	Plant Genetics Inc. (PGI)	Nitteh to market PGI alfalfa seeds in Japan
Olympus Corp. (U.S. subsidiary of Olympus Optical Co.)	Cetus Corp.	Cetus grants exclusive worldwide distribution rights to Olympus for its ProGroup automated blood-typing and screening device
Sankyo Junyaku	Du Pont	Japanese marketing rights to Du Pont's AIDS screening kits
Sanyo	Organon Teknika (Belgium)	Sanyo licenses enzyme immunoassay patents from Organon
Special Reference Laboratories (SRL)	Collaborative Research	Collaborative to perform genetic disease and cancer diagnoses on SRL samples
Special Reference Laboratories (SRL)	Integrated Genetics	Integrated to provide DNA probe diagnostic services for genetic disorders
Sumitomo Corp.	Celltech Ltd. (U.K.)	Sumitomo invests $3.4 million in Celltech equity
Teijin Ltd.	Zymogenetics	Teijin gains Asian rights to Protein C anti-coagulant
Toagosei Chemical Industry	Calgene	Calgene gains rights to use Bacillus thuringiensis genes isolated by Toagosei to engineer insect-resistant corn and cotton
Toray-Fuji Bionics	Cambridge BioScience	Toray-Fuji to distribute Cambridge's monoclonal antibody-based tests for rotavirus and adenovirus in Japan, Taiwan, and Korea
Toray Industries	Life Technologies	Toray gains exclusive Far East rights to Life Tech's nonisotopic DNA probe technology for detecting hepatitis B and human papillomavirus
Toyo Soda Manufacturing	Rohm and Haas	The new Toso Haas joint venture will market process equipment and supplies used for biological processing, as well as analytical equipment
Unicom	Chemicals (Canada)	Unicom to import and market Chemicals's monoclonals for blood-typing
Yamanouchi Pharmaceutical	T Cell Sciences	3-year, $3.7 million development agreement for T Cell's autoimmune disease and cancer diagnostic products
Yamanouchi Pharmaceutical	T Cell Sciences	Yamanouchi to distribute T Cell's interleukin-2 receptor test kits
Yamanouchi Pharmaceutical	Damon Biotech	Yamanouchi to pay $8.5 million for Japanese rights to Damon's tissue plasminogen activator

Data from Abstracts in BioCommerce, Japan Chemical Week and industry sources

(Extracted from Bio/Technology, Vol. 5, October 1987)

Rise in biotechnology product sales

Product sales among the large biotechnology companies rose 50 per cent from $20 million in 1985 to $31 million in 1986, according to an Arthur Young survey of 213 biotechnology firms, including diagnostic, therapeutic and agri-tech firms. Even at small companies, product sales accounted for over 50 per cent of revenues, which helps counter the belief that most biotechnology firms have few products on the market. Product sales ranged from 78 per cent of total revenues for diagnostic companies, a relatively mature sector, to 28 per cent for therapeutical companies.

Biotechnology sales, including instruments and reagents, will rise from $660 million in 1987 to $10 billion by 1997, according to Consulting Resources. The biotechnology industry is thus one of the best investment opportunities available. The financial performance to date has been disappointing because of heavy development costs. Marketing and production know-how will become increasingly important for the biotechnology companies. (Extracted from Chemical Marketing Reporter, 19 October 1987 and Chemical Week, 14 October 1987)

Big staffing increases for biotechnology

The biotechnology industry may expect healthy gains in employment, as well as above-average merit increases in salary and increasing use of financial incentives for top performers. So reports a salary survey released by the Industrial Biotechnology Association (IBA) in Washington, DC. Results are based on information gathered from 133 biotechnology companies. The study shows that about 40,000 people are employed in commercial biotechnology, with staffing expected to increase by 44 per cent by June of 1989. Difficult positions to fill, says the study, include biochemical engineers and research managers, as well as patent attorneys and immuno-engineers. In contrast, positions in oversupply include PhDs, biologists and organic chemists. Merit increases are projected to increase in 1988. To promote productivity, 60 per cent of participating companies use cash incentive compensation plans and 50 per cent use bonus plans. One company in fact authorizes its vice-presidents to write cheques at any time for up to $1,000 for employees demonstrating superior achievements. (Source: Chemical Week, 16 December 1987)

Biotechnology personnel will be in demand

The biotechnology industry desperately needs engineers who can scale up processes to industrial scale. J. Rady of G. D. Searle says there is no shortage of biotechnology personnel overall, but there is a shortage of qualified people for personnel to support scale-up operations. M. D. Dibner of the North Carolina Biotechnology Center says that the staff needed by biotechnology firms will rise 20-25 per cent/year in the next few years. Technically oriented people are needed not just in the laboratory and pilot plants, but in administrative positions as well. Particular difficulty will come in filling positions that must combine technical knowledge with regulatory affairs, patent law or marketing. Dibner predicts that the five rDNA drug products now approved for use in the US will rise to 20 by 1992.

Only a few US universities have biochemical engineering programmes. Bioprocess engineers are hard to find, as are pharmaceutical formulators to develop appropriate dosage systems. R. Curtiss III of Washington University (St. Louis, MO) predicts that students will begin to shift from medicine to biotechnology, since medical schools are full. Computerization of process systems might alleviate some need for trained personnel. Another possibility is increasing co-operation between universities and biotechnology firms to provide work experience. But in-house training is still the best solution in some cases. (Extracted from Chemical Week, 25 November 1987)

Biotechnology firms vie for farm products market

Biotechnological agricultural product sales will rise by 60 per cent/year to over $2 billion in 1995 versus 1985, according to a study by Kline & Co (US). The market will grow 100-200 per cent by the year 2000 versus 1995. Some 67 per cent of projected sales are for products that are impossible to create with conventional technology. The market is now worth some $14 million/year, with most products in the animal health therapeutics, disease diagnostics and micropropagated plants areas. By 1990 new ranges of products will appear, including animal health vaccines and genetically-engineered microbial insecticides. By 1995 this will expand to include herbicide- and pest-resistant crop varieties, hybridized, improved and modified crop varieties, and bovine and porcine growth hormones. Many major chemicals firms are now present in the market, and Kline expects a major shakeout to occur by 1995, removing many of the younger, innovative firms that have sprung into existence. (Extracted from European Chemical News, 26 October 1987)

New funds focus on biotech investments

Stock market turbulence aside, and even though biotechnology is not quite the novelty it was several years ago, several new funds have been formed recently to reap the benefits of investing in genetic engineering ventures.

The largest of this new breed is the Biotechnology Venture Fund S.A., incorporated in Luxembourg and advised by Abingworth Management Ltd. (London).

With its target of $50 million now raised - largely from European insurance companies and pension funds - the fund has begun investing in companies that emphasize biotechnology and health care. In addition to buying into several publicly traded firms, the fund so far has invested money into three private start-ups:

- Alkermes, which is to be located near Boston and will emphasize neurobiology;
- Immunetech Pharmaceuticals (La Jolla, CA), which has an anti-allergy peptide in phase III clinical trials and is developing a compound against auto-immune disorders; and
- Ultramed (La Jolla, CA), a medical company commercializing microsurgical appliances.

The Biotechnology Venture Fund hopes to invest soon in a privately held UK affiliate of a US company working in the cardiovascular area.

Major US corporations are also sponsoring biotechnology investment funds, with two of the most recent entries coming from E. R. Squibb (Princeton, NJ) and Westinghouse Credit Corp. (Pittsburgh, PA). The focus of Squibb Biotechnology Venture Capital Fund will be on molecular biology in health care. The dual goals are return on investment and attaining strategic advantage for Squibb by eventually forming relationships with portfolio firms. Such arrangements could include licensing, product development, distribution, or even Squibb's acting as an advisor.

Westinghouse Credit Corp., the money-managing component of Westinghouse Electric, had a somewhat different goal when it became the sole investor last spring in the $15 million MedCorp Development Fund. With the entire portfolio focusing on health care - and approximately one third going to biotechnology - Westinghouse is seeking nothing more than attractive return-on-investment, rather than any sort of window on technology.

On the public side, the little-known, two-and-one-half-year-old, Genetics Fund (previously called the Genetics Unique Fund) run by Ruggles & Associates (Boston, MA) represents what could be the purest play in public biotechnology stocks. Currently set up as a group trust available only to Ruggles' money management clients, the $8 million portfolio found itself badly burned by the stock market melt-down that shook Wall Street in the middle of October. In fact, the situation is so dire that Ruggles' new management is seriously considering liquidation of the Genetics Unique Fund. (Source: Bio/Technology, Vol. 5, December 1987)

Biotechnology Policy Center established

The US National Wildlife Federation last week announced establishment of a National Biotechnology Policy Center. Citing potential threats to the environment from rapid advances in bio-engineering, NWF's centre will oversee federal agency review of applications to release new organisms into the environment, review existing laws to determine whether new legislation is needed to regulate biotechnology, and carry on public education programmes. Headed by Margaret Mellon, an NWF attorney with a Ph.D. degree in biology, the centre is supported by a $210,000 grant from the Joyce Foundation. NWF is the US's largest conservation organization, with more than 4.8 million members and supporters and 51 affiliate organizations. (Reprinted with permission from Chemical and Engineering News, 21 December 1987. Copyright (1987) American Chemical Society)

New look at health in developing nations

In the poorest African and Asian countries, average life expectancy lingers in the 30s and 40s, evidence that modern medical science has had limited impact in much of the third world. A lack of substantial, sustained effort in research on health problems peculiar to developing countries is regarded as an important contributing factor. A new Independent International Commission on Health Research for Development is being formed to assess the issues and advocate new approaches.

To bolster its claim to independence, the commission intends to avoid the familiar posture of the First World prescribing for the third world. A majority of commission members will be chosen from developing countries for their direct experience in dealing with health problems in third world settings.

The commission will not be a grant-making organization. Its main objective will be to point out "gaps and opportunities" in health research, and it will be particularly alert to possibilities for applying advances in biotechnology to third world problems.

David E. Bell, who served as a consultant during the formative stages of the new commission said that a main impetus to its creation was the "shocking mismatch" between the volume of health research performed on behalf of the industrial countries and that specifically benefiting developing countries. Bell, a professor at the Harvard School of Public Health, said firm data are not available, but a rough estimate is that 95 per cent of the total health research effort in the world is focused on the problems of industrial countries.

He noted that although an "array of health research activities are directed at developing countries", these amount to an "accidental set". In some research areas solid progress is being made, as in the case of diarrhoeal diseases. In others, for example, acute respiratory diseases that take a heavy toll in developing countries, particularly among children, "virtually nothing is under way".

One example the commission might profitably consider is the development of oral rehydration techniques to treat diarrhoeal diseases. Success resulted from linking research with clinical and epidemiological work on cholera and other diseases, said Donald A. Henderson, dean of the Johns Hopkins School of Hygiene and Public Health, who also has been involved in the planning for the commission. Efforts in research and treatment advanced in parallel over the years to produce the current oral rehydration techniques that are practical for use in poor, third world countries. Much of the relevant work was done at centres overseas where research and care of patients were combined.

The new commission already has backing from major private foundations such as the Clark, Ford, Mobel, and Rockefeller foundations, the Carnegie Corporation, and the Pew Charitable Trust. At least by implication, formation of the commission seems a criticism of existing international assistance agencies. However, several - Canadian, Swiss, and FRG technical assistance agencies, the United Nations Development Programme, and the World Bank - have signed up as backers.

The idea of improving international health research through the work of a group like the new commission seems to have originated with the staff of the Edna McConnell Clark Foundation in New York. The plan began at a meeting convened by the foundation in 1985 to discuss how lessons from other sectors of development could be applied to health problems. After the meeting, the matter was pursued by Clark staff and representatives of Canada's International Development Research Center - the IDRC itself puts strong emphasis on the involvement of developing country scientists in research affecting their nations. Talks with Bell and his colleagues at the Harvard School of Public Health led to the school's becoming the base for the secretariat of the new commission.

The commission will not limit itself to an interest in research on infectious diseases. The commission intends to link social sciences with health sciences. At a meeting in July 1987, a wide range of topics were broached. There was agreement, for example, that women's health is a seriously neglected subject. Not only is maternal mortality much higher in developing than in industrial countries, but the importance of a woman's role in her family's health means that it merits close examination by the commission. Population issues and family health are regarded as important concerns for the commission.

The commission will get its formal start at a meeting early this month when it will start constructing an agenda. The group's chairman is John R. Evans, who heads Allelix, an Ontario biotechnology firm, and is chairman of the board of trustees of the Rockefeller Foundation. Deputy chairman is Celia T. Castillo, a professor of rural sociology at the University of the Philippines. The commission will have between 12 and 15 members when the recruiting process is complete.

The commission plans to set a brisk pace for itself. To reinforce the discipline of a deadline, it has a sunset clause in its charter programming it to go out of business after two years. In addition to an audience in industrial countries, the commission also expects to direct its message to governments of developing countries. (Source: Science, Vol. 238, p.740, J. Walsh, 6 November 1987. Copyright 1987 by the AAAS)

Research groups seal AIDS deal

The Institut Pasteur and the US National Institutes of Health (NIH) have signed an agreement which puts an end to the dispute over which group identified the AIDS virus first and, consequently, over the diagnostic test patents.

Last March, US president Reagan and France's prime minister Jacques Chirac announced the issue had been settled. The agreement is retroactive to January 1987 and provides that two foundations will be set up, a "Franco-American AIDS Foundation" and a "World AIDS Foundation" funded by 80 per cent of the royalties from diagnostic test licences.

Within these funds, 25 per cent is earmarked for research on AIDS in developing countries, while the balance will be divided between the Institut Pasteur and the NIH.

The 20 per cent not earmarked for the foundations is intended for the researchers in both countries which identified the AIDS virus. Since January 1987, $3.7 million worth of royalty fees have been collected and a cheque for that amount has been handed over to the Franco-American AIDS Foundation. (Source: European Chemical News, 14 December 1987)

A frustrating glimpse of the true AIDS epidemic

Each week the Centers for Disease Control (CDC) dutifully perform their grim arithmetic and update the number of reported AIDS cases. Yet more and more public health officials have come to see CDC's tally of full-blown AIDS cases as only a frustrating glimpse of the true epidemic. Today's AIDS cases are only a snapshot of the epidemic as it was five or 10 years ago when those individuals who are now ill were first infected with the virus.

In recent months CDC has been trying to figure out a way to do an extensive national survey to ascertain the extent of human immunodeficiency virus (HIV) infection in the general population. It was originally hoped that 50,000 randomly selected Americans would volunteer. But CDC is learning that it is easier to propose some projects than to execute them.

A recent survey conducted by the National Center for Health Statistics (NCHS) found that 31 per cent of the public said they would not allow their blood to be tested as part of a national seroprevalence study, even though assurances of privacy were given. The question was raised during a 15-minute interview with 2,250 persons. CDC is understandably concerned that the people who refuse to participate might be more likely to have risk factors and thereby harbour the virus.

James Curran, director of CDC's AIDS office, says feasibility studies for the large national survey will be "proceeding both rapidly and cautiously".

No one knows how many Americans harbour the AIDS virus. The Government's best guess is that one million to 1.5 million citizens are infected. But these figures, arrived at by panelists at a Public Health Service conference in Coolfont, West Virginia, in May 1986, are extremely soft. A more accurate picture of infection would be useful for marshalling prevention and education efforts, allocating resources, and charting the future course of the epidemic.

As it now stands, CDC relies on reported AIDS cases and data obtained by the labours of others to draw its picture of HIV infection. Both blood banks and the Department of Defense actively test their recruits, so to speak, and CDC relies on their numbers. Yet there are problems with making too many assumptions based on either population.

At American Red Cross blood banks, the incidence of HIV infection among blood donors today is extremely low, down to 17 cases per 100,000. This low incidence is almost certainly due to constant warnings to potential male donors not to give blood if, for example, they have had sex with another man since 1977, injected illegal drugs, or been with a prostitute in the previous six months. Making assumptions based on data gathered by the military is equally tricky.

While CDC mulls over the difficulty of doing its national survey, it has decided to rapidly expand what is known as the "family of surveys", a collection of smaller epidemiological studies being done by state and local health departments.

What CDC wants to do is expand or initiate surveys in 30 metropolitan areas, of which 20 cities are assigned high-risk status and 10 are relatively low risk. Anonymous blood samples will be collected from a variety of health care settings. At least two are familiar turf for AIDS epidemiologists: sexually transmitted disease clinics and treatment centres for intravenous drug abusers. CDC hopes to add tuberculosis clinics, "sentinel" hospitals, women's health clinics, and blood samples from newborns. Down the road, CDC also plans to do surveys in federal prisons, on college campuses, and with the Department of Labor's Job Corps, whose ranks are made up of disadvantaged, mostly teenaged, youths. Only scant information such as age, race, and sex is affixed to the blood samples. Since no prior consent is required, and since the samples are not linked to individuals, CDC will not be informing patients whether or not they have the AIDS virus.

The most revealing information about infection in the general population will probably come from the sentinel hospitals and the newborns. Since September 1986, CDC has been quietly gathering blood from four hospitals. Four more have recently been added, and it is hoped to have 40 hospitals participating in the programme by next year. The hospitals provide the Government with 300 samples a month, with the emphasis on young adults and children. (Source: Science, Vol. 238, 6 November 1987, p.747, W. Booth. Copyright 1987 by the AAAS)

Rise expected in child AIDS

The health care and foster care systems in the United States are overburdened and ill-equipped to deal with an expected increase in pediatric AIDS cases by the year 1991, according to a congressional report.

The House Select Committee on Children, Youth and Families said in its report that acquired immune deficiency syndrome was emerging rapidly as a major health threat to children and adolescents. The report marks the first time Congress has examined the figures on AIDS cases among the very young.

Of the estimated 279,000 Americans expected to contract AIDS by 1991, 3,000 will be under the age of 13, said the Committee, which based its estimates on figures from the Federal Centers for Disease Control. As of last month, there were 891 pediatric AIDS cases in the country out of 47,298 diagnosed cases.

A growing number of women of childbearing age are infected with the human immunodeficiency virus, which causes AIDS. About 80 per cent of AIDS cases in children have resulted from perinatal transmission from the mother. The rest have been caused mainly by contaminated blood transfusions. (International Herald Tribune, 10 December 1987)

B. COUNTRY NEWS

Australia

New consultative group

The Australian Government has established a biotechnology industry development consultative group to assess the future of the industry. The new group during the next six months will investigate and study the infrastructure that will be required to ensure continued national and international development. (Source: European Chemical News, 30 November 1987)

Austria

Vienna to gain biology centre

The University of Vienna announced its intention to build a Biozentrum in the city's third district. The centre will house five university institutes from the medical and science faculties.

The creation of the centre fulfils an informal promise that the Austrian Government made to Genentech and Boehringer Ingelheim when these two companies decided to locate their Institute for Molecular Pathology (IMP) in Vienna. The two institutions will be adjacent and will share support facilities.

The Austrian Government will pay about 300 million schillings ($25 million) for the Biozentrum, which will be ready for occupation in 1991. The project is an indication of the changing attitude of the Government towards basic research under new Science and Education Minister Hans Tuppy.

The university will endow two new chairs in general biochemistry and molecular genetics. Both positions should be filled in 1988 with the professors working in existing university laboratories or at the IMP until the Biozentrum is completed.

Some junior faculty members have already been hired. Director Birnstiel, who came from the University of Zurich to take the helm in 1986 reported that the IMP has almost completed its staff and will move into its new quarters in January 1988. The official opening of the IMP coincides with a meeting on "Genes in Control of Growth, Differentiation and Disease" to be held at the end of May 1988.

The Biozentrum, "inspired by" the institution of the same name in Basel, Switzerland, should attract Austrian researchers thinking of returning from abroad as well as foreigners, said Helmut Kutz of the general biochemistry department. "It has traditionally been hard to attract people with an international reputation to the University of Vienna," he said. (Source: Nature, Vol. 330, 31 December 1987)

Peptide vaccine

Researchers at the Sandoz Forshungsinstitut in Austria have prepared antibodies that could lead to the production of vaccines active against rhinovirus. Joseph McCray and Gudrun Werner have identified two highly conserved peptide regions and made synthetic analogues and site-specific antibodies to the sequences.

The scientists report that the antibodies are able to neutralize the infectious nature of the viruses. (Source: European Chemical News, 2 November 1987)

Brazil

Biotechnology agreement

Novo Industries of Denmark has signed a letter of intent to set up a factory and laboratory to produce enzymes and other biotechnology products in the southern Brazilian state of Panama. The entry of a new multinational company into the fine chemicals and biotechnology markets could signal increased flexibility in Brazil's attitude on increased foreign participation in these fields. With an initial $5 million investment and a royalty-free transfer of its technology to the Brazilian facility, the company intends to produce enzymes for the domestic market as well as export. (Extracted from The Financial Times, 8 May 1987)

Canada

Biotechnology programme

The National Research Council's biotechnology programme encompasses research and development leading to biotechnological innovations and processes that can be exploited by Canadian industry. The programme involves the work of three major NRC laboratories: the Plant Biotechnology Institute (PBI) in Saskatoon, the Division of Biological Sciences (DBS) in Ottawa, and the Biotechnology Research Institute (BRI) in Montreal. While the research carried out by these centres is national in scope and relevance, it is also sensitive to regional needs and concerns. For example, PBI with its emphasis on plant cell research is located in Canada's agricultural heartland, while BRI which houses one of the nation's largest facilities for pilot-scale R&D, is located in the centre of Montreal's growing biotechnology industry. DBS, committed to frontier research in the life sciences generally, is especially relevant to Ottawa's medical research laboratories.

As the nation's foremost laboratory doing research into plant improvement in the agriculture and forest industries, the Plant Biotechnology Institute focuses on new, exploitable methods for controlling and genetically altering plants, particularly at the molecular and cellular levels. More specifically, its objective is to advance the fields of gene and cell technology as well as biological chemistry to generate variability in crop plants, and thus to select superior individuals for integration into breeding programmes. The target crops are wheat, barley, rapeseed, sunflower, legumes, and several Canadian conifers. The plants are selected in terms of their growth and product quality and resistance to stress (cold, salinity, competition, insects, and disease). This central theme is complemented by innovation of technologies that have immediate application in agriculture and industry.

During the year, tissue culture methods led to the identification of wheat plants with heritable,

improved tolerance to cold, and barley with improved saline tolerance. Conifer biotechnology is firmly established at PBI with several modern culture facilities now containing treelets grown in vitro, the result of improved bud culture and multiplication methods applied both to juvenile and adolescent (15-18 year old) material from Douglas fir, white spruce, and western white pine. Technology permitting the formation of a multitude of somatic embryos from individual zygotic embryos has opened the way for genetic engineering of conifers, protoplast isolation and culture being the first step.

In molecular genetics, Bacillus thuringiensis toxin genes were successfully introduced into tobacco and rapeseed, the long-range goal being to make crop plants insect-resistant at the gene level. The construction of integrative and binary Ti vectors and additional markers for use in the transformation of dicotyledonous crop plants were also achieved. Plant productivity genes have been the subject of recent work, with concentration on two energy systems in green plants, photosynthesis and nitrogen fixation. The Rhizobial bacteria that infect legumes (making nitrogen fixation possible) are the subject of genetic engineering studies. The bio-organic chemistry group has isolated several plant components which control the behaviour of insect pests, including attractants and oviposition stimulants present in rapeseed, sunflower, and wheat. In addition, novel sex pheromone compounds have been discovered for use in monitoring the appearance of major insect pests of trees.

Plant cell metabolism work is aimed at cell fermentation for the production of phytochemicals; sanguinarine in poppy and catharacthine in periwinkle cell cultures have found particular interest with industry.

Finally, several projects were carried out under the Plant Biotechnology Fund, whereby part of the research programme is contracted out to other Canadian laboratories. This has allowed for rapid and effective solutions to specific problems.

The Division of Biological Sciences carries out research in specific areas of biotechnology that require a multidisciplinary approach. Programmes selected are appropriate to the expertise that exists or can be developed in the Division, and hold reasonable promise of success within the current state of knowledge in the field. Programmes must have potential for application, and if solved, lead to new technologies, products, or processes for Canadian industry.

Priorities of the Division currently include the work being done on the immune response to carbohydrate antigens, unique in Canada and which has very little international competition. The practical spin-offs from this research are new veterinary and human diagnostics and vaccines for bacterial infections. The immunochemistry group already has an outstanding record of collaboration with industry.

In collaboration with BRI and PBI, the Division is building up the protein engineering programme which has, as its ultimate goal, the design and construction of proteins with specific predictable functions. It is a high-profile topic of biotechnology internationally. Protein engineering is still a developing field in which results cannot be predicted, but the expected applications will have far-ranging effects in biotechnology.

The Biotechnology Research Institute carries out R&D activities in biochemical engineering, genetic engineering, protein engineering and immunology, in close collaboration with industry, universities, and public research agencies. The Institute is investing in fields where private sector financing of research and development cannot be justified economically because of the long-term commitment and risky return on investment. It also fosters the technology transfer of results and discoveries to Canadian firms and co-operates closely with Canadian universities in advancing basic knowledge in biotechnology.

During its initial phase, which may extend to approximately three years, the Institute is placing emphasis on setting up teams and projects to develop scientific and technological expertise. Human resources are the most important asset and the recruiting of scientists of international calibre, begun in 1984, remains a priority.

The web that connects NRC's three biotechnology research centres, bringing together scientists and engineers from Montreal, Ottawa and Saskatoon with their industrial and university colleagues, is the set of comprehensive programmes that have been established over the last two years. To date, these programmes touch on such areas as the genetics and biochemistry of lipid-modifying enzymes, anaerobic digestion of liquid wastes, the protein engineering of enzymes, an "artificial plant" bioreactor, and the micropropagation of conifers via somatic embryogenesis. The first programme will receive $340,000 a year over two years with a possible third year extension while the second will receive $500,000 a year, again over two years with a possible third year. Each of these totals includes a contribution to the industry involved in the programme. In addition, the conifer biotechnology programme was given a $100,000 continuation of funding to cover the fiscal year 1987-1988.

In keeping with the comprehensive programmes concept, a Technical Centre for Protein Structure and Design is being created, to be located at NRC's Montreal Road complex. It will draw on the expertise of each of the biotechnology divisions; known more commonly as Protein Engineering, this multidisciplinary field is at an early stage of development, and involves the modification of proteins through genetic alterations to improve their biological activity (of which enzymes are an important class) or the design of new proteins with novel functions. NRC's comprehensive programmes address major Canadian concerns, such as pollution, agriculture, health, and forestry. In addition, they have good prospects for medium-range applications, and they involve the participation of Canadian industries, universities, and other government laboratories. (Extracted from NRC, Canada, Annual Report, 1986/1987)

Task Force on Canadian Culture Collections established

An eight-member Task Force, composed of experts from industry, university and government, has been established by the Ministry of State for Science and Technology in co-operation with Agriculture Canada to collect information relating to Canada's storehouses of living micro-organisms and cell cultures. The study is being carried out in response to recent surveys by the Science Council of Canada and MOSST which identified concerns on the management and funding of culture collections housed in universities, industry and government.

Canada's collections of living organisms, including bacteria, fungi, viruses, plants and cell cultures, will be challenged by the increasing requirements of researchers, given the rapid advancement of bioscience. Therefore, the Task Force has been asked to investigate the situation and to

propose options to safeguard those collections which are critical to industrial biotechnology as well as to biological science.

The Task Force held its inaugural meeting on 5 October 1987 in Ottawa. At the conclusion of its investigation, in approximately six months, the Task Force will report to the Interdepartmental Committee on Biotechnology, which recommended the investigation.

As an element of InnovAction, the Canadian Strategy for Science and Technology, the Biotechnology Programme supports research and development in the strategic areas of health, agriculture, food, fisheries, forestry, mining, and waste treatment. In addition, through a series of national R&D networks in these strategic areas, the system fosters linkages between industry, university and government to bring together performers and users of biotechnology research.

For further information contact: Dr. Gordon Nelsn, Task Force Secretary, Agriculture Canada, (613) 995-7084 or Dr. David B. Shindler, Manager, Biotechnology, Ministry of State for Science and Technology, (613) 990-6322. (Source: News Release, 27 October 1987)

China

Insulin breakthrough

Chinese scientists are said to have made 'important breakthroughs' in research into insulin and nitrogen fixation using genetic engineering techniques.

An international meeting on biochemistry in Beijing has been told by the director of the China Biochemical Society, Zhang Youshang, that by using genetic engineering, Chinese scientists had developed a series of insulin substitutes which were significant to improving the use of insulin and public health. Hong Goufan, another director of the Society, was reported to have found a new way to activate the nitrogen-fixing gene through the study of plant nodules. (Source: Manufacturing Chemist, October 1987)

Cuba

Cuba focuses on monoclonals for health care

"Cuba has devoted massive resources to the development of monoclonal antibodies for human health care," according to Jorge Gavilondo-Cowley, the head of the monoclonal antibodies production department of this country's Centre for Genetic Engineering and Biotechnology (CIGB). In fact, the new, well-equipped facilities springing up around Havana, including those of the CIGB and the Immunoassay Centre, attest to the Cuban government's designation of biotechnology as a priority. And monoclonals represent a significant part of this biotechnology effort - which also includes a meningitis vaccine and various interferon preparations.

In Cuba, as in the rest of the world, monoclonals seem to be finding their best fit in diagnostics, with some specialized applications in therapeutics. The first monoclonals to be developed were for alpha-fetoprotein, T-lymphocytes, and alpha-interferon. This list has grown considerably; in fact, according to Gavilondo, the country now produces more than 30 antibodies in moderate quantities - on the order of grams per month.

Promising results of various clinical trials were reported at the International Workshop on Technology for the Production of Monoclonal Antibodies, held in October. Trials using anti-T lymphocyte antibodies to prevent the rejection of transplanted kidneys have been encouraging, reported Raúl Herrera of the Institute of Nephrology. He said that the monoclonal anti-T3 reduces T-cell proliferation by over 95 per cent.

Antibodies also seem to work on the skin lesions associated with B-cell lymphoma. Carlos García (Institute of Oncology and Radiobiology) said that his group is developing a whole panel of monoclonal antibodies as markers to identify normal and cancerous T and B cells. One of these antibodies, when applied as a topical cream to the skin lesions, clears them. García' group is also studying the phenotypic differences among lymphoid cells from patients with various B cell disorders; the researchers have found a high number of interleukin-2 receptors on cells from patients with progressive disease.

Still, most of the monoclonals produced in Cuban institutions - including the CIGB, the Institute of Oncology and Radiobiology, the National Centre for Scientific Research, and the Institute for Haemotology and Immunology - are for research or diagnostic purposes. These include antibodies against lymphocyte-leukocyte markers (used to classify leukaemias and lymphomas); tumour markers, including CEA (carcinoembryonic antigen); bioregulators and their receptors (such as anti-interleukin-2 receptor); human T cells; human foetal thymocytes; low-density lipoproteins; rotavirus antigen; hepatitis B surface antigen; Chlamydia; herpes simplex II; and cytomegalovirus.

In fact, many of these antibodies are being incorporated into a mass effort to diagnose the country's population for a variety of inherited defects and infectious diseases. (Extracted from Bio/Technology, Vol. 5, December 1987)

EEC

EEC poised to unveil first biotechnology directive

Brussels is hoping to present the European Environment Council with its proposals for a directive regulating the deliberate release of genetically altered organisms. Two other planned directives to regulate biotechnology are still under discussion and are unlikely to be settled until next spring.

Brussels is proposing that researchers wishing to release organisms into the environment for R&D purposes should notify and seek endorsement from the competent member State authorities. Companies planning to market genetically engineered organisms will have a different procedure.

The Commission is planning to introduce a procedure similar to the so-called sixth amendment which regulates the classification, labelling and packaging of dangerous substances. Endorsement would first be granted at a national level with a period for international co-operation.

Once the draft directive has received approval from the Environment Council the Commission will start to produce an annex laying down the information for a common standard of review within the EEC. Developing the directive has not been an easy task for the Commission and some problems will need to be solved.

The Commission is only proposing an endorsement procedure rather than one for approval. Strongest objections may still come from the FRG who are keen to introduce a five-year moratorium on deliberate release.

DG XI and the Commission's industrial affairs arm DG III have decided to merge their proposals for containment guidelines into one directive. Originally the two groups had planned to introduce separate guidelines but now the merged draft, which will also contain provisions for accident control, will be submitted to a meeting of member State experts in December. (Source: European Chemical News, 7 December 1987)

EEC raises commitment to biotechnology research

The European Commission has committed itself to biotechnology R&D until 1995 by agreeing to the BRIDGE Programme (Biotechnology Research for Innovation for Development and Growth in Europe). Taking over from the Biotechnology Action Programme (BAP), which runs out at the end of 1989, the new programme aims to improve biotechnology research in several areas.

After criticism on BAP-industry links, BRIDGE will attempt to woo biotech companies.

The Commission has already identified some of the hurdles it will have to overcome in order to achieve this. These include confidentiality of research findings and the structure of projects. Until now BAP has tended to break down R&D into sectors such as enzyme synthesis, microbiology and animal cell culture. BRIDGE will tackle some of the principles more fundamental to the technology as a whole.

Until now the size of research contracts has also inhibited industry participation. Averaging Ecu 95,000/year ($70,587) and two to three years long, contracts have been too small for large companies and too expensive for smaller concerns. The Commission plans to increase the value of some contracts to between Ecu 150,000 and Ecu 200,000 to pull in the larger companies. This will limit the number of projects.

BRIDGE, within the official framework programme, has already been earmarked Ecu 100 million - a substantial increase on BAP, which originally received Ecu 55 million. However, a further Ecu 20 million is being negotiated to revise BAP. This would allow the Portuguese and Spanish to join the programme.

Bio-informatics, risk assessment and training are areas where the Commission wants funding to carry out further research within BAP. (Source: European Chemical News, 30 November 1987)

Bioethanol plan shelved

The Commission has abandoned plans to use agricultural surpluses to subsidize the production of bioethanol on economic grounds.

Opponents of the scheme argued that production of bioethanol from agricultural surpluses would be more expensive than the current subsidized sale of surpluses and that more energy would be produced by simply burning the grain.

The proposal has always been opposed by the UK and the Netherlands while greatest support has come from France and Italy. European chemical companies with oil interests have also opposed the idea but the decision has angered Ferruzzi, the Italian agro-industrial concern which has been lobbying for subsidies. (Extracted from European Chemical News, 23 November 1987)

Egypt

New water-absorbing project

The Ministry of Reclamation and Japan's Ministry for International Trade and Industry will attempt to develop water-absorbing resin for use in desert agriculture. Water-absorbing resins are now chiefly used for diapers. MITI plans to build a plant in Egypt to produce water-absorbing resins in a five-year project. The material will be buried in lands at the edge of deserts to retain water. Attempts to plant trees to stop desertification have generally been fruitless, since there is not enough water to maintain the trees. The area around Cairo is in the path of advancing sandhills. Egypt's Desert Institute has asked MITI to provide the water-absorbing resin technology. If successful, MITI may extend similar aid to Oman, the United Arab Emirates and other countries. The Japanese market for the resin rose 10 times in 1981-1985, and the price of the resin dropped from ¥1,500/kg to ¥600-800/kg. (Extracted from Japanese Chemicals, 10 September 1987)

Federal Republic of Germany

Latest biotechnology achievements

The genetic centre in Cologne has made advances in the research of Alzheimer's disease. A group of scientists succeeded in identifying and cloning certain genes which characterize a protein closely connected with Alzheimer's disease. This supports an earlier hypothesis that this disease has mainly genetic causes.

At the genetic centre in Munich, genes of membrane-proteins of a highly pathogenic bacteria (Pseudonomas) have been isolated and identified. This bacteria has long been considered a "problem germ" because successful therapy with conventional antibiotics is not possible. The Munich scientists succeeded in identifying these genes in a nonpathogenic organism. The genetic products (proteins) can be used in the production of a vaccine for antibiotic-resistant pathogenic agents.

At a research centre in Heidelberg it has been possible to make considerable progress in the area of tumour diagnostics by using molecular biological methods. The objective is the development of a sensitive indicator of keratin in tumour cells.

A group of scientists in Munich demonstrated at the beginning of the year that interferon produced with genetic engineering methods represents an [effective] therapy for polyarthritis in 50 per cent of all cases. The experimental results are yet to be confirmed by large-scale clinical studies.

A group of scientists in Heidelberg succeeded in isolating and characterizing glycene and gaba receptors. This was also an important scientific advance on an international scale in that important basic neurobiological phenomena can be brought nearer to clarification. In the future, these phenomena will enable interesting applied research work in neurobiology. (Source: Technologie Nachrichten-Management Informationen, No. 459-460, 20 July 1987)

Embryo rules

The Federal Republic of Germany's Social Democratic Party, SPD, has called on the federal Government to accelerate plans for legislation to limit research with human genetic material.

In the draft of a bill to be introduced in the Bundestag in January, the party calls for a ban on experiments with embryos, cloning of human beings and crossing of human and animal, as well as surrogate motherhood.

Meanwhile, the Federal Minister for Research and Technology will press for the organization of an EEC-wide scientific conference on the acceptability of research with embryos. (Source: European Chemical News, 21/28 December 1987)

Hoechst faces insulin setback

Hoechst's plans to produce human insulin using recombinant DNA methods have received a setback. Approval of the company's plans to build the second stage (Fermtec) of a three-stage production set-up has been temporarily suspended by authorities in the Federal Republic of Germany State of Hesse after a formal objection, filed by a local environmentalist group, was accepted by an administrative court.

The company will have "no other choice" but to file a suit for immediate application of the state permit to avoid further delays to the human insulin production programme. Admittedly opponents of the project could receive an injunction against this permit, too.

Hoechst maintains that sterilization of its wastewater will prevent the escape of manipulated micro-organisms into the environment and its plans have been approved by the Federal Office for Biological Safety. But the environmentalists say they believe the plant poses a threat to public safety and that the granting of an operating permit should be made subject to a public hearing. (Source: European Chemical News, 23 November 1987)

HIV immuno-fluorescence assay

Diagen Institut, Molekularbiologische Diagnostik (FRG) has won marketing approval for an HIV immuno-fluorescence assay. The assay identifies both HIV-1 and HIV-2 antibodies, works at an earlier stage of seroconversion than ELISA tests, takes just 25 minutes to give results, and has nearly 100 per cent specificity and 99.5 per cent sensitivity. It can be used with whole blood or serum. It is based on an HIV isolate developed by the firm, unlike most HIV antibody tests that use H9 cells and HTLV-3b. The test is the firm's first product to reach the market, and is the only assay on the market that gives results so rapidly with the reliability of Western blot tests. (Extracted from Clinica, 21 October 1987)

New polymeric material being developed

Two methods to prepare anti-infectious and antithrombogenetic polymeric materials are being developed by modifying the surface and incorporating antibiotics into the polymers by B. Jansen of the University of Cologne's Hygiene-Institute. Infection and subsequent blood clotting in medical devices typically begin with the adhesion of bacteria to the polymeric devices, followed by colonization. Bacteria often produce a slimy matrix, insulating the infected area from host-defence mechanisms and antibiotic attack. Surface treatment to prevent adhesion by albumin coating has shown only limited success, while polymers containing antibiotics act as drug-delivery systems with prolonged antibiotic activity. Antibiotics can be bonded superficially to the surface or mixed in with the materials. (Extracted from Industrial Chemist, December 1987)

France

Joint venture set up to market hirudin

Sanofi, the French pharmaceutical giant, and Transgène SA, Strasbourg, have signed a partnership agreement to develop recombinant hirudin, a substance normally secreted in infinitesimal quantities by the salivary glands of leeches.

Sotragène, as the new joint venture is called, will concentrate initially on commercializing hirudin as a therapeutic in the prevention of re-thrombosis after acute myocardial infarctions. Animal trials of the protein have already demonstrated its efficacy. Sanofi will handle marketing, while Transgène researches hirudin's further applications, notably as a diagnostic agent in blood testing. (Source: McGraw-Hill's Biotechnology Newswatch, 5 October 1987)

German Democratic Republic

AIDS agent

The director of the GDR Institute of Virology at the Charite hospital in Berlin has said that the Institute has developed a chemotherapeutic agent which had proved as effective in tests as Wellcome's azidothymidin (AZT).

Prof. Rosenthal claimed they had developed an agent called fluorthymidin in collaboration with the Academy of Sciences. It was - at least in all tests - as effective as AZT and would presumably be tested in Western countries in the foreseeable future. Prof. Rosenthal said the German Democratic Republic would make it available as know-how to international health bodies. (Source: Manufacturing Chemist, November 1987)

German Democratic Republic goes genetic

The first pilot plant for the manufacture of micro-organisms altered by genetic engineering is being set up at the Academy of Sciences Central Institute of Microbiology and Experimental Therapy in Jena.

The Institute has been working on genetic engineering processes since the early 1980s and will be able to supply a series of parent microbes. The GDR's main pharmaceutical enterprise in Dresden will then process them into the preparations required. (Source: Manufacturing Chemist, October 1987)

India

New information network for biotechnology

The Government of India has decided to set up a biotechnology information network to co-ordinate research on development of the new generation of diagnostic tools and vaccines to prevent tropical diseases and control population growth.

It is aimed to bridge the interdisciplinary gaps on information and to facilitate closer links among scientists and organizations. The network would serve as a database organization in six identified areas involving nine specialized centres in seven cities, according to a biotechnology department report.

The network will take advantage of the large computers to be set up by the National Informatics Centre in Pune, Hyderabad, Bhubaneshwar and Delhi. Eighteen user centres located in different parts of the country would be able to communicate with external sources via 'Indonet' facilities which would be used wherever the service establishes links with outside systems.

Under the programme, the computerized service would be available for the storage and retrieval of information relating to papers, reports, books and patents covered by biotechnology.

With regard to queries from biotechnology centres, it is stated that they could be dealt with by micro-earth stations for telephone or telex. The report points out that each centre would have a recent collection of journals which are in heaviest demand, with a back-run of several years in specified areas.

Arrangements are also being made to access databases in other countries. (Source: Chemical Business of India, 20 August - 14 September 1987)

Ireland

Ireland launches national biotechnology R&D programme

The Republic of Ireland inaugurated its National Biotechnology Programme on 15 October 1987. The Government has allotted IE600,000 for 1987 as the first part of a IE10 million programme to promote biotechnology in Ireland. During the 'start-up phase', the Government will fund the infrastructure and staff for three R&D laboratories:

- Cell Tissue Centre at the National Institute for Higher Education in Dublin. Its temporary director, Martin Clynes, is involved in in-vitro toxicity work, financed by the European Economic Community. This centre will also expand production of monoclonal antibodies, and scale-up animal-cell culture for pharmaceutical production.

- University College, Galway, National Diagnostic Centre, temporary head Frank Gannon is working on solid-phase diagnostic components and hormone tests.

- University College, Cork, Food Biotechnology, Fergal O'Gara, temporary director, is developing biological control of crop pests with nitrogen-fixing organisms, and researching dairy starter cultures.

Ireland is considering starting a national biotechnology company to co-ordinate all administrative work for university centres. Equity would be held by universities, private-sector interests such as venture-capital companies and researchers. (Source: McGraw-Hill's Biotechnology Newswatch, 5 October 1987)

Improved salmon farms

Salmon eggs injected with an extra copy of the gene for growth hormone might produce larger salmon, according to J. Sreenan of the Agricultural Institute (Galway). Farmed salmon grow more slowly in Ireland than in Scandinavia. Salmon from 4,000 test eggs are now almost one year old, so the effect of the inserted gene may soon be measurable. (Extracted from New Scientist, 17 September 1987)

Israel

New system to produce amino acids

An artificial photosynthetic system that can produce amino acids from carbon dioxide using sunlight as the energy source has been developed by researchers at the University of Jerusalem and Hebrew University. The system can also produce methane and formic acid. All the products so far obtained have commercial applications. The amino acids produced are aspartic acid (used to make aspartame) and glutamaic acid (used to make monosodium glutamate). (Extracted from New Scientist, 31 December 1987)

Italy

New research centre

A virology research firm has been formed by Sigma Tau (Italy) and Merck Sharp & Dohme (US). It will build a research centre at Pomezia that will initially employ 80 researchers. It aims to persuade Italian researchers that have emigrated to the US to return. Its fields of study will include the AIDS virus. (Extracted from European Chemistry, 26 October 1987)

EniChem, Max-Planck link for plant studies

The study of viral diseases in plants is the basis of a fundamental research programme launched jointly by EniChem of Italy and the Max-Planck Institute of Crop Cultivation and Production Physiology in Cologne, Federal Republic of Germany. EniChem, an arm of Ente Nazionale Idrocarburi, the State-owned energy and hydrocarbons concern, will fund the work, aimed at developing novel crop varieties inherently resistant to viral infection. The programme is part of EniChem's long-term biotechnology thrust. Last month, the company launched a project at its recently completed laboratory facilities in Princeton, N.J., to seek genetically altered seeds that will produce crops with the ability to resist fungi and to absorb nutrients with greater efficiency. According to EniChem, the market for such genetically engineered seeds could reach $4.5 billion by the turn of the century. (Reprinted with permission from Chemical and Engineering News, 16 November 1987. Copyright (1987) American Chemical Society)

The Netherlands

Firm requests field tests of genetically altered potatoes

The biotechnological firm of Mogen in Leiden has requested that the Ministry of Housing, Planning and Environmental Protection grant it permission to carry out field tests of genetically altered potatoes.

The tests are intended to find out whether the potato plants will retain their familiar properties if genetically altered. The gene that is inserted into the potato species (among others, Bintje) in the laboratory tests contains hereditary properties which can protect the plant from a disease to which the plant is at present nonresistant. The tests are intended for the sole purpose of finding out whether the applied technique will also give good results when the plants are cultivated under other conditions than those of the laboratory. If this appears to be the case, various forms of resistance may be incorporated in the plants. An improved variety of Bintje may be of great commercial value. That potato is extremely popular, and cultivators have not yet been able to improve it. By the end of next year, with the help of field tests, Mogen hopes to demonstrate that a new 'geno-type' of Bintje may be produced. (Extracted from NRC Handelsblad, 18 September 1987)

Dutch firm forms biotechnology venture

The Dutch farm co-operative Cehave is setting up a biotechnology branch in 1988. One of these investments will consist of a laboratory for research on improving the ways in which animals take up and digest food.

Other research fields will include animal health and breeding techniques. Cehave has been working on environment-friendlier cattle-feeding for a number of years, resulting in chicken- and pig-feed with 10 to 15 per cent less phosphate.

Cehave's research plans include co-operation agreements with the technological institute TNO and Wageningen, the agricultural university. (Source: European Chemical News, 7 December 1987)

Gist-brocades tightens belt

Gist-brocades, the Dutch biotechnology group, is planning to rationalize its activities to buffer a projected slip in earnings and to release cash for acquisitions and new investment. The company is to shed 350 jobs and close bulk yeast production. The company plans to save about Dfl.40-45 million ($21-24 million).

Gist-brocades is now predicting that net income for the year will plummet 15 per cent from the Dfl.111 million earned in 1986. The dollar has also contributed to this downturn in prospects as about 70 per cent of the company's sales are conducted in foreign currencies.

The company is planning to expand its activity in aromatics from yeast derivatives, for which a new plant is currently under construction, to enzymes and pharmaceuticals based on biotechnology. But the company has decided to shift from its 1984 plan to grow through in-house development to one of growth through acquisitions. Extracted from European Chemical News, 30 November 1987)

Chemical company builds new plant

DSM Specialty Chemicals, part of the Chemical Products Division of the chemical group DSM, has started the construction of a plant for production of optically active amino acids at Geleen (Netherlands). The plant, to come on stream at the end of 1988, will have a capacity of several hundred metric tons per year.

The new facility will be used for biotechnological production of natural and non-natural amino acids, such as valine, homophenylalanine and proline, using enzyme technology developed by DSM.

DSM's decision to build the plant was based on the increasing use of amino acids as starting material for preparation of pharmaceuticals and agrochemicals.

DSM's enzyme technology combines traditional chemistry with biotechnological production techniques. With this technology a large number of natural and non-natural amino acids with a high degree of purity can be obtained, a company representative says. So far, this has not been really feasible on an industrial scale.

Non-natural amino acids can be widely used for production of agrochemicals and pharmaceuticals, for instance, anti-hypertensives (effective against high blood pressure) and antibiotics.

DSM is presently a producer of phenylglycine, starting material for ampicillin (a penicillin). In the near future, other amino acids will be developed in co-operation with the pharmaceutical and agrochemical industries. (Extracted from Chemical Marketing Reporter, 16 November 1987)

Japan

DNA deciphering process

The Science and Technology Agency has spent ¥766 million since 1981 on a project aimed at automating the DNA deciphering process. Five companies are involved: Fuji Photo Film, Seiko, Hitachi, Toyo Soda Manufacturing and Mitsui Knowledge Industry. Scientists believe that compiling a catalogue of the 3 billion pieces of genetic data in human DNA will help them better understand how the body works. It may also help them cure cancer and other diseases. Deciphering DNA involves many tedious laboratory procedures that are currently done by hand. The Japanese see the development of a DNA deciphering machine as an opportunity to make good use of their manufacturing expertise. Biology professor L. Hood of the California Institute of Technology believes they are definitely ahead. Some experts say it would take as long as 100 years and cost billions of dollars to completely decipher the human genetic blueprint using current methods. Automation will improve reliability, speed up the process and cut costs. Reading a single base pair in single gene costs about $1 now, but molecular biophysics professor A. Wada of the University of Tokyo says automation could reduce this to 10 cents.

The European Molecular Biology Laboratory (Federal Republic of Germany) and Lawrence Livermore National Laboratory have pioneered automated DNA sequencing technology, and several firms such as Applied Biosystems and DuPont (both US) have developed equipment to perform some DNA sequencing work. Japanese officials say the US Department of Energy is spending more than Japan to decipher genetic information, but claim the most advanced equipment is still being produced in Japan. Companies from various industries were brought in to the project because of their skills in specific areas. Seiko has rebuilt watchmaking robots to find tiny laboratory-grown cultures of DNA in petri dishes and transfer them to test tubes. Fuji Photo Film used its film technology to develop a gelatinous material for separating base pairs into visible patterns. The material is sandwiched between pieces of plastic. Hitachi and Fuji have developed a computer to convert the image of the base pairs into computer data. In 1988 the science agency will try to link the individual machines together. (Extracted from Asian Wall Street Journal, 14 December 1987)

Human thrombomodulin cloned

The DNA for human thrombomodulin has been cloned by researchers at Asahi Chemical Industry, Mie University and Kagoshima University. The cDNA has 3,461 base pairs and codes for a protein with 575 amino acids. When 18 amino acids are removed from the protein, it is transformed into a thrombomodulin of 117 amino acids. The gene inserted into a monkey's kidney stimulated production of thrombomodulin, which prevents blood clotting and can dissolve clots. (Extracted from Japanese Chemistry, 5 November 1987)

Virus-free asparagus cultured

Jujo Paper Manufacturing Co., Tokyo, has produced virus-free asparagus seedlings from shoot-tip culture. Together with its affiliate, Jujo Chemical in Akita Prefecture, the firm is developing an economical proliferation technique for these tissue-cultured shoots, as well as methods for mass-culturing garlic and onions. (Source: McGraw-Hill's Biotechnology Newswatch, 2 November 1987)

MAFF funds food enzyme R&D

Nine enzyme suppliers and three electronic equipment manufacturers are participating in a five-year project, Development of Enzyme-Conversion Technologies for the Food Industries, sponsored by the Ministry of Agriculture, Forestry and Fisheries. Funding from the government sector for this first fiscal year is ¥109.8 million ($773,000). The research projects and participating companies are:

- Protein engineering and analysis of enzymes to heat and acid resistance of soybean beta-amylase, Japan Maize Products Co. Ltd., Fujitsu Ltd.

- Increased heat-resistance and enzyme stability for starch-processing, by mutation of beta-amylase, cyclodextrin synthetase, and pullulan-degrading enzymes, Ezaki Glico Co. Ltd., Nagase Biochemicals Ltd.

- Altering the function of cell-wall-binding proteases of lactic-acid microbes to improve stability of casein-producing enzymes, Yakult Honsha Co. Ltd., Nippon Electric Co. Ltd.

- Altering the function of proteases from "yellow koji" microbes to improve salt tolerance of alkaline protease, and expanding the substrate range of neutral proteases, Green Cross Corp.

- Development of a heat-resistant bacterial lipase, Amano Pharmaceutical Co. Ltd., Fujisu Ltd.

- Altering the functions of lipase and phospholipase to improve heat and acidic resistance, Nisshin Oil Mills. Ltd., Toyo Jozo Co. Ltd., Nippon Electric Co.

(Source: McGraw-Hill's Biotechnology Newswatch, 2 November 1987)

Experiments in space

Mitsui is trying to persuade other Japanese firms to undertake biotechnology experiments in space using protein crystallization equipment developed by the Federal Republic of Germany's space experiment firm Introspace. The equipment is to be loaded onto a Chinese rocket to be launched in October 1988. More than 80 per cent of the equipment's experimental space has been booked by West European firms and Mitsui hopes that the rest will be taken by Japanese firms. (Source: European Chemical News, 30 November 1987)

New mushroom

Scientists at Nippon Shokuzai Kagyo (Osaka), working in collaboration with colleagues at the Agricultural School at Miyazaki University, have used protoplast fusion to produce a novel hybrid mushroom. The new hybrid was obtained by fusing protoplasts derived from two species of the agratic (tree) mushroom hiratake (Pleurotus ostreatus): the Japanese tamogi-take and a species of hiratake that is native to Scotland. The taste and consistency of the new hybrid was reported to be excellent. Nippon Shokuzai Kagyo anticipates that the new mushroom will be widely used in cooking and will quickly gain acceptance in the marketplace. (Source: Bio/Technology, Vol. 5, October 1987)

Vitamin research

Scientists at Japan's Nippon Zeon have reported the first results of a joint research programme with French genetic engineering concern, Transgène, to develop a fermentation route to the vitamin biotin (vitamin H).

The bio-b gene of B sphaericus, a micro-organism known to produce biotin has been cloned and sequenced by researchers and expressed in E. coli. The discovery could mark the first step in the commercialization of a fermentation route biotin, replacing the costly chemical process.

The vitamin, which is involved in the metabolism of fats and carbonydrates, is now increasingly used as a supplement for human and animal nutrition and in cosmetic preparations. (Source: European Chemical News, 19 October 1987)

DNA cleaver

Mitsuo Matsuura and co-workers at Kyoto University have used bleomycin to cut DNA selectively. Although researchers knew this anti-tumour drug cleaves DNA, they had not realized that the cleavage could be made site-specific and more efficient in the presence of activated oxygen and iron. The new method cuts DNA between guanosine-cytidine and guanosine-thymidine pairs with nearly 100 per cent efficiency. The increased ability of bleomycin to cleave DNA may also lead to more effective anti-cancer therapies. (Source: Bio/Technology, Vol. 5, November 1987)

Prototype cell-sorter unveiled

Sumitomo Electric Industries Ltd. (SEIL), Osaka, has developed prototype equipment to select a single fused cell from more than 100 million cells. SEIL is developing the cell-sorter as a part of Japan's anti-cancer programme and plans to introduce it by the end of 1988. The compact, 5.7-square-metre prototype system does three chores automatically: monitors fused cells and replaces HAT (hypoxanthine-aminopterin-thymidine) culture solution as needed; detects antibodies in fused cells, and separates out those cells containing desirable antibodies. The monitoring, which also distinguishes live from dead cells, is done by imaging. The series of operations performed by the machine supplants the work of three researchers, SEIL claims. Cell-selection capacity is equivalent to 60 glass plates; SEIL is trying to raise the capacity to the equivalent of 200 plates. (Source: McGraw-Hill's Biotechnology Newswatch, 5 October 1987)

MAFF to buy US plant-gene maps

As part of an emergency programme to buy more foreign goods, to rectify the trade imbalance between Japan and the USA, the Ministry of Agriculture, Forestry, and Fisheries (MAFF) will acquire genetic maps of plants. MAFF has revised its 1987 budget to spend an additional ¥290 million ($190,000) to purchase restriction-fragment-length polymorphism maps of tomato and corn, for cross-breeding experiments. Additional MAFF procurements will include gene sequencers, analysers and measuring instruments. (Source: McGraw-Hill's Biotechnology Newswatch, 5 October 1987)

TMV-resistance gene hits viral coat

By using recombinant DNA to create mutant strains of tobacco-mosaic virus (TMV), Yoshimi Okada, biology professor at Tokyo University, has determined that the tobacco plant's N'-resistance gene recognizes the viral-coat protein, and disrupts its function. The L strain of TMV causes only slight localized necrosis in tobacco varieties such as Bright Yellow, which possess the dominant N'-resistance gene. However, when Okada swapped the TMV coat-protein genes of strain OM for the same segment from the L strain, the virus caused mosaic-mottling symptoms in the plant. But when the L-coat protein was spliced into the OM strain, the once-virulent virus caused only localized damage. (Source: McGraw-Hills Biotechnology Newswatch, 5 October 1987)

Mexico

Foetal tissue transplants

Researchers have received government approval to transplant human foetal cells into patients in an attempt to cure Parkinson's disease. Neurosurgeon, I. Madrazo and cellular physiologist, R. Drucker, are experimenting with the implantation of adrenal tissue

from human foetuses into the brain. Other researchers see the method as a way to repair damaged nerves and treat various neurological diseases without drugs. Foetal cells are attractive because they multiply so rapidly and are not affected by the body's system of rejection of foreign tissue if the foetuses are under 14 weeks old. Although there is much potential for these techniques, there is also much controversy about using living foetal tissue in medicin . Most researchers will look to use cultured human cells, which are already being produced by Hana Biologics. (Extracted from Business Week, 7 December 1987)

Puerto Rico

New pharmaceutical facility

Genentech (the South San Francisco biotechnology company) has optioned a 100 acre tract in Canovanas, where it will build a $40 million, 100,000 sq. ft. plant (125 workers at start-up) to make Protopin (for hormone deficiencies) and Activase (for relief of cardiac attacks). (Extracted from Business Week, 2 November 1987)

Sweden

Swedish-American biotechnological company formed

A formal agreement to set up a Sweden-based biotechnical research company, called Karo Bio, was made in Stockholm in September between Swedish investors and Californian Biotechnology Inc., one of the leading American companies in this field.

The new company is to be based at Novum, a developing biotechnology centre adjacent to Huddinge Hospital, south of Stockholm. Its medical research centre is an extension of the Karolinska Institute in the capital, and medical and technical researchers work in close cross-disciplinary collaboration. (Source: SIP, November 1987)

Pharmacia acquires biotechnology R&D firm

Sweden's Pharmacia is strengthening its interest in cancer research with the acquisition of Stena Diagnostics, established in 1983 to develop diagnostic reagents based on monoclonal antibodies for the early detection of cancer. It has already developed a number of reagents used in the Delfia test system marketed by Pharmacia Diagnostics.

Pharmacia is particularly interested in Stena's research into the production of antibodies for use in the treatment of cancer tumours. The companies have jointly received a development grant from the Swedish industrial development fund. R&D operations will be carried out in close co-operation with the University of Gothenburg. (Source: European Chemical News, 19 October 1987)

United Kingdom

New SERC bioseparation initiative

The Science and Engineering Research Council (SERC) has launched a new £1 million initiative focusing on separation processes. The initiative is jointly supported by SERC's Biotechnology Directorate and the Process Engineering Committee of the Engineering Board. Five areas have been selected for special support at present: (1) membrane separations; (2) selective absorbents; (3) solvent extraction; (4) separations in centrifugal and high-intensity magnetic fields; and (5) highly selective separations.

Prof. Jack Richardson of the Department of Chemical Engineering at University College, Swansea, has been appointed as programme manager to oversee the initiative. The present activity in the first area, membrane separation, will be subsumed in the new initiative, but will continue to be co-ordinated by Prof. Pat Meares of the University of Exeter.

In many cases, separations will involve components with only marginal differences in physical and chemical properties, for example isomers, and the material may be sensitive to high temperatures and shear rates. Also, many of the present processes are becoming uneconomic because of the very high energy costs involved. The initiative will not only encourage innovative engineering, but will also support studies in areas of basic underlying physical science. These areas may include surface chemistry, thermodynamics and physical property determination and prediction. Details from: Prof. Jack Richardson, Department of Chemical Engineering, University College Swansea, Swansea SA2 8PP or on 0792 295194. (Source: Biotechnology Bulletin, Vol.6, No. 11, December 1987)

Biochemical engineering strategic centres

A new grant from the Biotechnology Directorate of the Science and Engineering Research Council (SERC) will support a four-year research and training programme at Birmingham University and University College London (UCL). The main purpose of the work, which will involve close collaboration with industrial partners, will be to translate the basic results of research into industrial biotechnology processes.

Among the companies already involved with the two universities are Glaxo, RHM and Unilever. The latter, for example, is working with UCL on the biochemical transformation of plant oils and fats into high-grade fats, such as cocoa butter. Birmingham, meanwhile, has persuaded RTZ Chemicals to endow a new chair of biochemical engineering.

Dr. Geoffrey Potter, head of the SERC biotechnology directorate, has said that he hopes that two further university research centres will also join the research programme. Much of the funding is expected to come from industry, with matching funds from the Department of Trade and Industry. Details from: Science and Engineering Research Council, Polaris House, North Star Avenue, Swindon, Wiltshire SN2 1ET or on 0793-26222. (Extracted from Biotechnology Bulletin, Vol. 6, No. 12, November 1987)

New company formed

A new company, Oxford Virology Ltd. (OV), has been formed to develop the production of diagnostics and vaccines for human and veterinary health care using insect viruses. The use of insect viruses is expected to ensure dramatically lower production costs.

The main research effort is being carried out, under the direction of Prof. David Bishop, at the Natural Environment Research Council's Institute of Virology (IoV), which carried out the first release of genetically marked virus in the United Kingdom.

The main products OV is developing are diagnostic tests and vaccines for hepatitis B, AIDS and Rantaan fever for human health care applications and, in the veterinary sector, for bluetongue. The company has already entered into a number of agreements with international firms covering these products.

At the same time, OV has obtained research contracts from a number of companies for the production of biologically active proteins using the insect virus expression systems. Details from: Oxford Virology Ltd., 10 Storey's Gate, Westminster, London SW1P 3AY or on 01-222 9272. (Source: Biotechnology Bulletin, Vol. 6, No. 9, October 1987)

CRB launches oncoprotein antibodies

Recent research has led to the isolation and identification of oncogene products (oncoproteins) as causative agents in the development of certain tumours. Following these developments Cambridge Research Biochemicals (CRB) is releasing a range of monoclonal and polyclonal oncoprotein antibodies.

Using innovative methods to determine immunologically accessible sites, CRB says it has identified discreet peptide sequences from a number of nuclear, membrane and cytoplasmic oncoproteins. Using the mild conditions of Fmoc-polyamide mode of solid-phase peptide synthesis technology, developed at Cambridge, CRB has synthesized these fragments of the oncoprotein primary sequences and used them to raise monoclonal and polyclonal antibodies. The Immunobiology Unit at CRB has extensive experience in this area and already produces a number of anti-peptide antibodies for its catalogue and Custom Antibody Service.

Oncoprotein antibodies scheduled for the range include myc, ras, fos, myb, erb-B, mas, mos, abl, neu, int-1, inc-2, ets, and antibodies to the EGF Receptor.

Contact: Cambridge Research Biochemicals, Button End, Harston, Cambridge, CB2 5NX; tel: (Freefone) 0800 585396. (Source: Manufacturing Chemist, October 1987)

Drugs company funds research at Oxford

The American drugs firm Squibb announced a deal with Oxford University to provide a new building for its department of pharmacology and to support research into potential treatments for brain diseases. The announcement coincided with the launch by the university of a multi-million-pound appeal: cuts in government funding have forced administrators to meet running expenses from the university's financial reserves, now rapidly dwindling. In return for the money, the company will own intellectual property rights to work that it funds.

Workers on such projects must pledge to keep secret anything that might prejudice the commercial interests of the company, for example during seminars. They must also agree to notify the company before they submit results for publication in a journal. The idea of this is to give the company time to take out patents.

Under the terms of the deal, Squibb will pay £9.6 million for a new building almost twice the size of the existing department. The building will be next to the Medical Research Council's projected building and be linked with it. The Council's unit will be ready in September 1990; the rest of the building a year later.

The company will also inject £10.4 million into research in five areas over the next seven years. They are: degenerative diseases of the nervous system (such as Alzheimer's disease and Parkinson's disease); epilepsy; psychoses, such as schizophrenia; the control of blood pressure by the central nervous system; and control in the peripheral nervous system. After five years it will review progress and consider funding a further five years' work.

Squibb will have first option on funding the department's projects in these five areas. If it chooses to support a project, the company will retain the intellectual property rights on the work, allowing it to take out patents on any discovery. The university will receive royalties on commercially-successful products.

Researchers working outside the five designated areas will carry on as before, applying for grants from government, charities or other commercial sources of funds. They will be free of other restrictions. At present, the five areas represent about 30 per cent of the department's workload, but this may now increase to 50 per cent.

The deal, the biggest Oxford University has ever undertaken, represents a unique experiment in uniting academic and commercial interests. (Extracted from New Scientist, 22 October 1987)

UK firms establish diagnostics venture

Agricultural Genetics Company (AGC), the Cambridge, UK-based biotechnology concern, is reinforcing its push into diagnostics with the formation of Stirling Diagnostics, a new joint venture with Tulbero of Scotland. The new firm, based at Stirling University's Innovation Park, will focus on the development and marketing of dagnostics kits, vaccines and associated services to the agricultural and fish farming industries.

By merging the diagnostics interests of AGC, including the Agricultural Diagnostics Company (ADC), with those of Tulbero, a Stirling-based fish farming diagnostics outfit, the partners hope to achieve the critical mass required to impact the West European diagnostics market.

Stirling Diagnostics is planning to launch its first products next year. The firm will first focus on kits diagnosing diseases affecting salmon and trout and fungal attacks on potatoes and cereals.

The first series of products will be based on colour change immunoassay technology but the new company is working with a Finnish group to develop DNA hybridization techniques to produce kits based on DNA probe technology.

Stirling Diagnostics hopes that other companies will use its marketing resources for their own products.

The Scottish firm will have a limited production capacity for pilot-scale requirements but intends to subcontract kit manufacture elsewhere in the UK. Initially the company will focus on the EEC but will push the US and Far East within 18 months. (Extracted from European Chemical News, 21/28 December 1987)

Celltech to produce hormone

Celltech Limited, Slough, UK, says it has been awarded a "multi-million dollar" contract from Ortho Pharmaceuticals, Inc., to produce erythropoietin (EPO) from mammalian cell culture over the next two years. EPO is used in the treatment of kidney failure.

Ortho Pharmaceuticals, New Jersey, has a license to market EPO for renal failure and to develop it for other indications. Clinical trials are currently under way in the US, Europe and Japan for which Celltech is producing the product as well as for early marketing.

A subsidiary of Johnson & Johnson already has installed and commissioned a specialist, dedicated plant at Celltech's production facility. Approximately 200 g of EPO are expected to be produced by the end of 1989. This represents a significant proportion of world supply that is expected to be on the order of 500 g to 1.5 kg per year, depending upon the success of clinical trials. Celltech has begun negotiating with the necessary regulatory bodies for product and manufacturing licenses for EPO. (Extracted from Chemical Marketing Reporter, 7 December 1987)

United States of America

The Administration re-engineers biotechnology regulation

Presidential Science Adviser William Graham has transferred the policy-making powers of the Biotechnology Science Co-ordinating Committee (BSCC) - which pulled together the federal Government's biotechnology regulation framework last year - to a new Committee on Life Sciences (CLS), a unit of the Federal Co-ordinating Council for Sciences, Engineering & Technology within the White House Office of Science & Technology Policy (OSTP). Since most of BSCC's members also will sit on CLS the biotechnology committee's future role is unclear. Previously, BSCC worked closely with the working group on biotechnology of the White House Domestic Policy Council, which will still play a role in government-wide biotechnology policy. CLS's mission will be broader than BSCC's. CLS will be involved in aquatic and marine research, plant science research and international science, as well as risk assessment biological diversity and a human genome project. It will be chaired by Beverley Berger, now assistant director for life science at OSTP. (Source: Chemical Week, 16 December 1987)

New research centre

The US Department of Agriculture in collaboration with the University of California at Berkeley has established an agricultural biotechnology research centre. The centre, which will be run by the USDA's research arm, will focus on determining the mechanisms by which plant genes are switched on and off. An understanding of these mechanisms will lead to greater chances of producing new crops. (Source: European Chemical News, 14 December 1987)

Occupational Safety and Health Administration proposes rule on biological hazards

For the first time, OSHA is beginning to explore ways to protect workers from biological hazards in the workplace - specifically, ways to prevent infections of human immunodeficiency virus, and hepatitis B virus. At this early stage, OSHA is seeking scientific and technical data on a number of issues related to these hazards, including the scope of coverage for such a regulation, the degree of risk that exists for workers, technologies that could control exposures to the viruses, protective clothing and equipment, medical surveillance requirements, and training and education issues. (Reprinted with permission from Chemical and Engineering News, 7 December 1987. Copyright (1987) American Chemical Society.)

Strawberry plants attacked in Californian field tests

In the latest incident in California's battle between environmental groups and biotechnology, sabotage has delayed a test of genetically engineered frost-preventing bacteria by the Oakland-based company Advanced Genetic Sciences (AGS).

On 30 November, just two days before the test was to begin, vandals slipped past guards, scaled a fence and spread rock salt on the test site, a strawberry field east of San Francisco. The radical environmental group Earth First!, which advocates sabotage, claimed responsibility.

So far, all three California field tests of genetically engineered bacteria - two by AGS and one by the University of California at Berkeley - have been damaged by vandals.

Although the environmental groups have not succeeded in stopping the field tests, they have in some cases reduced their scientific value, and have cost both AGS and the University of California millions of dollars in delays and court battles.

Trevor Suslow, director of product research for AGS, said the rock salt was removed from the field and the plants seem not to be damaged. But, as the vandals claimed to have sprayed a slow-acting herbicide as well, AGS will wait a few days before proceeding with the experiment.

Suslow said that AGS needs several more field tests before its frost-preventing bacteria will be ready for market. He said the company will not give up Californian field tests, despite the harassment. But as the Organization for Economic Co-operation and Development irons out its regulations for such tests, the company may look abroad for countries more sympathetic to environmental release experiments. (Source: Nature, Vol. 330, 10 December 1987)

AIDS education in United States

The largest effort to date to study the effectiveness of AIDS education in preventing infection by the virus is being funded by the National Institute of Mental Health (NIMH) and the National Institute of Drug Abuse (NIDA) at three centres around the country. Those who have been calling out for more research into AIDS prevention will say that the initiative is long overdue.

Although public health officials agree that education programmes are virtually the only tool for combating the spread of HIV (human immunodeficiency virus) infection, evaluating these programmes is just getting under way.

The University of California at San Francisco (UCSF) centre is a collaboration between the university, the San Francisco Department of Public Health, and MIRA (Multicultural Inquiry and Research on AIDS), a group of researchers who study the impact of AIDS on minorities.

Research at the UCSF centre will include improved epidemiological studies to learn the prevalence of high-risk behaviour, and research to test the effectiveness of educational programmes in reducing that behaviour. The centre is also conducting a study of high-risk behaviours in Rwanda, and an international exchange programme to help researchers from Africa and Latin America study AIDS prevention in their own countries.

A second centre is Columbia University's HIV Centre for Clinical and Behavioural Studies in New York. The New York Psychiatric Institute and Columbia Presbyterian Hospital are partners with Colombia University in the centre, and other regional hospitals will participate in the centre's activities.

Three of the five studies proposed by the centre will analyse the effectiveness of AIDS prevention education, with the emphasis on how best to reach adolescents.

A third AIDS centre at the University of Miami School of Medicine received a five-year grant from NIMH and NIDA in November 1986. Called the Biopsychosocial Centre for the Study of AIDS, the Miami centre is focusing its attention on the development of AIDS dementia and on how social and psychological factors influence the course of HIV infection. (Source: Nature, Vol. 330, 12 November 1987)

Molecular modelling laboratory set up

A molecular modelling laboratory equipped with advanced computer graphics stations and software capable of modelling a wide range of structures has been established at the Department of Energy's Pacific Northwest Laboratory in Richland, Washington. The laboratory is the first phase of a planned $120 million molecular science research centre, to be completed by 1992. A full-time staff as well as visiting scientists will conduct research in areas such as coal chemistry, high-temperature superconductivity, thin-film materials, and protein structures. The modelling laboratory has begun operating in existing facilities while a new building is being constructed. (Reprinted with permission from Chemical and Engineering News, 19 October 1987. Copyright (1987) American Chemical Society.)

ASTM Board approves new subsidiary insitute for standards research

The ASTM Board of Directors recently approved the formation of the ASTM Institute of Standards Research, Inc. The subsidiary will provide a management system for the solicitation of funds for the accelerated development of technical information in support of ASTM standards-writing committees.

As ASTM (formerly the American Society for Testing and Materials) approaches the last decade of the twentieth century, both the industrial and service sectors of the US economy face many challenges and opportunities. Rapid globalization of the marketplace, coupled with an ever-widening spectrum of emerging technologies, mandates a more responsive and dynamic course of action for ASTM. In response to these challenges, and in order to position ASTM firmly in the twenty-first century, the concept of an ASTM "Institute for Standards Research" emerged.

The Institute for Standards Research will do no actual research, but will serve as the intermediary between the technical community and the public or private agencies that could supply needed research and technical service for the ASTM standards writing community. The corporation is incorporated under the General Corporation Law of the State of Delaware exclusively for charitable and educational purposes. (Source: ASTM News Release, 6 October 1987)

New riboflavin plant

On 30 November 1987, Coors Biotech Products Company dedicated its new plant in Winchester, Kentucky for the production of riboflavin from an improved micro-organism developed by Synergen. Vitamin production in the new plant is to begin in January, with sales beginning by the end of the first quarter. Riboflavin, or vitamin B2, is widely used in food production, commercial vitamin supplements and animal feed.

Synergen applied its proprietary techniques of genetic strain improvement to significantly increase production levels of riboflavin over existing processes. Coors Biotech developed the fermentation and scale-up techniques and will be responsible for production and marketing activities. Although Synergen's share of revenues is not expected to be substantial, this event is a milestone in Synergen's development of products using biotechnology.

In human pharmaceuticals, four of Synergen's recombinant human proteins are now in advanced preclinical studies and all are showing positive results. The firm expects that wound healing uses for its angiogenesis factor (FGF) will be the first product in human clinical trials, and it anticipates that treatment of pancreatitis with the trypsin inhibitor should follow into the clinic shortly after. (Extracted from Company News Release, 30 September 1987)

Ecogen awaits approval for its cotton biofungicide

Hoping to be the first company to have a biological fungicide registered by the Environmental Protection Agency (EPA) for use on crops, Ecogen (Langhorne, Pa.) has submitted an application for Dagger G biofungicide, which relies on a naturally occurring strain of Pseudomonas bacteria. The product, says Ecogen, combats damping-off disease, a fungal disease that destroys cotton plant seedlings. The application to EPA follows three years of field trials which showed Dagger G "to be equal in effectiveness to a currently used chemical fungicide," says Ecogen. (Source: Chemical Week, 4 November 1987)

Kodak will build a biotechnology plant

A plant for the production of biotechnology products, including food additives and pharmaceutical intermediates, as well as industrial enzymes and specialty chemicals, will be built by Eastman Kodak in Cedar Rapids, Iowa. Kodak says that a major factor in its choice is the city's proximity to several suppliers of processed corn and soy products. Each year, the plant - which is scheduled for completion in 1990 - will use thousands of tons of processed corn and thousands of pounds of soy-based products. (Source: Chemical Week, 11 November 1987)

Phillips forms biotechnology venture with Dallas group

Phillips 66 Biosciences Corporation and Wadley Technologies, Inc., of Dallas have formed a jointly owned corporate venture, Wadley Biosciences Corporation, to develop new pharmaceutical products.

Wadley Biosciences will use genetic engineering and monoclonal antibody technologies to identify, isolate and develop new human immune proteins for the treatment of cancer and viral diseases including AIDS. Wadley Biosciences will be located in Dallas. Its initial research and product development projects will be funded with $5 million.

Phillips has developed a proprietary recombinant DNA yeast expression system which has proven utility in the production of various recombinant products. (Extracted from Chemical Marketing Reporter, 30 November 1987)

Sandoz acquires granulocyte macrophage colony stimulating factor supplies

Genetics Institute, the US biotechnology firm, has signed a supply deal with Sandoz for granulocyte macrophage colony stimulating factor (gmcsf). The biotechnology product is believed to have a potential for treating infections associated with AIDS and cancer.

Both firms have been working on gmcsf for a number of years and the drug is only one of many that the Swiss major has in its potential biotechnology arsenal. (Extracted from European Chemical News, 30 November 1987)

Biotechnology companies merge

DNA Plant Technology (DNAP), Cinnaminson, N.J., and Advanced Genetic Sciences, Oakland, California, have agreed in principle to merge. The agreement calls for Advanced Genetics shareholders to receive two thirds of a share of DNAP stock for each share of

Advanced Genetics they now hold. The deal is worth $38.5 million at the current market price of DNAP shares. Both companies concentrate their efforts on agricultural biotechnology. According to a company spokesman, the combined company will maintain both its East and West Coast facilities and will have a combined work-force of more than 200. Advanced Genetics recently drew EPA's ire when the agency alleged that the company conducted open-air testing of genetically altered bacteria to retard frost formation without the proper agency permits. (Reprinted with permission from Chemical and Engineering News, 21 December 1987. Copyright (1987) American Chemical Society.)

RAC extends guidelines to r-DNA plants and animals

Proposed guidelines for research with genetically engineered whole plants and animals, originally drafted by the US Department of Agriculture (USDA), were endorsed by the Recombinant-DNA Advisory Committee (RAC) to the National Institutes of Health (NIH) at its September meeting. If accepted by NIH Director James B. Wyngaarden, the guidelines will be enforced for all recombinant plant and animal experiments funded by USDA, which has decided not to issue separate rules of its own. The guidelines will apply to large animals such as cows and pigs, and to greenhouse experiments.

The new provisions have four biosafety containment levels, consistent with those for micro-organisms. The least restrictive, level 1, allows open greenhouses for plants, and fenced enclosures for animals, with the latter primarily intended to prevent sexual reproduction. The most restrictive, level 4, specifies enclosed structures designed to prevent escape of organisms with "recognized potential for significant detrimental impact on managed or natural ecosystems".

Transmission of plant pathogens is radically different than transmission of animal pathogens, noted the chairperson of the working group's plant-subgroup, Nina V. Fedoroff, who heads the Department of Embryology at Carnegie Institute of Washington in Baltimore, Md. Therefore, "biological containment" - such as conducting experiments in the winter when plants are not germinating - was considered as important as physical containment. Consequently, her subgroup rejected most of the suggestions of the Environmental Defense Fund (EDF), which wanted stricter level 1 containment of plants that are modified with recombinant vectors.

The RAC unanimously adopted a proposal to add Bacillus stearothermophilis to the guidelines' grampositive exchanger list for extra chromosome elements. The organism was previously excluded, according to Richard Novick and June Polak of the Public Health Research Institute of the City of New York, because natural transfer had not been demonstrated in the laboratory. This, they said in a letter, is an "arbitrary" criterion, because "these species naturally contain plasmids that are indistinguishable from pBC16".

Finally, the RAC heard a proposal to change its guidelines, submitted by Jeremy Rifkin, president of the Washington-based Foundation on Economic Trends. Currently, the RAC rules are applicable "to projects done abroad, if they are supported by NIH funds". Rifkin proposed defining "projects" to include "any research or development of the recombinant organism or other product or process in question, including all such work that is reasonably foreseeable when the NIH support is received". Also, NIH support would include "both money grants and any type of in-kind support, including research conducted directly by NIH, supplies, equipment, the use of facilities, and biological research materials". (Extracted from McGraw-Hill's Biotechnology Newswatch, 5 October 1987)

California eases the rules

Americans are increasingly criticising the Food and Drug Administration (FDA) for being too cautious in its testing and approval of drugs for AIDS. Although the FDA passed new rules last May to make experimental drugs available to people with no-hope diseases, none has as yet been approved for testing under the new scheme. Now California has decided to take matters into its own hands by passing legislation that will get round the FDA regulatory processes.

A bill allowing the testing and eventual approval of an AIDS drug without FDA approval was signed by Governor George Deukmejian on 28 September. Apart from helping to speed up the approval of AIDS drugs, the hope is that the new bill will also put to an end the growing black market that has emerged across the border in Mexico, where all sorts of unapproved AIDS drugs are available for high prices in "guerrilla clinics".

About one in five of America's AIDS sufferers lives in California. The State authorities have been under increasing pressure from doctors and victims alike to be seen to be doing something about finding new treatments for the disease. (Extracted from The Economist, 3 October 1987)

Surveys will scrutinize thirty American cities

The Centers for Disease Control (CDC) in Atlanta, Georgia, has begun working with health officials from 30 American cities in an attempt to obtain a more accurate picture of the prevalence of the human immunodeficiency virus in the US. Current estimates say that between one million and two million Americans are infected.

The survey will cover 20 cities, including San Francisco, Los Angeles and New York, which researchers believe are high-risk areas for catching the virus. The other 10 cities are in low-risk areas. Health workers will collect blood samples from people in hospitals, prisons and clinics for sexually transmitted diseases.

Meanwhile, the CDC has held up a more ambitious programme to take random blood samples from 45,000 American households. Preliminary surveys indicate that there may be a widespread unwillingness to participate, and the CDC is worried that this reluctance could distort the results of such a large survey.

Researchers in California, however, have recently completed a survey of HIV infection among intravenous drug users in California. (Extracted from New Scientist, 29 October 1987)

Anonymous tests for HIV carriers

Public health officials in the US have begun testing people anonymously for antibodies to the human immunodeficiency virus, using blood collected for other purposes.

Early results from surveys at four hospitals in the US found that 0.32 per cent of the people who attended hospital for problems other than AIDS were infected with HIV.

Tests on blood from military personnel, college students, prisoners and patients in hospital casualty departments are also under way. More widespread testing of the population in 30 American cities will begin in May 1988.

Doctors will take blood samples at random from patients at selected hospitals and at clinics for sexually transmitted diseases, drug addiction and tuberculosis. The records will hold only the age, sex, race and area of residence of the people tested. It will not be possible to identify or inform anyone whose blood yields a positive result.

The President's Commission on AIDS, which critics have accused of disorganization and a lack of expertise produced a progress report which contained no conclusions, but listed four urgent problems on which the 13-member panel will concentrate before its final report in February. These are: lack of data on the prevalence of the virus; lack of home care for people with AIDS; the inadequacy of programmes for treating intravenous drug users; and the slow pace of testing new drugs to treat AIDS. (Extracted from New Scientist, 10 December 1987)

USSR

Soviet scientists synthesize zidovudine

Scientists at the Soviet Academy of Sciences are claiming to have developed a process to synthesize azidothymidine (AZT, or zidovudine). They are now planning to develop the process for commercial scale quantities.

The synthesis developed at the Institute of Molecular Biology of the USSR Academy of Sciences has been reported in a number of Soviet publications. The Soviets are also hoping to develop AIDS test kits and a vaccine. Scientists at the Ivanovsky Institute of Virology have introduced several AIDS genes into smallpox vaccines and tests on monkeys are scheduled within the next few months. (Source: European Chemical News, 14 December 1987)

AIDS vaccine

The Soviet Union has recently stepped up research to find an anti-AIDS vaccine or prophylactic, according to Academician V. I. Pokrovskii, president of the Soviet Academy of Medical Sciences.

Voluntary anonymous testing facilities for HIV have been available for some time, but a recent decree on mandatory testing of suspected carriers and the heavy legal penalties it imposes on carriers who knowingly place others at risk make it difficult for many people in high-risk category to trust fully in the promised confidentiality. Moreover, if the Soviet Union continues its policy of compulsory testing, it could encounter difficulties internationally. As Pokrovskii stressed, international co-operation is all-important in AIDS research. But the Hungarians who had also passed a new law on the mandatory testing of high-risk groups, now say that they may have to abandon it in the light of the agreement rejecting compulsory screening adopted by a recent conference in Paris.

In the mean time, research efforts continue, and receive considerable publicity. The popular science journal Nauka i Zhizn recently described the development of 'nuclear filters' at the Dubna Joint Nuclear Research Institute. These filters, it was explained, are produced by directing a beam of charged particles at a polymer film, and can be tailored to trap the HIV virus, which would interact with the material of traditional member filters. (Source: Nature, Vol. 330, 3 December 1987)

Gene engineering producing interferon

A new technology for interferon production was developed by the Soviet Academy of Sciences. Until recently, it was almost impossible to preserve interferon, a basic antiviral substance released by cells exposed to the action of a virus. Another danger was that interferon might include the virus against which it was produced. So, a few years ago scientists at the Institute of Bio-Organic Chemistry (the USSR Academy of Sciences) led by Academician Yuri Ovchinnikov undertook to produce interferon out of natural organic elements at the molecular level.

Today, the scientists have produced two kinds of interferon - leucocyte and immunologic. The former is effective against infections and the latter against tumours.

Yuri Ovchinnikov showed samples of interferon tablets, ointments and ampoules at the latest meeting of the Academy Presidium. He said their mass production was now the task of medical industry.

Soviet gene engineers have developed several organic compounds, including insulin and a growth hormone. Several new preparations are undergoing clinical tests. (Source: Science Age, November 1987)

Zaire

Soldiers prepare for vaccination

Large-scale tests of a vaccine against AIDS, developed by the French researcher Daniel Zagury, may soon go ahead in Zaire. French and Zairian researchers want to test the vaccine on soldiers and have asked the country's president, Sese Mobutu, for permission to do so.

Researchers would divide subjects of the trial into two groups. One would receive the vaccine, the other a placebo. The researchers want to test the vaccine on soldiers because their lifestyle raises their risks of infection. Preliminary tests of the vaccine on humans, including Zagury himself, confirm that the vaccine is safe. If all goes according to plan results should be available within one year. (Source: New Scientist, 19 November 1987)

C. RESEARCH

Research on human genes

Gene inactivation by dominant negative mutations

A number of techniques are now available for the cloning of genes, that is, determining their nucleotide sequence. Molecular biologists are, however, increasingly being faced with the problem of assigning a function to genes that have been cloned. The classical approach is to inactivate the gene and see what effects this has, but as yet this method is not suitable in the case of mammalian genes. I. Herskowitz of the Department of Biochemistry and Biophysics, University of California, San Francisco, USA, has suggested a new approach to this problem that involves the manipulation of a cloned gene to create what are known as "dominant negative" mutations. Such mutations could, in fact, provide information on the in vivo function of a diverse array of cloned genes and gene segments.

The new approach involves blocking the function of a gene at the protein level. The ability to manipulate genes in the laboratory makes it possible now to design inhibitory products based on the principle that the activities of a protein can be separately mutated. The method has the genetic virtue

of causing a conditional defect and, being dominant, allowing functional inactivation of redundant genes. In practice, the cloned gene is altered so that it encodes a mutant product capable of inhibiting the wild-type gene product in a cell, thus causing the cell to be deficient in the function of that gene product.

The California biologist believes that dominant negative mutations may provide a route to new information on protein-protein interactions and, hence, on designing new inhibitory polypeptides. It is possible that the type of mutation suggested by him might be responsible for some cases of cellular transformation, since both recessive and dominant mutations are known to be able to cause cellular transformation. There is every reason to believe that loss of function could also result from dominant negative mutations. What is more, production of a dominant negative oncogene in vivo could involve precisely the same type of events as those described for generating a dominant negative mutation by in vitro manipulations. (Source: Science Age, November 1987)

Synthetic DNA reagents

DNA-cleaving reagents with greater specificity than naturally existing restriction enzymes have been synthesized by M.E. Mosher and P.B. Dervan of the California Institute of Technology (Pasadena), who prepared 9 DNA probes - each 11-15 nucleotides long and specific for a different DNA sequence - in which the nucleotides were a mixture of thymine and cytosine. One thymine nucleotide in each probe was covalently attached to ethylenediamine tetracedic acid (EDTA), which cleaves DNA in the presence of ferrous ions and a reducing agent such as dithiothreitol. The synthetic DNA reagents cleaved DNA from various organisms at sites complementary to the reagents. Mosher explains that reagents are more specific than most restriction enzymes because restriction enzymes require a complementary match of only 4-8 nucleotides in a DNA strand, versus 11-15. (Extracted from Chemical Week, 25 November 1987)

Earlier detection of genetic defects in embryos

Researchers may someday be able to detect genetic diseases by examining pre-embryos. Women at risk for bearing genetically diseased children may then be able to choose if they want a pregnancy to continue. Some genetic diseases such as Tay-Sachs are inevitably fatal after no more than two-three years of life. Others do not kill but are debilitating. If genetic defects could be detected before the embryo begins to develop, women might be more willing to terminate a pregnancy than if the defects are not detected until later in the pregnancy. Possible routes to pre-embryonic genetic monitoring include measurement of waste products secreted by the cells or biopsy of the cells, at any of several points in the pre-embryo's development. Polar bodies or cells of the mural trophectoderm (which do not add to the embryo itself) can be taken for examination with no damage to the pre-embryo. Measurement of protein production or the use of DNA probes to locate possibly defective genes might provide information about genetic defects. (Extracted from New Scientist, 10 December 1987)

Purposely created genetic defects

Genetic defects purposely created to simulate genetic disorders can be produced with some accuracy using a new technique developed by M.R. Capecchi of the University of Utah. The technique may facilitate research on diseases such as cystic fibrosis and muscular dystropny. The procedure is a variation of a technique used in 1980 to produce a black-and white haired mouse by injecting a black hair gene into an albino mouse embryo. The human hypoxanthine phosphoribosyl transferase gene was mutated and then injected into mouse stem cells. The altered cells were then injected into mouse embryos. Long DNA strands are used to improve the exchange of genetic information with other genes. A selection system that allows only desired cells to live can increase the odds that a desired mutation will be present to 50-50. The same techniques might eventually be used in human bone marrow. (Extracted from Science News, 21 November 1987)

Huntington's marker

Scientists have located what they say is the best marker yet for the Huntington's disease gene.

The new marker, called C4H, is a DNA sequence positioned about 4 million base pairs closer to the gene - which is located on chromosome 4 - than the previous marker, G8. In fact, C4H may even be on top of the gene, because a study of 150 people with the fatal neurological disorder has shown that C4H travels with the gene in all cases. The previous marker travelled with the gene 96 per cent of the time.

The new marker will allow better presymptomatic testing for the disease. Research testing is being done at Johns Hopkins University in Baltimore, Columbia University in New York City and Massachusetts General Hospital in Boston.

The next step is to find the gene itself, which requires finding a DNA segment that produces a protein that may be responsible for the disease.
(Source: Science News, Vol. 132, 28 November 1987)

Protection against diabetes?

A unique subset of T cells may protect against diabetes, according to D.L. Greiner of the University of Connecticut. The RT6-positive cells account for about 10 per cent of the total lymphocyte pool in rats. When the cells were removed from rats, 50 per cent of them developed diabetes. When the cells were injected into diabetes-prone rats, their susceptibility was virtually eliminated. If a comparable cell population can be discovered in humans, lymphocyte transfusions may prevent diabetes in people who are genetically predisposed. The RT6-positive cells are absent in diabetes-prone rats, due to a defect in bone marrow stem cells that produce lymphocytes. Some factor produced or induced by the cells apparently prevents the immune system from destroying pancreatic beta cells. Tests of RT6-positive cells might be done on human twins, when one has diabetes and the other does not. Isolating the factor produced by the cells might also allow successful islet cell transplants. (Extracted from Medical World, 12 October 1987)

Aging

What is new about aging is that its chemistry has been determined by a scientist of the Radcliffe Infirmary in Oxford, England. There is a methyl (CH^3) group in all genes; when it is erroneously positioned, it fails to make proteins and this leads to aging.

Biologists are now sure about the key role the methyl group ($-CH^3$) plays in genes and any alteration in the group's link in the DNA sequence can alter the gene's expression in an individual. About 4 to 5 per cent of the DNA have links of methyl groups near the cytosine portion of the chain. This seems to be an inherited trend in all mammals. This position of the methyl group near cytosine - a constitutent of DNA - plays a significant role in aging.

The genetic clue to aging comes from S. Fairweather who reported at a meeting of the International Association of Gerontology that nucleic acids without methyl groups result in aging. As long as the nucleic acid remains methylated near the cytosine residue, the genetic character of aging remains unexpressed.

A comparision of time-span of the existence of the methyl groups showed that human cells lose them slowly while the loss is fast in short-lived animals. Cells under the control of certain viruses become immortal and exhibit a constant presence of methylation in the DNA. Probably the virus enzyme aids in methylating the nucleic acid chain while the presence of 5-azacytidine, a cytosine analogue, retards methylation.

How does methylation relate to aging? The answer is that as cells age, methyl groups are no longer seen in the cytosine region. The enzyme methylase, as a result, slows down in its activity and the genes begin to express themselves differently. The proteins synthesized by such unmethylated genes, it seems, can be harmful. (Source: Science Age, December 1987)

Human monoclonals in therapy and diagnosis

Human monoclonals may soon replace many of the mouse monoclonals now in use in therapy and diagnosis. Human monoclonals might be more active but less immunogenic than mouse monoclonals. C. Cabot of Centocor says the technology for making human monoclonals is about three years behind that for mouse monoclonals. Antibody-producing B lymphocytes are fused to long-lived lymphocytes such as plamocytoma or lymphoblastoid cells. The resultant hybridoma cells are screened for cells that produce the antibody of interest. Recent advances in getting the B cells to merge with the lymphocytes will aid human monoclonal production. (Extracted from Medical World, 9 November 1987)

Left-handed DNA segment assay

An assay to detect left-handed segments of DNA in living cells has been developed by researchers at the University of Alabama (Birmingham). The assay may allow researchers to determine what role the backwards twisted DNA plays in genetically influenced disorders, including heart disease and cancer. There is evidence for left-handed DNA in test tubes but researchers will now be able to search for it in living cells. Left-handed DNA should be highly mutagenic. The assay is based on the fact that methylation is necessary for some DNA cleaving enzymes to work, but left-handed DNA is resistant to methylation. Left-handed DNA might affect DNA transcription and cell repair. (Extracted from Science News, 14 November 1987)

Unravelling the human genome

Prof. Walter Gilbert, previously chairman of Biogen, has set up a company to sequence the human genome and thinks that the entire sequence can be completed and checked for $300 million. Others, including Prof. James Watson of the Cold Spring Harbor Laboratory, predict a much higher figure. Biologists, who are increasingly excited about the idea of producing even a relatively crude overall genetic map of the human chromosomes, are now talking of the initiative as biology's "Moon shot", and the feeling today is that the project is viable.

A workshop organized in August by the US Office of Technology Assessment came up with an initial listing of the key components of such a programme: a genetic map, showing the locations of known genes; a physical map, consisting of a complete, ordered set of DNA fragments; and the sequence itself - the exact chemical order of the 3 billion nucleotide base pairs that make up the human genome. Overall, the cost is likely to be at least $1-2 billion and the project could still be running in the early years of the 21st century.

The importance of having a genetic map has been demonstrated by the recent discovery of genes implicated in such diseases as cystic fibrosis and Duchenne's muscular dystrophy, and in manic-depressive illness. A thousand or more genetic markers have been found in the last five years, facilitating such discoveries and holding out the promise of further advances. If such markers, which signpost the position of particular genes, can be located across the genome, the resulting "map" would have enormous clinical value. Its usefulness, however, would very much depend on its "resolution", determined by the distance between the identified markers. The greater the resolution, the greater the overall cost.

Luckily, the task is being made progressively easier by the development of new sequencing technologies. In the early 1970s it took more than a year for a skilled biologist to work out the nucleotide sequence of a single gene.

By the late 1970s, this rate had risen to 15,000 bases a year. Then, in 1986, Leroy Hood and his colleagues at the California Institute of Technology developed the first automated DNA sequences, which potentially could sequence 10,000-15,000 bases a day.

Applied Biosystems introduced a sequencer based on Hood's technology earlier this year and says it has sold about 100. Du Pont's competing Genesis 2000 was announced in October. Du Pont expects to begin delivery of its systems, priced at $90,000 apiece, in February. However, even instruments as advanced as these are still considered to be too slow by the US Department of Energy, which is playing a leading role in the Human Genome Project. It is currently exploring "far-out" technologies which might allow the sequencing of thousands of bases a second. (Source: Biotechnology Bulletin, Vol. 6, No. 10, November 1987)

Genetic linkage map completed

Scientists in the US have created the most detailed map yet of the human genome. The map is a rough chart of molecular signposts along the 23 pairs of human chromosomes.

The map is the culmination of five years' work by Eric Lander of the Massachusetts Institute of Technology in Cambridge, Massachusetts, and researchers at Collaborative Research, a biotechnology company in nearby Bedford.

The map contains 403 markers each separated by about 10 million chemical bases, the small chemical units of DNA.

Each signpost is called a restriction fragment length polymorphism (RFLP). When the chromosomes of two persons are exposed to an enzyme that cuts DNA, there are variations - RFLPs - between the two sets in the spots where the enzyme slices through. Consequently, there are variations in the sizes of the resulting fragments. The variations are called polymorphisms.

Certain polymorphisms appear only in the chromosomes of people with an inherited disease, of which there are about 4,000. Researchers seek polymorphisms that distinguish a person with, say, cystic fibrosis, from his or her close family, whose members share an almost identical genome.

The polymorphisms become markers for that disease. The marker, however, is not necessarily the gene itself, which is somewhere else nearby on the chromosome. The fewer or further away the markers are from the actual gene at fault, the more room for error in genetic diagnosis.

The map of hundreds of polymorphisms will guide researchers closer to the genes that cause disease and will make tests more reliable. It also paints a finer picture of human variation in association with disease.

With the map, Collaborative Research and its associates claim to be able, with 95 per cent certainty, to assign a new marker to its place along the human genome.

Collaborative Research claims to have the largest collection of genetic markers in the world. The company found 305 of the 403 polymorphisms in the map; the rest came from other researchers. The DNA for the work came from 40 families over three generations supplied by the Centre for the Study of Polymorphisms in Paris (France).

The publication puts the company ahead in a hotly-contested race, however. Raymond White, a genetic scientist at the University of Utah, is preparing his own map with even more markers than Collaborative Research lays claim to. However, the restriction fragment length polymorphism map is much less precise than the complete human genome map planned by US Department of Energy scientists to identify all three billion base pairs. Collaborative Research hopes to recover the $12 million research cost of the five-year project by using the data to develop diagnostic tests. The markers on the map are about 9 million base pairs apart from each other, on average, while US Department of Energy's cosmid maps will have a resolution of about 30,000 base pairs, and will cost $50-100 million to construct. (Extracted from New Scientist, 10 October 1987, and Medical World, 9 November 1987)

Skin generated from muscle tissue

Skin for burn victims might be regenerated from muscle tissue, according to I. Yannas of the Massachussetts Institute of Technology. The researchers first developed an artificial skin in 1975 from collagen fibres and a carbohydrate polymer from shark cartilage. This skin may be commercialized if the Federal Department of Agriculture approves. Inoculating the skin with young cells from the upper epidermis layer can result in generation of a new epidermis and interlying basement membrane. The finding that underlying muscle can regenerate skin is based on animal studies, in which new skin starts to develop on a wound when encroaching skin from the edges of the wound may still be one centimetre away from skin forming under a polymer patch in the centre of the wound. Fibroblasts and stem cells from the muscle move into the polymer to generate the skin. (Extracted from Science News, 12 September 1987)

GM-CSF to boost white blood cell counts

Granulocyte-macrophage colony stimulating factor (GM-CSF) may be effective at increasing the number of white blood cells in AIDS patients, according to researchers at the New England Deaconness Hospital, Harvard Medical School, Sandoz Research Institute and University of California at Los Angeles. GM-CSF is nontoxic and capable of boosting white blood cell counts. Intravenous infusions of GM-CSF for two weeks significantly increased levels of neutrophils, monocytes and eosinophils in proportion to the dosage administered. GM-CSF could be used in conjunction with zidovudine in the treatment of AIDS. The GM-CSF therapy did not increase the number of T-cell lymphocytes, which is the main cell type affected by AIDS. However, the cell-stimulating growth factor granulocyte macrophage colony stimulating factor can cause blindness and death in mice, according to researchers at Duke University (Durham, NC) and research institutes in Parkville and Melbourne, Australia. The research was done on mice that had been genetically engineered to produce excess amounts of the compound, which in small amounts is needed to stimulate the proliferation of some white blood cells. The drug has been given to AIDS patients in an attempt to increase the production of white blood cells. The engineered mice produced 40 times the normal amounts of GM-CSF. All the mice had opaque eyes ravaged by excess macrophages. Lens and retina were affected. Many of the macrophages that heavily infiltrated all parts of the mice were abnormal, with 2-18 nuclei. Almost all the recombinant mice died by 5 months. The macrophages in the engineered mice were reacting to the GM-CSF and also producing the compound.

There was no evidence of GM-CSF production in the bone marrow, however, which is where the compound normally is produced. Researchers point out that the mouse results are not directly applicable to use of the drug in humans, since humans receive it in small doses as adults, whereas the mice received huge amounts very early in development. (Extracted from Science News, 12 September 1987 and 12 December 1987)

Tests screen for teratogens

Two tissue culture assays together can detect chemicals that cause birth defects with 75 per cent accuracy, according to blind tests using teratogens and non-teratogens. The assays were studied by Richard E. Morrissey, a research scientist with the National Institute of Environmental Health Sciences, Research Triangle Park, N.C., working with researchers at Northrop Services, also at Research Triangle Park, and at Microbiological Associates, Bethesda, Maryland. One assay, the mouse ovarian tumour attachment inhibition assay, detects a chemical's interference with cell-matrix binding essential in embryo tissue formation. The other assay, the human embryonic palatal mesenchymal growth inhibition assay, detects a chemical's inhibition of cell division. The two mechanisms are considered major causes of birth defects. (Reprinted with permission from Chemical and Engineering News, p.18, 7 December 1987. Copyright (1987) American Chemical Society)

DNA adducts separated by chromatography

Researchers at Northeastern University, Boston, have developed a chromatographic method for separating DNA adducts based on hydrogen bonding. Detecting DNA adducts in humans is important because they signal exposure to possible carcinogenic or mutagenic chemicals. The researchers use a liquid chromatographic column that mimics the multiple hydrogen bonding that occurs between complementary bases in double-stranded DNA. Normal DNA monomers "should be highly retained on such a column," they note, but adducts (altered monomers) "tend to hydrogen bond abnormally and thereby elute rapidly from the column". The Northeastern chemists were able, for example, to separate a derivative of the adduct 3-methylthymidine from a thymidine derivative on a column containing silica gel bonded with an N,N'-2,6-pyridinediylbis (alkanamide) derivative. This phase forms triple hydrogen bonds with thymidine but not with the 3-methylthymidine derivative. (Reprinted with permission from Chemical and Engineering News, p.18, 7 December 1987. Copyright (1987) American Chemical Society)

Hybrid peptide cleaves DNA

A hybrid peptide formed by combining a DNA-binding peptide and a metal chelator can cleave DNA at specific sites, according to researchers from California Institute of Technology. Peter B. Dervan and James P. Sluka of the division of chemistry and chemical engineering collaborated with Suzanna J. Horvath, Michael F. Bruist and Melvin I. Simon of the division of biology to create the new molecule. They attached an iron chelator, ethylenediaminetetraacetic acid (EDTA), to a synthetic 52-amino acid peptide that binds to a specific DNA sequence. In the presence of ferrous ion, molecular oxygen and a reducing agent, the EDTA-peptide oxidatively cleaves DNA at a specific location. (Reprinted with permission from Chemical and Engineering News, p.11, 23 November 1987. Copyright (1987) American Chemical Society)

Genes travel out of cell nucleus

The transfer of genetic material in a cell is not a one-way process, according to two Federal Republic of Germany researchers. This discovery undermines the long-held view that genes in structures outside the nucleus, in the cytoplasm of a cell, can move only to the nucleus.

These structures in the cytoplasm - mitochondria and chloroplasts - generate energy for the cell through respiration and photosynthesis. They contain their own genes because they are remnants of once free-living bacteria which colonized cells early in the evolution Most of the genes are active - that is they produce an RNA intermediary or a final protein product. These active genes are either copied in the nuclear genome, or lost altogether to the nucleus. Hence researchers assumed that genes from mitochondria and chloroplasts could move only in one direction, into the nucleus.

Wolfgang Schuster and Axel Brennicke at the University of Tübingen have found evidence to suggest that the transfer of genetic material is not all one-way, from organelle to nucleus. They have discovered genes in mitochondria that have come from the nucleus. Furthermore, these are active genes, transcribed into RNA.

The researchers suggest that genetic material may have been transferred into mitochondria as RNA, and then copied to DNA in the mitochondria by a special enzyme. We already know that retroviruses contain an enzyme with just such an ability to convert RNA into DNA, reverse transcriptase.

Remarkably, Schuster and Brennicke also found signs of this enzyme in the genome of mitochondria. The gene that seemed to have moved from the nucleus to mitochondria is flanked by a sequence that makes a polypeptide very similar to part of the reverse transcriptase molecule. The mitochondrial version most resembles the reverse transcriptase that is linked to "jumping genes" - mobile genetic elements known as transposons that can move from one site in the nuclear genome to another.

The researchers suggest that moving genes from one compartment to another in the form of RNA is an efficient way of transferring only important genes, because only those normally transcribed into RNA could move. (Source: New Scientist, 10 December 1987)

Purified blood-clotting factor approved

The US Food and Drug Administration has approved marketing of a purified form of blood-clotting Factor VIII:C by Armour Pharmaceuticals for treatment of haemophilia A, the most common form of the disease. Removal of 99 per cent of contaminants often present in other preparations minimizes risk of contracting hepatitis B, non-A/non-B hepatitis, and acquired immune deficiency syndrome. Tests used now sometimes fail to detect viruses that cause these diseases. Armour's technique is to filter blood plasma through resin beads covered with monoclonal antibodies. These antibodies are designed to identify and attach to von Willebrand's factor, which is itself normally attached to Factor VIII in a loose chemical "bond". This means the chemical complex of Factor VIII and von Willebrand's factor sticks to the resin beads, and other proteins and viruses in the blood plasma pass through the filter.

The next stage is to add a solution of calcium ions to the resin beads. This breaks the bond between Factor VIII and von Willebrand's factor, so that Factor VIII comes free for collection as an almost pure product. Armour is also developing antibody-purified Factor IX for haemophilia B, as well as Factor VIII:C and Factor IX produced by recombinant DNA techniques. (Extracted from Chemical and Engineering News, 26 October 1987 and New Scientist, 22 October 1987)

IG's transgenic mice yield human TPA in their milk

Hard on the heels of an announcement from Scotland that transgenic sheep are being milked for human Factor IX (Newswatch, 17 August, p. 1) a US company announced that it is milking transgenic mice for human tissue plasminogen activator (TPA), a protein that quickly dissolves blood clots in heart-attack victims.

Scientists from Integrated Genetics, Inc. (IG), Framingham, Mass., and the National Institutes of Health (NIH) announced they have demonstrated that transgenic animals could yield hundreds or thousands of times more TPA than mammalian cell cultures - the technique currently used by Genentech, Inc.

Like the Scottish method for winning the blood-clotting factor, the technique developed by IG and NIH involves injecting the human gene for TPA, linked to a milk-protein sequence, into the fertilized egg of a mammal. When the animal matures and lactates, it will secrete relatively large quantities - grams or tens of grams - of TPA in each litre of milk. This compares with milligrams per litre of effluent from cell cultures, points out IG's scientific director Alan Smith. Several generations of the genetically engineered animals must be raised and cross-bred to ensure a dependable line, he notes.

The biotechnology company plans to extend the technique next year to large animals, such as cows, goats, or sheep. The same technology can produce other useful pharmaceutical proteins, including human growth factor and blood-clotting factors, as well as industrial enzymes, with a potential worldwide market.

The NIH researchers have been trying to determine why particular genes express proteins in one organ and not another. Mouse mammary glands are convenient organs for study, as they produce large quantities of specific proteins. IG's interest is primarily commercial and joint IG/NIH patent applications were filed last year. However, before IG's mammary method of making TPA can be approved for human use, it will have to be accepted by the Food and Drug Administration. To date, even Genentech's TPA has not been cleared for marketing, although FDA Commissioner Frank Young says that a decision is "imminent" as to the adequacy of the firm's clinical data. Weighing against the transgenic approach, S. Robert Kupor, financial analyst says, is the far greater variability from animal to animal than between batches of cell cultures produced in a laboratory.

Even if Integrated Genetics does manage to go head-to-head with Genentech, the profit margin for TPA is expected to be so large that a hundred-fold production advantage may still not give IG a significant market advantage. Genentech is expected to charge $2,000 a dose for its TPA, the analyst points out, while its production costs are estimated at only $200 to $300 a dose. So it may not matter much if IG can produce a dose for $20 or even $2. (Extracted from McGraw-Hill's Biotechnology Newswatch, 2 November 1987)

G-Proteins

The role of guanine-nucleotide-binding-protein (G-proteins) membrane-spanning receptors is examined. When G-protein-associated receptors, located in the cell membrane, are activated by a signal from outside the cell, they cause G-proteins bound to them to release a form of guanine nucleotide, guanosine diphosphate (GDP), and bind another form, guanosine triphosphate (GTP), where the G-protein activates the next step in a chain of events that eventually leads to a cellular response. G-proteins generally either regulate the activity of an enzyme or open or close channels in the cell's membrane that allow passage of cations. G-proteins also slowly hydrolyze the GTP attached to them to GDP, terminating the regulatory effect of the G-protein and leaving it available for reactivation when the receptor receives another signal from outside the cell.

The G-protein system seems to work for cell functions as diverse as vision, olfaction, control of cell proliferation and cellular regulation by various hormones and neurotransmitters. Major diseases such as cholera and whooping cough are now believed to be caused, at the biochemical level, by interference in cellular communication pathways. (Abstracted with permission from Chemical and Engineering News, 21 December 1987. Copyright (1987) American Chemical Society)

IL-1 may induce hormone secretion

Interleukin-1 (IL-1) can induce secretion of adrenocorticotropic hormone by the pituitary gland. This hormone, in turn, stimulates secretion of other hormones by the adrenal glands. IL-1 is therefore a key intermediary between the immune system and the hormonal system. It is still not clear, however, if IL-1 acts directly on the pituitary or indirectly, via the hypothalamus, since contradictory results have been obtained. Researchers at Stanford University and the Salk Institute say IL-1 stimulates release of corticotropin-releasing factor, which then induces adrenocorticotropic hormone (ACTH) secretion. This finding is supported by experiments done at Free University (Amsterdam, the Netherlands) and at the Schweizerisches Forschungsinstitut (Davos-Platz, Switzerland). However, studies at Walter Reed Army Institute of Research say that IL-1 can directly stimulate cultured rat pituitary cells to secrete ACTH.

M.D. Lumpkin of Georgetown University says both findings may be correct, since there are two forms of IL-1. One form may affect the brain and the other affects the pituitary. The sex of the experimental animals may also affect the findings, since oestrogen makes cells more receptive to factors that stimulate ACTH production. (Extracted from Science News, 31 October 1987)

Chloroquine-resistant malaria parasites

Some strains of the malaria parasite Plasmodium falciparum are resistant to the drug chloroquine whereas other strains are susceptible to its effects; kinetic studies of accumulation and release of the drug indicate why this is so. Both resistant and susceptible parasites accumulated chloroquine at the same initial rate but, in resistant strains, the rate of accumulation fell off rapidly after four minutes: resistant strains released 50 per cent of accumulated chloroquine in two to three minutes, but susceptible strains took longer than 85 minutes to release the same amount of drug. The accelerated release of chloroquine by resistant strains could be slowed by several calcium channel blockers, an antibiotic, and an inhibitor of microtubule function. D.J. Krogstad and colleagues at the Washington University School of Medicine, St. Louis (MO), point out that because some of these same decelerating substances slow drug release from multi-drug-resistant cancer cells as well, drug clearance in these two systems may be mediated by similar cellular mechanisms. Furthermore, the rapid efflux phenotype may be a common feature of certain resistant Plasmodium strains in all regions of the world - West Africa, South America, and South East Asia - where they have appeared. (Extracted from Science, p. 1,209, 27 November 1987, copyright 1987 AAAS)

Roles for HDL in Chagas' disease

Chagas' disease is common in Latin America; it begins as an acute infection but leads to chronic heart and intestinal problems. It is caused by the parasite Trypanosoma cruzi. New data suggest that serum high-density lipoprotein (HDL), a transporter of cholesterol, may also play some part in pathogenesis. The epimastigote stage of the parasite that multiplies in the gut of a blood-sucking insect and the trypomastigote that infects mammalian cells both have the enzyme neuraminidase on their surfaces; enzyme activity is typically low in epimastigotes but is high in trypomastigotes. Neuraminidase activity was known to be inhibitable by a serum component named cruzin, and cruzin has now been shown to be structurally and functionally the same as HDL. R.P. Prioli and colleagues at the Division of Geographic Medicine and Infectious Diseases, New England Medical Center Hospitals, Inc., Boston, MA suggest that the binding of HDL to the epimastigote may fill a nutritional need, because the multiplication rate, which is slow for epimastigotes grown in lipoprotein-depleted medium, can be restored by the addition of HDL; epimastigotes cannot make their own cholesterol. Exposure of trypomastigotes to HDL blocks neuraminidase activity and enhances infectivity; neuraminidase and the receptors for HDL are thus in close association on the parasite's surface. (Extracted from Science, Vol. 238, p. 1,333, 4 December 1987, copyright 1987 AAAS)

Structure of HLA determined

The structure of the human leukocyte antigen (HLA) molecule has been determined by researchers at Harvard University and Stanford University. HLA is essential to the body's killer cell immune complex. Knowledge of the HLA structure could open new doors to fighting diseases and immune abnormalities. Existing immunomodulators affect antibody-mediated, not HLA-mediated immune responses. X-ray crystallography indicates the molecule is folded into a flat-bottomed ravine with each wall made up of an amino acid coil. The ravine is just large enough to accommodate a foreign peptide. Killer T-cells apparently straddle the ravine and read the amino acid sequence of the captured peptide, thus programming themselves to attack identical proteins. The immune system might thus be programmed with all sorts of peptides to provide a new type of vaccination.

A genetic error that results in the substitution of a single amino acid in an immune system molecule can greatly increase one's chances of getting insulin-dependent diabetes mellitus, new research suggests. The finding supports earlier evidence that

inherited forms of diabetes may result from an autoimmune response against insulin-producing islet cells in the pancreas.

John A. Todd, John I. Bell and Hugh O. McDevitt of the Stanford University School of Medicine performed detailed analysis of HLA molecules in 39 diabetic patients and compared them to normal controls. The researchers found that the 57th amino acid on a particular HLA protein chain was highly predictive of diabetes. Of 20 possible amino acids for that position, one, called asparagine, is most common and appears to confer protection against islet-cell autoimmunity. The presence there of any other amino acid, however, apparently alters the HLA molecule so that it is more likely to mount an autoimmune response against the insulin-producing cells. (Extracted from Science News, Vol. 132, 10 October 1987 and 17 October 1987)

New studies clarify genetic links in alcoholism

Researchers studying children of alcoholics are detecting biochemical and behavioural differences in their responses to alcohol that may be a key to why these children are prone to becoming alcohol abusers themselves.

For years, scientists have been reporting that a tendency to become an alcoholic can be inherited. With new findings appearing almost monthly, researchers are identifying some inherited physiological differences among children. The differences may, researchers say, indicate a predisposition to alcoholism.

The newest studies reflect the resourcefulness required in facing one of science's most elusive challenges: identifying genetic factors in human behaviour.

One much-discussed finding is that college-age sons of alcoholics tend to have better eye-hand co-ordination and muscular control when they drink. They also tend to have a lower hormonal response to alcohol and to feel less drunk when they drink too much as compared to young men whose parents are not alcoholic.

Another group of researchers has shown that college-age daughters of alcoholics exhibit most of the same traits as the sons.

And young boys who do not drink themselves but whose fathers are alcoholics tend to have the same unusual brain wave patterns seen in alcoholics, another research group finds.

What researchers strongly suspect is that children born with these various traits are more likely than others to actually become alcoholics.

Strong evidence indicates that this reflects genetic as well as social factors. Recent studies of adopted children of alcoholics indicate that 30 to 50 per cent become alcoholics, regardless of the drinking habits of their adoptive parents. In contrast, 10 per cent of the general population is dependent on alcohol.

Among the first to study the children of alcoholics was Dr. Marc Schuckit of the University of California at San Diego. So far, he has studied 400 men; half had alcoholic fathers and none were alcoholic themselves at the time of the study. Dr. Schuckit and all the other researchers restricted themselves to children of alcoholic fathers to exclude the possibility that an alcoholic mother could have affected her child by drinking during her pregnancy.

Recently, Dr. Jack Mendelson and Dr. Barbara Lex of McLean Hospital in Boston repeated Dr. Schuckit's experiments, this time with daughters of alcoholics. The researchers have studied about 50 women so far and their results, according to Dr. Lex, are in general agreement with Dr. Schuckit's.

Women had not been studied previously because hormonal changes during their menstrual cycles can change their responses to alcohol. Dr. Mendelson and Dr. Lex overcame that obstacle by making sure, with blood tests, that all the women in their study were at the same hormonal stage in the menstrual cycle when they were tested.

Dr. C. Robert Cloninger, an investigator in Swedish study, has recently proposed that there are subgroups of alcoholics and that inheritance is more pronounced among those that use alcohol because it releases their inhibitions.

When Dr. Begleiter looked at sons of alcoholic fathers who fit this particular subgroup in Dr. Cloninger's classification, he found that 89 per cent had the deficits on the brain wave test. (Extracted from International Herald Tribune, 12 November 1987)

Duchenne muscular dystrophy gene

Patients with Duchenne muscular dystrophy (DMD) have severe cardiac and mental abnormalities; those with Becker muscular dystrophy have similar but milder pathologies. In 20 women, these diseases have been associated with a gene that maps to a region of the X chromosome where a piece of chromosome 21 has been translocated; although only one X chromosome has this diagnostic translocation, carriers develop disease because their normal X chromosome is preferentially inactivated. S.E. Bodrug, P.N. Ray and R.G. Worton of the University of Toronto, Canada studied the sequence of nucleotides at the translocation junction of the disease-causing X chromosome of one woman with DMD; comparisons were made with sequences at corresponding regions of derived and normal (unrearranged) X chromosomes and chromosomes 21. No major structural changes were found at the junction. However, small deletions (about 100 base pairs total) and some minor differences were found; in addition, a repeated tetranucleotide - possibly a recognition site for an enzyme catalyzing the translocation process - was found on both sides of the breakpoint. How these or other minor changes occur and whether they are causally associated with the development of disease remain to be determined. (Source: Science, Vol. 237, p. 1,551, 25 September 1987, copyright 1987 AAAS)

Borrowed cells repair dying muscles

Research into inherited muscle diseases has progressed considerably in recent years. Perhaps the most important advance was the discovery of the gene involved in Duchenne muscular dystrophy.

Jennifer Morgan and her colleagues at the Charing Cross and Westminster Medical School in London recently showed that it might be possible to replace diseased muscle by implanting new muscle precursor cells.

Muscle tissue poses a particular repair problem because the cells are fused into "syncytia", with each muscle fibre formed from a large number of muscle cells. Morgan and her colleagues found that they could repopulate a dying muscle with muscle precursor cells from newborn mice.

The researchers took a muscle from the toe of a mouse, and killed it by repeated freezing and thawing. They then grafted the dead muscle back into the mouse and injected muscle precursor cells. After allowing time for regeneration, Morgan found that the killed muscles had partly reformed.

To demonstrate that the reformed muscle tissue had grown from the injected precursor cells, the scientists used precursors from a different strain of mouse that carry a genetically marked muscle enzyme (an isozyme). When they looked at the enzyme in the reformed muscle, they found that it contained isozyme from both types of mice - from the precursor cells and from the cells of the mouse that received the implanted cells. This meant that the regenerating muscle was repopulated with muscle cells not only from the implant, but also from muscles lying next to the damaged muscle.

Taking the experiment further, the scientists implanted precursor cells from an identical strain of mouse, to prevent the recipient's immune system from rejecting the implant. Under these conditions as much as 50 per cent of the muscle reformed.

Morgan's technique has a long way to go before it can be used to treat people. But these experiments show that there is more than one way to develop treatment for inherited muscle diseases. (Source: New Scientist, 29 October 1987)

Blood clot agent's genes are read

The protein responsible for triggering blood clots in the body has been cloned and its genetic code cracked, researchers report. The new information, they say, could eventually lead to the development of a new class of anticlotting drugs to combat heart attacks and strokes.

The protein, called tissue factor, is one of eight major proteins involved in coagulation. But unlike the other clotting proteins, which circulate in the blood, tissue factor is bound to cell membranes within blood vessel linings. Because of the difficulties in working with such membrane-bound proteins, and because the protein is present in extremely minute quantities, tissue factor did not succumb easily to genetic analysis.

The research was a collaborative effort by scientists at Yale University in New Haven, Conn., and the Mount Sinai School of Medicine in New York City. The work could lead to the development of antibodies or assays to measure tissue factor availability. Such tests might detect early signs of thrombosis - the blocking of blood vessels due to unwanted clots - so as to allow early intervention with clot-dissolving drugs. The research could also facilitate the discovery of natural clot inhibitors capable of blocking coagulation before it even begins.

And not surprisingly, the amino acid sequence of tissue factor is remarkably different from other clotting factors - evidence that tissue factor has separate evolutionary roots. Whereas other clotting factors rely upon proteolytic activation by blood-borne enzymes, tissue factor triggers coagulation in response to tissue damage. It is the last of the blood clotting proteins to have its genetic sequence completely deduced. (Source: Science News, Vol. 132, 15 August 1987)

Changing a gene's message to suit a cell's needs

A team of British biologists may have discovered a new way for a gene to do different things in different cells - by generating a normal messenger RNA in some cells and a specifically mutated messenger RNA in others.

For a gene to become active the double helical DNA of the gene must be copied into a matching single strand of messenger RNA (mRNA). The base sequence of the mRNA matches the base sequence of the gene, so that the mRNA carries the same genetic information as the DNA "master copy". The mRNA then moves from the nucleus to the cytoplasm, where it directs the manufacture of a protein whose structure (determined by its amino acid sequence) depends entirely on the base sequence of the mRNA, and hence of the gene that gave rise to it.

That is what normally happens, but a research team, led by Lyn Powell of the Medical Research Council's Clinical Research Centre in Harrow, Middlesex, has found a fascinating novelty imposed upon that general scheme.

The team has discovered a gene which yields a normal mRNA in liver cells, but an altered or "mutant" mRNA in intestinal cells. So one gene gives rise to two mRNAs, and therefore two different proteins, depending on the type of cell it is in.

Powell does not know how the base sequence of the intestinal mRNA is altered. It might happen during the initial manufacture of the mRNA, when it is copied from the DNA of its gene, or it might be the result of a modification of the mRNA some time after it has been produced.

However it happens, it is an interesting genetic novelty in its own right; but if it proves to be the first example of a general phenomenon, then the biochemistry textbooks will have to be rewritten to include this new way in which identical genes can do different things in different types of cell. (Source: New Scientist, 15 October 1987)

No extra genes in Alzheimer's disease

The search for a cure for Alzheimer's disease has suffered a setback. Three studies have failed to find any evidence that patients with the disease have an extra copy of the gene making the abnormal protein that accumulates in their brains.

Alzheimer's disease involves the progressive degeneration of certain areas of the brain, resulting in the intellectual devastation known as dementia. There is no cure.

The cause of the disease is also a mystery; but there is strong evidence that genes might be involved. In a small number of families, Alzheimer's is inherited: anyone in these families has a 50 per cent chance of developing the disease if one parent has it. Earlier this year, Peter St. George-Hyslop and his colleagues at Harvard Medical School found that the affected members of these families had a defective gene on chromosome 21.

At about the same time, researchers in the Federal Republic of Germany and the US identified the gene making the main protein component of a substance called amyloid. The areas of degenerating nerve cells, called senile plaques, in the brains of Alzheimer's patients have a dense core of amyloid at their centres. The amyloid gene is also on chromosome 21. At the time many thought it might be the same as, or at least very close to, the gene for familial Alzheimer's.

People with Down's syndrome have an extra copy of chromosome 21, and they all develop the characteristics of Alzheimer's disease if they live long enough.

Alzheimer's patients do not have an extra chromosome. If they had an extra copy of the amyloid gene, however, this might account for the deposits of

amyloid in the brains of non-familial cases. Familial cases might have a defective version of the gene, with the same catastrophic results.

However, J.M. Delabar and his colleagues in Paris reported that in three patients with the non-familial form of the disease, there was indeed an extra copy of the amyloid gene. But in September, an international group established that the amyloid gene was definitely not the gene that was defective in familial Alzheimer's.

St. George-Hyslop and his colleagues also failed to find any link between variants (alleles) of suspect genes on chromosome 21, including the amyloid gene, and people with the disease. They conclude that "neither gene is the site of the primary defect causing Alzheimer's disease". Like other researchers, they suggest that amyloid accumulates in the plaques for some reason other than a simple genetic defect. And that means much more research into the whole question of what regulates the production and deposition of amyloid. (Source: New Scientist, 19 November 1987)

Alzheimer's: A cancer-like mechanism?

Peter Davies, of the Albert Einstein College of Medicine in New York City, reported last year the first (and still the only) marker - a protein found in the brain tissue of Alzheimer patients but absent in the normal elderly. Researchers still don't know what role the protein plays in the course of the disease, but more information should be forthcoming once its amino acid sequence is determined. That process may be completed in a matter of months, Davies says.

Meanwhile, Davies presented some surprising new evidence that the protein in question, called A68, is not entirely unique to Alzheimer patients, but is found in the normal developing foetus and infant. One intriguing possibility, he says, is that the protein may be involved in the "programmed killing" of brain cells that is characteristic of early brain development. Scientists have long known that during the first years of life the brain makes more neurons than it needs, and that many of these neurons are systematically killed. Davies says A68 distribution in the immature brain is similar to the distribution of cells that are known to die during periods of programmed killing.

The protein's reappearance in adults with Alzheimer's may represent an error in gene regulation similar to that seen in certain cancers. Cancer involves the repeated replication of adult cells as if they were still in their early development stages. Davies adds that such a model is compatible with current scientific knowledge about Alzheimer's disease, including the apparent combination of both genetic influences and unidentified environmental factors that seem to play a role in triggering the disease.

Alzheimer researchers are finding increasing evidence of immune components in the brain, including T cells, natural killer cells and human leukocyte antigens. They say this suggests that the blood-brain barrier may not be as impermeable as scientists have assumed, or that the central nervous system may even have its own independent immune arsenal. (Extracted from Science News, Vol. 132, 28 November 1987)

DNA probes for spotting a predisposition to cancer

The use of DNA probes to assess an individual's inherited risk of developing certain forms of cancer is the aim of a $1.8 million, five-year contract to Integrated Genetics (Framingham, Mass.) from the National Cancer Institute. The probes would analyse the DNA from blood samples for the presence of specific segments of DNA, known as "gene markers", that have been shown to be closely linked to defective genes believed to be related to cancer. (Source: Chemical Week, 21 October 1987)

Clinical trials for brain cancer treatment

Nova Pharmaceutical (Baltimore) will begin clinical trials of a new treatment for brain cancer at a number of US medical institutions. The treatment is based on a biodegradable polymer - made of 80 per cent sebacic acid and 20 per cent carboxy-phenoxy propane - that is implanted in the brain during standard brain cancer surgery. The polymer is designed to deliver - at a controlled release rate - the widely used cancer drug N,N-bis(2-chloroethyl)-N-nitrosourea at concentrations 10,000 times greater than is possible through injection. Because the polymer is biodegradable, additional surgery is not required to remove the implant. (Source: Chemical Week, 28 October 1987)

Trials begin for an antilymphoid cancer drug

Scripps Clinic and Research Foundation (La Jolla, California) has started clinical trials on a new antilymphoid cancer drug: 2-chlorodeoxyadenosine (2-CdA). The drug causes chromosome breaks in cancer cells, making replication impossible. It is said to have low toxicity and to be active against both resting and dividing cancer cells. (Source: Chemical Week, 28 October 1987)

Lung cancer genes located

Molecular biologists have found the key genes that, when damaged, lead to lung cancer. Charles Buys and his colleagues of the State University of Groningen, in the Netherlands, and Ben Carritt of the Medical Research Council's Biochemical Genetics Unit in London have discovered that a stretch of DNA is missing from cells in all forms of the disease.

The discovery is further evidence that some forms of cancer develop when a pair of "tumour-suppressing" genes malfunction or are lost. Such a pair of genes probably produce some chemical that controls the growth of cells. If a small "point" mutation develops in one of these genes (one allele), the cell goes into a precancerous state. The product of the remaining functioning allele on the other chromosome is enough to stop the development of a full-blown cancer. If something happens to the second allele - if it is lost, say, during division - the cell goes out of control and becomes cancerous. Cells in a precancerous state may divide more frequently and thus increase the risk of losing the second allele.

Such a two-stage process accounts for the development of two rare hereditary cancers of childhood, retinoblastoma and Wilms tumour. In these diseases, a child inherits one malfunctioning allele, and develops the cancer only if something later goes wrong with the second allele. These cancers are called "recessive" because they remain hidden until a second "hit" unmasks the inherited mutant gene. The new research on lung cancer suggests that even a common cancer, with little hereditary basis, can develop through a similar two-step process.

Even though researchers have now identified the region of chromosome 3 that carries the tumour-suppressing genes, it will not be easy to find the gene.

Only one of the tumour-suppressing genes has yet been cloned. Robert Weinberg of the Massachusetts Institute of Technology recently isolated the gene that malfunctions to cause retinoblastoma.

Researchers are also studying "dominant" genes that can actively transform a cell into a cancerous one. These genes, known as oncogenes, were first detected in some human tumours about six years ago. Twenty per cent of human cancers have an altered oncogene known as ras. Many more genes underlying cancer have yet to be discovered.

A "cure" for lung cancer is still further off. Buys suspects that the malfunctioning genes in chromosome 3 are just the first step in the development of cancer. "After that there are many more changes in the cells, which will make it very hard to reverse the process." The long search for the cancer genes has only just begun. (Source: New Scientist, 17 December 1987)

Cancer gene gap mapped

As chromosome mapping techniques improve, more and more diseases are being linked to specific genetic defects. Small-cell lung cancer - a particularly deadly form of lung cancer - became the latest disease to have its genetic origins identified, but although scientists still don't know what causes the genetic defect that leads to the disease, the researchers who discovered the link says cigarette smoking is a candidate.

The research, which points to a missing pair of genes on chromosome 3 as the cause of the cancer, was performed by scientists at the National Cancer Institute and the Uniformed Services University of the Health Sciences in Bethesda, Md., and the University of Texas Health Sciences Center in San Antonio. (Extracted from Science News, Vol. 132, 10 October 1987)

New compound against ovarian cancer

New radioactive compounds that act like oestrogen can be targeted specifically at ovarian cancer cells, where they destroy the genetic material with lethal doses of radiation, according to chemists at the Argonne National Laboratory and the University of Chicago. The new drugs are made by attaching a radioactive atom, bromine 80m, to synthetic forms of oestrogen. In vitro tests have been successful, and animal studies are now under way. Advanced ovarian cancer does not respond well to conventional treatments - surgery, chemotherapy and radiation - with only a 35 per cent cure rate, versus 75 per cent for other cancers of the reproductive organs.

The drugs capitalize on the fact that many ovarian tumours need oestrogen for growth. Nearly 50 per cent of ovarian cancers have increased numbers of oestrogen receptors, molecules on the cell surface that capture oestrogen and draw it into the cell. Once inside the cell, the drug concentrates in the nucleus, where the bromine 80m is incorporated into the DNA. The bromine quickly decays, emitting lethal particles that damage the DNA molecule, breaking it into pieces and killing the cell, according to E. DeSombre of the Bemay Institute at the University of Chicago, who is overseeing the preclinical tests. While some normal ovarian cells also have oestrogen receptors and can be affected by the therapy, O.T. DeJesus of the University of Chicago notes that cancer cells reproduce much faster and take up the radioactive compound more rapidly than normal cells. (Extracted from Industrial Chemist, August 1987)

How radiation causes cancer

Radiation causes cancer because cells turn cancerous when failing to repair radiation-inflicted damage, according to St. Andrew's University, Scotland. Translocation or accidental transfer of DNA to the wrong place occurs when cells try to mend broken chromosomes. For research purposes damage similar to that caused by radiation can be inflicted on cells by genetic engineering techniques under laboratory conditions. (Extracted from The Times, 11 September 1987)

New compound effective against tumours

A new amino acid compound is effective in preventing the formation of tumours, according to researchers at the National Institute of Health, Bethesda, Maryland. The compound, called peptide-11, was synthesized in the laboratory and its potency was demonstrated in test-tube experiments and tests with rats. Two groups of rats were injected with lung cancer cells. One of those groups also received injections of peptide-11. All of the rats were killed three weeks later, and the ones that received no peptide-11 had an average of 51 lung tumours each. Those who had been given high doses of the amino acid compound had none.

Peptide-11 apparently prevents cancer cells from penetrating blood vessels and entering an organ, according to H.K. Kleinman. Ordinarily, to pass through the blood vessel wall, a cancer cell attaches itself to the wall membrane and then erodes it. Peptide-11 seems to prevent the cancer cell from adhering to the membrane. The cell remains in the bloodstream, where it either dies or is destroyed by the immune system. Existing anticancer drugs are usually toxic to cancer cells but can also damage healthy cells. According to Kleinman, peptide-11 has been tested on a number of tumours and has caused few side effects. It has also been effective against Kaposi's sarcoma. Kleinman calls the drug 'very, very promising', but adds that years of laboratory tests may be needed before human trials begin. (Extracted from New York Times, 20 November 1987)

Cancer cells and differentiation factors

Biochemicals called differentiation factors may induce normal maturation of what would otherwise become cancer cells, according to J.J. Jiminez and A.A. Yunis of the University of Miami School of Medicine. Granulocyte colony stimulating factor may be a member of this mysterious class of substances. No one knows how many such factors there are or how they work. Until now, all that has been known is that there is some substance in extracts of certain mammalian organs that can induce differentiation in leukemic cells. The Miami researchers worked with myeloid leukemia cells. A lack of differentiation factors may allow leukemic cells to remain in the undifferentiated state. Adding larger amounts of differentiation factor to leukemic cells induces more of the cells to differentiate into normal mature white blood cells. Injections of the differentiation factor into rats helped them to survive injections of leukemic cells. Caged cells within the rats' bodies were also shown to differentiate when a differentiation factor was injected into them, indicating that the leukemic cells had not simply been killed off by an immune response. (Extracted from Science News, 5 December 1987)

Research on animal genes

Brain disease in cows

Vets at the Ministry of Agriculture have identified a new disease in cows that is causing dairy farmers some consternation. The fatal disease, which they have called bovine spongiform encephalopathy, causes degeneration of the brain. Afflicted cows eventually become unco-ordinated and difficult to handle. The first case was reported in 1985. Now there are 92 suspected cases in 53 herds, mostly in the South of England. So far 21 cases in 18 herds have been confirmed. All are Friesian/Holstein dairy animals.

No one yet knows the cause of the disease but there are some similarities with a group of neurological diseases caused by the so-called "unconventional slow viruses". This group of progressive diseases includes scrapie in sheep and goats, chronic wasting disease in mule deer and transmissible mink encephalopathy. In humans kuru and Creutzfeld-Jakob disease, both fatal neurological diseases, come into the same category. The precise nature of the agents causing this group of diseases is a matter of intense debate but all are infectious.

Like scrapie and the other diseases, bovine spongiform encephalopathy is insidious and progressive. A farmer is unlikely to suspect that a cow has the disease until it has almost run its course. Previously healthy animals become highly sensitive to normal stimuli, they grow apprehensive and their movements uncoordinated. In the final stages the cows may be frenzied and unpredictable and have to be slaughtered.

At autopsy, Gerald Wells and his colleagues at the Central Veterinary Laboratory in Weybridge, Surrey found that some areas of the brain were full of holes, giving it a spongy appearance. The pattern of holes shows some similarity with that in the other unconventional encephalopathies. In all these diseases an important diagnostic feature is the presence of proteinaceous fibrils seen in brain extracts in the electron microscope. No one knows for certain what the fibrils are - whether they are the agents of the disease, a type of subviral particle, as some researchers suggest, or are a product of the disease. The veterinary researchers analysed the brain tissue from cows that died from the disease and found similar fibrils. Brain tissue from healthy cows did not contain fibrils.

Scientists at the Neuropathogenesis Unit will look for evidence of transmission in experiments on mice, while Wells and his colleagues try to transmit the disease in cows. It will take at least two years of experiments before transmission can be proved.

What is certain is that the number of reported cases is increasing rapidly. Not all reports will turn out to be bovine spongiform encephalopathy. Farmers and vets might just be getting better at recognizing symptoms. If the disease turns out to be transmissible then it might spread to other breeds of cows. Many countries ban the import of sheep from areas where scrapie occurs. (Source: New Scientist, 5 November 1987)

Lactating for drugs

Genetic engineers in the US have created mutant mice that secrete a valuable human drug in the female's milk. The scientists say their technique, the first ever to turn lactation into drug manufacture, could make goats, cows or any lactating mammals into protein factories.

Integrated Genetics, a biotechnology company in Framingham, Massachusetts, and the National Institutes of Health unveiled "transgenic" mice that harbour a human gene for expressing tissue plasminogen activator (TPA). The protein can dissolve blood clots in humans.

Until now, companies have been vying for the new TPA market by creating the drug in vats of genetically altered micro-organisms. Alan Smith, a British molecular biologist who now directs research at Integrated Genetics, said transgenic animals can outproduce bacteria or yeasts in bioreactors by 10 to 100 times.

The scientists located and cloned the gene for producing TPA. They then fused it with a region of the genome that switches genes on and microinjected this "construct" into a fertilized mouse egg at the single-cell stage. The adult mouse, and offspring through five generations, integrated the gene and secreted TPA. (Source: New Scientist, 29 October 1987).

Female calves cloned

American Breeders and researchers at the University of Wisconsin have successfully cloned female calves. American Breeders, a division of W.R. Grace, says the accomplishment is a step toward reproducing the best traits of genetically superior animals in dairy herds. Nuclei were taken from 16-cell bovine embryos and implanted in single-cell bovine eggs from which nuclei had been removed. The engineered embryos were implanted in cows that then gave birth to the calves. Multiplication of a single embryo is potentially unlimited, allowing production of genetically equivalent animals. (Extracted from Chemical Week, 9 September 1987)

Lack of a protein lays down fat

Not all fat people eat too much. Certain metabolic and genetic disorders cause obesity, regardless of how much is consumed. A team of scientists, at Harvard Medical School, Boston, has identified a protein called adipsin in rodents which could provide a useful marker for some obesity disorders.

Adipsin is synthesized and secreted by cells involved in lipid metabolism, such as adipocytes and sciatic nerve cells (but not muscle cells). The protein comes in two forms, with molecular weights of 37 and 44 kilodaltons each. The difference depends on whether a side-chain has another group attached.

The exact purpose of adipsin is a bit of a mystery, even though researchers have identified and cloned the gene that produces it in mice. One clue to its function is that up to 77 per cent of its sequence of amino acids is the same as those found in such protein-digesting enzymes as trypsin, chymotrypsin and elastase. Jeffrey Flier, Bruce Spiegelman and their respective research groups at Harvard, isolated adipsin messenger RNA (mRNA) from three types of rodents. The first were genetically obese while the second had metabolic obesity induced in them, by injecting monosodium glutamate (which causes permanent disruption of the hypothalamus). The third type were normal rodents fattened on a "cafeteria-type" diet.

Compared with control animals, the genetically and metabolically obese rodents had levels of adipsin mRNA that were barely detectable and that could not be raised by fasting. In contrast, rodents on the "cafeteria diet" had normal levels of adipsin mRNA. The changes in the level of adipsin mRNA also correspond exactly to changes in the amounts of adipsin protein secreted by the rodents. Thus obesity, caused by sheer gluttony, can be distinguished from that caused by genetic or metabolic disorders.

If the same trend in adipsin levels can be found among humans, then this protein could become a useful clinical marker for genetic or metabolic obesity. (Source: New Scientist, 29 September 1987)

Better animal models for genetic defects

A new technique, developed by University of Utah biologists, perhaps will make it easier to understand why mutated genes cause such diseases as cystic fibrosis and muscular dystrophy. Researchers want to know, for instance, whether mutated genes underproduce or overproduce certain substances, such as enzymes.

Eventually, the technique, which makes good and bad genes interchangeable, may allow researchers to reduce the occurrence of genetic diseases in humans. They also may be able to place mutated human genes in mice to see which of the 50,000 genetic defects in humans they cause, according to Mario R. Capecchi.

Using a variation of gene therapy that researchers first used in 1980 to produce a black-and-white-haired mouse by injecting a black-hair gene into an albino mouse embryo, Capecchi and Kirk R. Thomas mutated the human hypoxanthine phosphoribosyl transferase (HPRT) gene and successfully injected it into mouse stem cells. Stem cells are embryo-derived cells that have not yet decided what they want to be.

The next step will be to inject the altered cells into mouse embryos, which would then express the mutated gene. The cell insertion step, Thomas says, is difficult, but it has been done in several other laboratories.

In humans, the mutated HPRT gene causes Lesch-Nyhan syndrome, characterized by mental retardation and self-mutilation, including finger biting, eye gouging and head banging. The normal HPRT gene produces an enzyme that converts a nucleic acid, guanine, into precursors for RNA and DNA. It is not known why reductions in the enzyme cause the syndrome.

To accomplish the change, Capecchi and Thomas went against a common perception among scientists: when DNA strands are injected into stem cells, they will randomly exchange information with other genes, but only 1 of 1 million interchanges will be correct. The researchers showed that they could increase the number to 1 of 1,000 by using larger strands and that they could increase the odds to even money by setting up a selection system that allows only the cells undergoing the preferred recombination to live.

The two researchers placed modified guanine into a dish of stem cells. Those cells undergoing the unwanted recombination died because the HPRT gene manufactured an enzyme that tried to convert the modified guanine into RNA and DNA precursors. The few remaining cells survived because they made the precursors from smaller building blocks. It is not known why a similar process is not sufficient in humans with mutated HPRT genes.

While this procedure will allow interchangeability between good and bad genes in mouse stem cells for experimental purposes, the same techniques may be used in human bone marrow, which would make the change only in that individual. Exchanging good genes for bad in human stem cells, however, poses technical and ethical problems. (Source: Science News, Vol. 132, 21 November 1987)

Research on plant genes

Identifying and improving nitrogen-fixers

Brazilian scientists may have discovered a new, acid-tolerant, nitrogen-fixing bacterium associated with sugar-cane - thereby adding to the growing body of evidence that nitrogen fixation occurs in grasses, as well as legumes.

Speaking at an international symposium on nitrogen fixation held in August at the Indonesian mountain resort of Cisarua, Johanna Dobereiner (a research scientist with Brazil's national agricultural research centre, EMBRAPA) said that 20 strains of the suspected nitrogen-fixing bacterium have now been isolated from the roots and the stems of five sugar-cane varieties from several locations. The isolates grow on a pure sugar-cane juice medium containing as much as 30 per cent sugar. They fix nitrogen at a pH as low as 2.8, which kills most other bacteria. Dobereiner says that the bacteria actually use the sugar to produce huge amounts of gluconic acid as a source of food.

There are only three known acid-loving bacteria - Frateuria, Gluconobacter, and Acetobacter - to which the new isolates could be related. None of these three, however, fixes nitrogen. The Brazilian scientists are now collaborating with a Belgian team to identify the new bacterium - preliminarily named Saccharobacter nitrocaptens - by DNA and ribosomal RNA sequencing. The assays have already determined that it is not Frateuria, the genus with which it shares the most phenotypic characteristics.

If confirmed, the research will have enormous implications for sugar producers around the world.

New results in mapping the genome of a species of Rhizobium have implications for the organization of DNA in other nitrogen-fixing bacteria. To this end, research on Rhizobium phaseoli - the symbiont of the common bean, Phaseolus vulgaris - is being conducted by several scientists at Mexico's Centro de Investigación sobre Fijación de Nitrogeno (Centre for the Investigation of Nitrogen Fixation). Rafael Palacios, who was the first to discover that R. phaseoli has several copies of nitrogen fixing gene sequences, reported that this pattern of repeated gene sequences is common to several other species, as well. According to Palacios, the presence of repeated gene sequences is responsible for frequent genetic recombination which can alter and even eliminate the symbiotic capability of the bacterium. Palacios explained that the lack of stability has important implications for the preparation of nitrogen-fixing soil inoculants. He also stressed the necessity of gaining better insight into how much and in what way genetic information is transferred between strains in field environments.

To identify specific gene functions, Palacios cut the bacterium's plasmid into several fragements, which he then reintroduced into R. phaseoli (cured of its plasmid) to determine the function of each fragment. To study the interaction of particular bacterial genes in the overall bacterial-plant symbiotic relationship, Palacio's colleague, Frederico Sanchez, has been introducing specific-gene-mutated bacteria into bean plants and a tree legume (Leucaena esculenta). This procedure should ultimately permit genetic engineering for improved characteristics. Nearer-term, a genome diagnostic kit is being developed, which will allow breeders and farmers to determine whether a given bacterium is a good nitrogen-fixer.

Another symbiotic relationship being dissected is that of an aquatic fern, Azolla, and its cyanobacterial symbiont, Anabaena azollae. Azolla is one of the most commonly used nitrogen-fixing plants; it is difficult to exploit commercially, however, because superior strains rarely survive transfer into a new environment. But the bacteria might. According to Jacek Plazinski (Australian National University), the difficulty with determining the success of such a transfer has been the phenotypic similarity among many different Anabaena genotypes. But, with the advent of DNA hybridization techniques, a research team of Australian, French, and Chinese scientists hope to surmount this problem.

The group has developed three DNA probes to aid in the positive identification of Anabaena genotypes. The first probe - based on nifH and nifS nitrogenase genes isolated from a non-symbiotic Anabaena (sp. PCC 7120) - is able to differentiate between Anabaena species. And RuBisCo (ribulose-1, 5-biphosphate carboxylase/oxygenase) and rRNA probes

isolated from Anacystis nidulans can differentiate between different Anabaena isolated from the same Azolla plant (all would appear the same from a taxonomic point of view). The third probe - based on a native Anabaena plasmid subfragment - permits conclusive identification of the nine Anabaena genotypes known to exist. (Source: Bio/Technology, Vol. 5, October 1987)

Grass grows to keep out salt

Plants that live in the most extreme environments are usually adapted physiologically to cope. Now, it seems, the structure of such plants also alters to give them an advantage in their harsh conditions. That is the conclusion of T. McNeilly, M. Ashraf and C. Veltkamp from the University of Liverpool who studied with a scanning electron microscope the leaves of three species of grass that can tolerate salt. They collected Agrostis stolonifera, Holcus lanatus and Dactylis glomerata from an exposed sea cliff at Abraham's Bosom on Anglesey, North Wales, and compared them with leaves from plants from the university's botanic garden.

In all three species the stomata on the upper surface of the leaves of the coastal plants were sunk deeper into the epidermis than those on the inland plants. Moreover, the researchers saw plates of wax on the guard cells of the stomata.

A. stolonifera and H. lanatus showed other differences: the salt-sprayed Agrostis had small papillae on its upper epidermis, and the Holcus leaves from the coast were much hairier than usual. These features reduce the permeability of leaves to salt spray and so reduce the chance of salt entering the leaves, either through stomata or through the cuticle of guard cells. (Source: New Scientist, 15 October 1987)

Ultrasound used to fuse living cells

Living cells can be fused using ultrasound, according to U. Zimmerman of Wurzburg (FRG). An earlier study used alternating electric current to fuse a petunia cell and a human blood cell to form a new cell with the characteristics of a plant but also with the ability to produce haemoglobin. The cells prefer to be in a salty solution, however, which conducts the electricity too well. But the cells can be put in a salty solution and fused using ultrasound. The technique has worked with mouse cells in solution. An electric current is still used to force the cells into a string like a necklace. Twenty-microsecond bursts of direct current then burst the cell membranes long enough to allow the cells to fuse but not long enough for contents to spill out. (Extracted from New Scientist, 10 December 1987)

Yams help themselves to fertilizer

One of the great hopes of agriculture is to make crop plants grow their own fertilizer. Yams offer an alternative "self-grown" bacterial fertilizer - on their leaves.

Most plants of the yam family, the Dioscoreaceae, have long tips at the ends of their leaves. These help to drain water from the leaves during heavy downpours. But the tips also contain "glands" buried deep inside folds running along their margins. The glands shelter bacteria.

To find out what relationship the bacteria have to the yam, I.M. Miller and M. Reporter, of the Batelle-Kettering Laboratory in Yellow Springs, Ohio, examined the leaves of the West African yam, Dioscorea sansibarensis, under the microscope. They also tested them chemically for signs of nitrogen fixation.

The two botanists found an intimate relationship between bacteria and the yam. The glands in the leaf are hollow chambers containing numerous microscopic hairs, some of which are packed with a range of Gram-negative bacteria. Slime exuded from the other hairs fills the hollow of the chambers. The tissues around the glands are highly folded, providing a large surface through which to absorb nutrients oozing from the bacteria and trapped by the slime. The area is well plumbed with vascular tissue for carrying away nourishment to the rest of the plant.

Miller and Reporter also found that plants deprived of their leaf bacteria grow more slowly and produce only a few yellowy leaves instead of the lush green foliage of plants that are infected with bacteria. The plant and the bacteria have a symbiotic relationship, the plant providing the bacteria with a protected home and the bacteria supplying some sort of nourishment to the plant. Yet the classic test for nitrogen-fixation failed. If the bacteria were not fixing nitrogen, what exactly are they passing to the plant? No one yet knows. Genetic engineers, however, should be attracted to this relationship that already benefits the yam, which is an important crop in Africa. (Source: New Scientist, 29 October 1987)

Genetically modified cabbage

Plantech Research Institute, a joint venture of Mitsubishi and Mitsubishi Chemical Industries, has genetically modified cabbage for the first time in the world. A kanamycin-resistant gene was inserted into cabbage with a binary vector developed from a cabbage mosaic virus and a wild strain of agrobacterium. Crown galls produced by the inoculated cabbage can be made to produce buds, from which can be grown kanamycin-resistant cabbage. (Source: Technology Update, 28 September 1987)

Research on yeast and fungus genes

Growing algae for drugs

Algae grown in "photobioreactors" may provide drugs for the future. British research on culturing algae in controlled conditions is approaching the stage when it will be a commercially viable operation. The products can be used to produce various high value organic compounds for the food and drug industries. Some of the most promising products that can be extracted from algae are polyunsaturated fatty acids such as ecosapentanoic acid and gamalinolenic acid. Algae and fish oils are the only sources of these. They are widely used as diet supplements, or to counter arthritis, for example.

Fermentation is a time-honoured way of producing a valuable organic chemical, alcohol, from micro-organisms. The organism involved in this case is yeast, which is a fungus. Scientists in the microbiology department of Queen Elizabeth College, London, have developed the idea one stage further. They are using algae to produce valuable products by growing them in tubes under controlled environmental conditions.

John Pirt, the head of the department, explains that the photobioreactors convert sunlight much more efficiently than growing algae in open-air ponds, for example. Although ponds are much deeper and can, in theory, have a greater depth of algae to absorb the sunlight, photobioreactors can accommodate over 200 times the densities of algae. This is mainly because the system is totally closed and much easier to control.

To grow algae in a photobioreactor, all nutrients and carbon dioxide must be supplied. However, none of these materials can escape and their concentrations in

the culture solution can be controlled for optimum productivity. Temperature, acidity and salinity of the solution can also be regulated and contamination with other strains of algae can be prevented. The algae can be harvested continually by sedimentation. Oxygen, produced as a waste produce of photosynthesis, can also be collected from the reactor.

Other products that can be made by algae include betacarotene, a naturally occurring yellow food colouring which is now replacing the synthetic dye tartrazine and one red alga can be cultured to produce a red dye, phycoerytnrin, which now costs £100 per thousandth of a gram. (Source: New Scientist, 1 October 1987)

Research on bacterial genes

Progress in fermentation of biotin

Nippon Zeon (Tokyo) and French biotechnology company Transgène (Strasbourg), which have been co-operating since September 1985 to develop an efficient fermentation route for vitamin H, biotin, reported some promising results in a paper presented to the 60th annual meeting of the Japanese Biochemical Society. Researchers from the two companies say that they have expressed the bio-b gene of Bacillus sphaericus, a bacillus that produces high levels of biotin in Escherichia coli, and that they have achieved improved biotin synthesis rates. Biotin, sold as a supplement for human and animal nutrition and in cosmetic preparations, commands an annual market of $100 million/year, say the companies. (Source: Chemical Week, 21 October 1987)

Canadian company offers rhizobacteria

Allelix Agriculture offers naturally-occuring plant growth-promoting rhizobacteria (PGPR). Allelix has not modified the bacteria, but says that inoculating soil with the bacteria can improve crop yields up to 30 per cent. Strains now in field trials can aid the growth of leguminous crops. Other strains might aid the growth of other crops. How the bacteria aid plant growth is not clear, but they appear to promote root growth, perhaps by suppressing harmful bacteria or by producing compounds that promote growth. Field trials at the University of Guelph have increased yields 1-15 per cent for all crop types in all soil types. PGPR products could be on sale by 1990. Allelix estimates the market at $50 million. (Extracted from New Scientist, 15 October 1987)

New antibiotic

Abbott Laboratories has developed a new class of antibiotic that inhibits production of lipopolysaccharide, a component of bacterial cell membrane. Without lipopolysaccharide, the bacteria is unable to reproduce. The bacteria are also more susceptible to conventional antibiotics. The bacterial enzyme that is inhibited (CMP-KDO synthetase) was identified and cloned and its structure determined by NMR. Once the structure was known, scientists designed an inhibitor to mimic the enzyme's natural target. The affected enzyme is unique to gram-negative bacteria. Researchers still need to develop a way to deliver the inhibitor into the bacterial cell. Carriers now being tested do not enter all gram-negative bacteria equally effectively. Once inside the cell, the inhibitor is cleaved by other bacterial enzymes. The carriers now being tested are also very short-lived in the human body. (Extracted from Science News, 19 September 1987)

Bacteria produce magnets

Bacteria have been isolated to reduce large amounts of ferric iron to the magnetic iron ore magnetite, Fe_3O_4, by D.R. Lovley, G.L. Nord and E.J.P. Phillips of US Geological Survey and J.F. Stolz of the University of Massachusetts (Amherst). The bacteria, GS-15, are the first organisms known to effectively couple oxidation of organic matter to reduction of ferric iron during growth under anaerobic conditions. The bacteria produce two moles of carbon dioxide and reduce eight moles of ferric iron to ferrous iron for every mole of acetate they oxidize.

Unlike magnetotactic bacteria, GS-15 organisms do not respond to an applied magnetic field, suggesting that magnetite is formed outside the cell from ferrous irons sent across the cell membrane. The researchers believe that the bacteria's novel metabolism may account for much of the magnetite in oxygen-depleted sediments and in ancient iron formations and hydrocarbon deposits. (Abstracted with permission from Chemical and Engineering News, 23 November 1987. Copyright (1987) American Chemical Society)

Bacterium used to breed root cultures

Louisiana State University researchers use a bacterium to breed root cultures for their valuable elements used to make drugs, fragrances, dyes and pesticides. Left on their own, plant roots often do not develop fast enough to be commercially useful. By exposing plants to a bacterium that causes hairy root disease, researchers have been able to get plant roots to overproduce the hormones that stimulate root division so they rapidly grow hair-like rootlets. The roots are then chopped off, treated with antibiotics to kill the bacteria, and raised as root cultures that grow virtually without end. Plant roots that make pesticides are currently being tested, but a number of sweeteners and fragrances made by plants such as jasmine, licorice and sandalwood are also being considered. (Extracted from Business Week, 7 December 1987)

Deep sea microbes fix carbon without light

A team of American scientists has shown experimentally that some marine organisms can fix carbon directly using sulphur.

Biologists have known for some years that habitats rich in sulphides, such as terrestrial hot springs, support large numbers of bacteria. These micro-organisms acquire their energy to convert inorganic compounds to organic compounds, not from the Sun, but from the oxidation of hydrogen sulphide, a process called chemosynthesis. The general equation for the process is:

$$CO_2 + H_2S + H_2O + O_2 \longrightarrow [CH_2O] + H_2SO_4.$$

These bacteria, like green plants, are primary producers. They also occur around hydrothermal vents, hot spots on the deep ocean floor, either living freely or in close association with animals, such as clams and tube worms. These "chemolithotrophs" could form the base of the food chain at vents, providing nutrients for other animals in the community. Scientists studying the communities around vents have assumed that this is probably the case for some time. Researchers have shown that a marine animal can fix carbon using sulphur compounds. (Journal of Experimental Biology, Vol. 133, p. 1).

James Childress and his colleagues at the University of California, Santa Barbara, performed their experiments on Solemys reidi, a burrowing, gutless clam that has symbiotic sulphur-oxidizing bacteria in its gills. This particular clam lives, not in the deep sea but in sediments rich in sulphur, such as the effluents from pulp-mills and around sewage outfalls. Last year, Mark Powell and George Somero of the Scripps Institution of Oceanography at La Jolla, California, showed that the first step in sulphur oxidation takes place in the clam's own tissues rather than in the bacteria they

mouse. This reaction provides energy, in the form of molecules of adenosine triphosphate (ATP), to enable the bacteria to fix carbon.

The researchers proposed that the clam oxidises sulphide in its tissues and generates ATP in the process. Another major product of the reaction is thiosulphate, which is transported to the bacteria living in the clam's gills. The bacteria further oxidize the thiosulphate to sulphite, and probably also to sulphate. These reactions also generate ATP and the electron carrier NAD(P)H, which provide the energy to fix carbon. If the concentration of oxygen is too low or that of sulphide too high, the sulphide diffuses into the animal's tissues and blocks the action of cytochrome c oxidase, one of the enzymes essential for normal aerobic metabolism in the clam and the bacteria. Normal metabolism then stops. (Source: New Scientist, 24/31 December 1987)

Research on viral genes

Herpes latency makes "anti-sense"

A backwards genetic message may be the reason why herpes simplex viruses lie dormant between occasional attacks on their human hosts, scientists reported this week. Because such latency periods are characteristic of genital herpes and cold sores, as well as some other viral diseases like shingles, the researchers say that further studies on the unusual gene may suggest a way to keep inactive those viruses that persist in the human body.

It is well established that once a person is infected with herpes simplex type 1 viruses, the viruses "rest" - or at most grow very slowly - somewhere in the nerves throughout life, waiting to reactivate and ambush the host with painful attacks. Why and how the viruses remain inactive is of considerable interest in terms of public health.

Scientists at the National Institute of Allergy and Infectious Diseases (NIAID) in Bethesda, Maryland, hunted for dormant herpes simplex viruses in facial nerve tissue taken from cadavers that did not have signs of active herpes infections. The NIAID group found large amounts of RNA similar in structure to a previously identified viral gene that forces infected host cells to produce a viral protein called ICPO and helps regulate subsequent steps in viral replication. But the new RNA was a mirror image of the ICPO gene, and therefore is what geneticists call "anti-sense" RNA.

The NIAID researchers, with collaborators from the Office of the Chief Medical Examiner in Baltimore, say that the anti-sense RNA may cause latency by either blocking activity of the normal viral RNA, or coding for a protein that interferes with virus growth. If the RNA turns out to be a regulator, it would be the first time such a mechanism would be demonstrated outside bacteria.

The current study is an extension of work in laboratory mice reported earlier this year by University of California researchers in Los Angeles and Irvine. More experiments must be done to prove whether the anti-sense RNA is really the key factor in establishing and maintaining latency, and whether it comes from the virus. The approach also may be useful in studying factors like stress, which is known to reactivate the herpes virus and in studying latency in other viral infections. (Extracted from Science News, Vol. 132, 5 December 1987)

Herpes virus transplanted with organs?

The virus causing genital herpes apparently can be transferred to transplant recipients from contaminated donor organs and tissues, say scientists from the University of Minnesota Hospital in Minneapolis. Although the stress of organ transplantation has been known to reactivate latent herpes viruses in a previously infected patient, disseminated herpes infections seen in two transplant recipients at the Minnesota hospital were caused by viruses in the donated organs. The transplanted heart and pancreas were suspected after the two patients - previously uninfected with herpes simplex virus type 2 - developed severe herpes infections of the blood and liver. One of the patients eventually died from the infection. Subsequent testing of blood samples from the donors showed a previous infection, suggesting that this virus may move from the genital site and become latent in other areas like the donated organs, says Jesse L. Goodman. Earlier this year, similar transmission occurred in two kidney recipients in Pittsburgh. Although this type of viral transmission is very rare in the transplant field, care should be taken when organs or tissues from infected donors are used. (Source: Science News, Vol. 132, 17 October 1987)

Viruses in search of "compatible" diseases

Despite massive efforts by medical science to match diseases with specific causes, new agents of disease can appear without warning and disrupt any scientific self-confidence. The viral cause of AIDS, for example, existed for many years, yet researchers only recently identified the human immunodeficiency virus (HIV) and its devastating results. Scientists have emphasized that there are other "new" viruses whose complete medical consequences are undiscovered. These viruses include those that may be responsible for foetal death, the controversial chronic fatigue syndrome and lymph node cancers.

One such agent, human parvovirus B19, was "a virus looking for a disease" until 1981 - when it was first associated with aplastic crisis, a shutdown of the bone marrow's production of blood cells, says Larry Anderson of the Centres for Disease Control (CDC) in Atlanta. Researchers later tied the virus to severe skin rashes and arthritis.

This year, says Anderson, reports indicate that the virus also may be responsible for some foetal deaths, as well as for bone marrow failure among patients with defective immune systems. Scientists now think the threat of parvovirus B19 may be most severe for AIDS patients, who cannot defend themselves against additional infections. Studies are under way to determine the prevalence of B19 infection in the general population and to confirm the link between the virus and specific diseases.

The human B-lymphotropic herpes virus (HBLV), first described in 1986, is another example of a virus with an incomplete medical history. The virus is unusual in that it is released from infected cells in membrane-bound packets, rather than through disruption of the cell. But this lack of cell "lysis" during HBLV infection does not mean the virus is harmless. Preliminary studies by Zaki Salahuddin of the National Cancer Institute and others have found HBLV in patients with various lymph node cancers, although no direct association between the virus and malignancy has been established.

Scientists are developing an assay for a herpes virus they recently isolated, which appears to be identical to the HBLV found by Salahuddin's group. Using the test, the scientists are tracking the virus, which they call human herpes virus VI (HHV-VI).

Antibody production against HHV-VI apparently peaks sometime early in life, then "dwindles" as a person ages. Despite its apparent affinity for children, the virus is being considered, along with Epstein-Barr virus, as a possible cause of the adult condition called chronic fatigue syndrome, which scientists say may or may not be a distinct medical disorder.

Other early data suggest that HHV-VI can be sexually transmitted, and that in the general population, women are more likely than men to be infected. Another curious aspect of the new herpes virus is that it apparently inhibits HIV replication in cell cultures by 50 per cent. (Extracted from Science News, Vol. 132, 17 October 1987)

Irradiated viruses might delay disease

Viruses inactivated by irradiation will form the basis of a new potential therapy for people who are infected by HIV but have not yet developed any symptoms. If the first tests are successful, the preparation could act as a vaccine in uninfected people.

Researchers in California hope to begin testing the therapy on humans, subject to approval by the Food and Drugs Administration of the US. Doctors at the University Medical Centre in Sacramento have asked for 40 volunteers for the trial, only half of whom would receive the therapy. The preparation that these people will receive will contain HIV that has been irradiated so that it is inactive and unable to infect cells. Scientists at the University of California at Davis will check each batch of irradiated viruses to ensure that is pure and noninfective.

The company which will produce the preparation is the Immune Response Corporation of La Jolla, in California in collaboration with Jonas Salk, head of the Salk Institute, also in La Jolla. Salk developed a vaccine consisting of inactivated whole virus against poliomyelitis in 1954. (Extracted from New Scientist, 1 October 1987)

Babies may be at lower risk than first thought

Information on the likelihood of an infected woman passing HIV infection to her unborn child is hard to come by in the West because so few heterosexuals are infected. One study, in Edinburgh, of children born to women who are intravenous drug users, found that the rate of transmission to the child is about 50 per cent.

Results from Zaire, however, from studies of much larger numbers of women, suggest that the rate of transmission may be of the order of 25 per cent. The research also suggested that the woman is more likely to transmit the virus if she has AIDS, or severe disease related to HIV infection, than if she is infected but asymptomatic.

Researchers with Project Sida in Kinshasa, Zaire, and colleagues from the US, studied women attending two hospitals in the city. At the Mama Yemo Hospital, which serves a relatively poor part of Kinshasa, tests showed that 332 (5.7 per cent) of 6,000 pregnant women were infected with HIV. Of the 332, 50 per cent had AIDS, and 15 per cent had disease attributable to HIV infection.

The researchers, led by B. N'Galy, went on to test 70 of the children born to infected mothers, at delivery, for antibodies of the type known as IgM, which would suggest that the children were themselves infected. (Antibodies can cross the placenta, but only IgG antibodies, not IgM.) They found that 17 (24 per cent) of the 70 babies had IgM antibodies.

Seven months later, the researchers followed up the original test. They found that 18 per cent of the children born to infected mothers had died, compared with only 1 per cent of children born to sero-negative mothers.

The research is still continuing. There may also be a risk of infection via breast milk, which these studies do not take into account. (Source: New Scientist, 15 October 1987)

AIDS mothers'-milk risk

Mothers infected with the AIDS virus could pass the disease on to their infants in between 25 to 50 per cent of cases, according to recent suggestive evidence revealed by the World Health Organization (WHO) as a result of its June Consultation on Breast-Feeding/Breast Milk and HIV Infection. In view of the importance of breast milk and breast-feeding for the health of infants and young children, and of the increasing prevalence of human immunodeficiency virus (HIV) in many parts of the world, WHO's Special Programme on AIDS and its Division of Family Health organized the meeting in June to review currently available information.

WHO says the risk of transmission may depend on a number of factors including: the timing of the mother's HIV infection; the mother's immunological and overall health status; her parity and intercurrent infections; and other possible factors.

Transmission of HIV from infected mothers to their infants may occur before, during or shortly after birth. That HIV could be transmitted through breast-feeding/breast milk is supported by a report that HIV can be cultured from breast milk from infected mothers. A substantial number of infants born to infected mothers have been breast-fed without their having any evidence of acquiring HIV infection. On the other hand, there are a few reported cases where mothers became infected post-partum through blood transfusions, and where their infants, in turn, became infected, possibly through breast-feeding. This does not necessarily imply, however, that such transmission occurs among mothers who were infected with HIV before or during pregnancy.

The immunological, nutritional, psychosocial and child-spacing benefits of breast milk/breast-feeding are well recognized and have been reflected increasingly in national and international policies on maternal and child health.

Breast milk is also important in preventing intercurrent infections which could accelerate progression of HIV-related disease in already infected infants. Therefore, its importance for the survival and development of infants and young children should continue to be emphasized in all health and nutrition policies.

In August, the Special Programme on AIDS announced that over $US 13 million has been raised for AIDS prevention and control activities in the coming year for Ethiopia, Kenya, Rwanda and Tanzania. These countries join Uganda in having achieved full funding for the first year of operation of comprehensive national AIDS programmes. The funds will ensure that scarce resources are not diverted from other important health priorities. (Source: Development Forum, Vol. XV, No. 9, November-December 1987)

Dementia may strike before other symptoms

Evidence is accumulating that the human immunodeficiency virus may damage the brain long before signs of disease surface elsewhere in the body. Changes in behaviour, memory and control of movement can appear relatively early in the course of infection. It also seems that the brain becomes a principal reservoir for the virus soon after infection.

Tests on patients with early symptoms due to HIV infection, such as lymphadenopathy (persistently swollen lymph glands), have shown signs of brain disease.

It is difficult to separate those symptoms that are due to HIV from the psychological effects on people who know that they are infected. Another problem is that tests of memory, concentration and

psychomotor ability need further refinement. None the less, the available results are worrying. One difficulty is now to determine the ability of seropositive people to cope with high-performance jobs. The US forces have begun their own studies of neuropsychological effects among seropositive individuals. Some results of studies on civilians are already available, however.

Unlike Alzheimer's disease, which affects the cerebral cortex, AIDS dementia results primarily from damage to the deep structure of the brain. The central white matter of the brain is most severely affected, particularly the basal ganglia and thalamus. Imaging techniques such as computerized tomography and magnetic resonance imaging show enlargement of the furrows - called sulci - on the surface of the brain, and of the ventricles (cavities) inside it.

A variety of symptoms result from these abnormalities. First, affected people may experience difficulty in concentrating or in performing complex sequential mental tasks. They may have to read paragraphs several times in order to understand them. They become confused by the plots of television programmes. They complain of missing appointments and start keeping lists to aid their short-term memory.

Early motor symptoms usually involve the legs, resulting in clumsiness, weakness and altered gait. Handwriting may change. Sufferers may drop things more frequently. Behavioural changes include apathy, loss of spontaneity, social withdrawal and change in personality.

Examinations for AIDS dementia complex usually include standard tests for neurological impairment. Affected individuals take longer to put grooved pegs into the holes on a board. They are unable to remember series of digits. They are slow to respond to stimuli, whether with speech or movements. For example, they may have difficulty in moving their eyes to focus on an object.

As the impairment progresses, the patient becomes mute, confused and incontinent.

Scientists are gradually beginning to formulate theories about how the virus mediates these effects on the nervous system. Several researchers have shown that the virus enters the brain in macrophages, large mobile cells of the immune system that fight infection. According to the "Trojan Horse" hypothesis, infected macrophages cross into the brain, perhaps in response to an infection such as cytomegalovirus. Once there, these cells harbour the virus. Such infected macrophages may be the origin of the abnormally large cells with many nuclei which are sometimes present in the brains of AIDS patients. These "multinucleated giant cells", as they are called, resemble cells in laboratory cultures that fuse together when infected with HIV.

David Ho, of the Cedars-Sinai Medical Centre in Los Angeles, and his colleagues Roger Pomerantz and Joan Kaplan, have suggested two hypotheses to explain how the virus does its damage. First, the infected macrophages might release toxic chemicals. These substances might damage the nerve cells of the brain and the glial cells, which protect the nerve cells and manufacture the insulation around their fibres. Or, the toxins might attract inflammatory cells which carry out the damage themselves.

The second possibility is that the infected macrophages might affect the cells of the blood-brain barrier in some way, with the result that the permeability of the barrier changes. The blood-brain barrier keeps the bloodstream separate from the fluid that bathes the central nervous system. A change in its permeability would alter the delicately balanced environment of the central nervous system, upsetting the function of the nerve cells.

Another hypothesis is that HIV may be able to infect glial cells. Investigators have also found evidence on rare occasions for HIV infection in nerve cells. But it is still not clear to what extent such infection accounts for the malfunctions of the nervous system in people with AIDS.

One hypothesis is that viral proteins released by infected macrophages could interfere directly with the function of nerve cells. Recent work, again by David Ho, but this time with Mark Lee and Mark Gurney of the University of Chicago, provides support for this theory. They have shown that part of the envelope glycoprotein of HIV is similar to a substance called neuroleukin. Neuroleukin, a protein which is found in human skeletal muscles, brain and bone marrow, prolongs the life of embryonic nerve cells in laboratory cultures.

Ho, Lee and Gurney found that, in the absence of neuroleukin, 90 per cent of embryonic nerve cells died within 48 hours in a laboratory culture. If they added neuroleukin, however, up to 45 per cent of cells began to grow and develop within 12 hours. The same thing happened if they added a substance called nerve growth factor. The team then tried adding HIV to cultures of nerve cells supported by either neuroleukin or nerve growth factor.

They found that HIV consistently suppressed the growth of the nerve cells supported by neuroleukin, but did not affect those cells grown in nerve growth factor. After further tests, they concluded that the viral envelope protein, gp120, was able to inhibit the activity of neuroleukin, but not that of nerve growth factor. Subsequent analysis of the sequences of amino acids in both neuroleukin and gp120 showed that they shared the same amino acids at 14 out of 47 sites - a similarity of about 30 per cent. This nomology, Ho and co-workers say, appears in all isolates (strains) of HIV for which information is available on the sequence of gp120.

Ho, Pomerantz and Kaplan say that these results suggest that the viral envelope protein may complete with neuroleukin for binding to nerve cells. Those cells to which gp120 binds probably die sooner.

Whatever the mechanism that causes dementia, researchers are left with the problem of how to evaluate objectively their patients' symptoms.

Fortunately for patients, preliminary research suggests that zidovudine (formerly known as AZT), which can cross the blood-brain barrier, can relieve dementia. But further research is needed to find out whether the dementia is reversible. (Extracted from New Scientist, 10 December 1987)

Blood blot samples

Fast and inexpensive ways of taking blood samples for AIDS tests are needed in developing countries where well-equipped laboratories are few. Scientists at Johns Hopkins University in Baltimore, Maryland, have found that a few drops of blood on filter paper are sufficient and can even be kept for several weeks.

Homayoon Farzadegan, an epidemiologist at the school of public health, first applied the method to test blood for the cost of the hepatitis B virus. Recently, he took blood from African AIDS patients and from healthy hospital workers, using both finger pricks and standard venepuncture. The blood from finger pricks went onto filter paper, was dried

overnight at room temperature and then sealed in plastic bags. Tests for antibodies to the AIDS virus showed that the two methods were equally accurate. Further tests showed that the paper samples can be kept for up to eight weeks without altering test results.

Farzadegan says the best method for shipping the blood is to use a hole punch on the paper blots to create small discs of the sample. These "stamps" save space and avoid complaints by postal workers about leaking samples. (Source: New Scientist, 12 November 1987)

Threat to younger women

Although the ratio of HIV infection in men and women in Africa is commonly quoted as being about 1:1, several researchers reported finding many more cases of infection in women than in men - in younger age groups, at least. A.R. Neequaye, of Accra in Ghana, said that in 1986, the ratio of infected women to infected men was 11.6:1. By 1987, the ratio had dropped to 6.3:1;

This fall suggests, Neequaye said, that HIV infection had only recently been introduced into the country by returning travellers. One of the risk factors for AIDS in Ghana is a stay in a neighbouring country.

Prostitutes are also a high-risk group in Ghana. Four out of 162 prostitutes tested were seropositive for HIV antibodies, compared with none of 288 blood donors, and none of 168 laboratory workers. One route by which HIV could have entered the country is via prostitutes who go to neighbouring Côte d'Ivoire to work.

Other groups of investigators reported that more women than men were infected in younger age groups. In older age groups, sometimes more men than women had the virus. One suggestion for this observation was that men, young and old, may prefer to have sexual intercourse with younger women. (Source: New Scientist, 15 October 1987)

Spermicides with anti-HIV activity sought

R&D proposals are being sought on chemicals and/or delivery systems for spermicides with virucidal activity against HIV, the virus that causes acquired immune deficiency syndrome (AIDS). The proposals are being sought by the Contraceptive Research & Development (CONRAD) Programme, sponsored by the US Agency for International Development to develop improved contraceptive technology. Additional funding has been supplied by the agency, since one aspect of the programme is development of improved chemical and mechanical barriers against sperm. Virucidal activity that would prevent AIDS transmission is seen as a natural extension of the concept. Those interested can contact: Henry L. Gabelnick, Director of Extramural Programmes and Product Development, CONRAD Programme, 1611 North Kent St., Suite 806, Arlington, Va. 22209. (Reprinted with permission from Chemical and Engineering News, 12 October 1987. Copyright (1987) American Chemical Society)

Advances on AIDS

Further hope for AIDS sufferers came recently with announcements that a potential therapy for preventing one of the diseases associated with AIDS has been encouraged by the US Government in the hope of accelerating research on it, and that an antibiotic may be effective against the virus.

The US Food and Drug Administration has given orphan drug status to the aerosol form of pentamidine, a pneumonia therapy now given by injection, as a preventative treatment for Pneumocystis carinii pneumonia (PCP), a common opportunistic infection in people infected with the AIDS virus.

The drug company Fisons is filing a new drug application for this form of pentamidine with the FDA, which could give the company exclusive marketing rights for seven years.

According to Fisons, preliminary clinical trials show that aerosol pentamidine may be effective in inhibiting PCP and causes no serious side-effects. The injected form, however, can have severe side-effects such as liver damage and nausea.

Meanwhile, researchers at the University Hospital of Copenhagen and the Clinical Research Centre in Harrow, UK, have found that fusidic acid, a steroidal antibiotic made by Leo Laboratories, is active against the AIDS virus in vitro and produced "striking clinical improvement" in a 58-year-old man with AIDS.

The researchers found that fusidic acid had no effect against the viral reverse transcriptase, and suggested that it may act as an inhibitor of the viral protease, because its antibacterial action is due to protein synthesis inhibition. (Source: Chemistry and Industry, 19 October 1987)

Relative of AIDS virus appears in Italy

Another retrovirus that infects humans has emerged. Scientists in Rome recently isolated the new virus and named it human T-cell lymphotropic virus type 5 (HTLV-5). The virus is related to but distinct from the human immunodeficiency virus (HIV) that causes AIDS. Instead, it appears in people suffering from a rare lymphoma called mycosis fungoides.

A team of scientists at the University of Rome and the University of L'Aquila had been studying the human T-cell leukaemias caused by HTLV-1 and HTLV-2. Robert Gallo of the National Cancer Institute in the US classified these as the first human retroviruses - that is, viruses that infect cells and transform their own RNA into the host's own DNA.

The Italians discovered a patient whose lymphocytes behaved as if they were infected with a human retrovirus. Yet tests for HTLV-1, HTLV-2 and HIV proved negative.

Tests with gene probes and with restriction enzymes, which cut DNA in distinctive patterns, confirmed that the patient's virus was a distinct variety. It was not the recently discovered retrovirus from Africa, called HIV-2, which seems to cause a less rapid form of AIDS.

HTLV-5 was found by Vittorio Manzari and his colleagues in Italy. They had seven patients infected with the same mysterious virus. All were Italian males over the age of 50, who were at no apparent risk from AIDS. They all had mycosis fungoides. The new virus, like HTLV-1, induces immune cells to proliferate, but in this case, the affected class of immune cells is different. Some of Manzari's patients eventually developed leukaemia and died. One of those infected was the wife of a patient, suggesting that the virus might, like the other human retroviruses, be transmitted sexually.

Like HTLV-1 and HTLV-2, the Italian virus causes certain lymphocytes, the cells of the immune system,

to proliferate. Laboratory tests also suggest that, physically, the new virus is closest to HTLV-1. HIV-1 and HIV-2 do just the opposite: they kill lymphocytes, thus destroying the body's immune system. (Source: New Scientist, 17 December 1987)

Decoy protein tempts AIDS virus away from body's defence system

Scientists in the US have manufactured a cellular protein that in laboratory experiments acts as a decoy for the AIDS virus, preventing it from attacking the body's immune system.

Scientists hailed development of the decoy protein as exciting and promising, but also cautioned that the technique is by no means proven and that it must first undergo tests in animals and humans.

At least three US biotechnology companies are vying to develop the technique. Scientists from Genentech of south San Francisco and from Harvard Medical School in Boston, announced that in a test tube they had saved more than 99 per cent of T-4 cells, a key component of the immune system, from infection. Two days earlier, Smith Kline and French Laboratories in Philadelphia announced that it had achieved similar results working with scientists from Columbia University in New York. Biogen, a biotechnology company in Cambridge, Massachusetts, is also in the race.

The technique, developed jointly by Genentech and Harvard, which is similar to what each of the companies is doing, involved using mammalian cells to clone the CD4 receptor protein, a protein on the surface of the T-4 cells. The envelope glycoprotein, gp120, on the surface of the AIDS virus binds to CD4 receptor when the virus attacks the immune system.

The scientists made soluble, free-floating versions of the receptor that were not attached to T-4 cells. The free-floating cells, manufactured in large numbers, acted as a decoy and scavenged the invading virus before it reached the normal receptors on the T-4 cell. Trans-membrane and cytoplasmic regions were removed from the cloned protein so that once it had bound to gp120, it would not enter the T-4 cells.

Several crucial questions will have to be answered before the technique is verified. Scientists do not know how much of the virus needs to be destroyed before there is a therapeutic effect.

Another problem is the possibility that soluble CD4, by swamping the receptor on the T-4 cell, will cause suppression of the immune system itself. The normal function of the CD4 receptor on the T-4 cell is not known, but may involve recognition by the immune system of invading antigens. (Source: New Scientist, 24/31 December 1987)

Soluble protein blocks AIDS virus infection

The initial step in the infection of human T lymphocytes and other cells by the AIDS virus (HIV-1) is the attachment of the virus' envelope glycoprotein, gp120, to its cellular receptor, a glycoprotein called CD4. A team of researchers at the biotechnology firm Genentech and Harvard Medical School is investigating the possibility of blocking this pivotal step with soluble, truncated versions of CD4 that will tie up the viral glycoprotein. The team has produced soluble CD4 that binds gp120 "with an affinity and specificity comparable to intact CD4 and is capable of neutralizing the infectivity of HIV-1" in vitro. Soluble CD4 also might be able to inhibit HIV-infected cells from spreading the infection by cell-cell fusion, they speculate. However, it is still too early to tell whether this approach will be clinically useful, especially since soluble CD4 may be too toxic. Nevertheless, a number of other groups also are pursuing this approach. (Reprinted with permission from Chemical and Engineering News, 21 December 1987. Copyright (1987) American Chemical Society)

HIV monoclonal antibody

Baylor College of Medicine has developed the BAT123 HIV monoclonal antibody that is 1,000 times more effective than alternative antibodies. It prevents transmission of the virus to healthy cells from infected ones. It will start human trials on terminal AIDS patients and infected pregnant women in 1989. It currently fuses mouse cancer cells with spleen cells from deactivated HIV-injected mice to produce the antibody, but will transfer production to human cells. Potential applications included vaccines, prevention of AIDS development in carriers and stopping spread of the disease in sufferers. (Extracted from SCRIP, 9 September 1987)

Researchers find AIDS virus may be blocked

Scientists have developed a technique that may prevent the AIDS virus from invading cells that are its prime targets by flooding the body with synthetic proteins that in laboratory dishes absorb the AIDS virus.

In the human body the protein CD4 normally helps spread AIDS from one T-4 immune system cell to another by binding to the AIDS virus. By synthesizing recombinant CD4 cells, which act as decoys, diverting the virus from the body's authentic proteins, the virus is stopped from entering healthy T cells.

Genentech Inc. research scientists Daniel J. Capon and colleagues report that the genetically engineerd CD4 proteins have kept more than 99 per cent of T cells from being infected with AIDS.

The synthesized proteins are produced by inserting the human gene that directs its manufacture into animal cells, which make the protein.

Scientists warn the new technique may not eliminate AIDS, but could halt the progression of the disease.

Genentech is said to be one of at least four groups racing to synthesize CD4. Biogen, Smith Kline & French Laboratories, as well as scientists at the Dana Farber Cancer Centre at Harvard, all hope to test the protein on patients.

Dr. Anthony Fauci, director of the National Institute of Allergy and Infectious Diseases in Bethesda, Maryland, says if animal tests of safety and efficiency are successful, the federal agency would lend its full support to human clinical trials. It is not likely that the cloned protein will be toxic, experts say. They also say that in addition to AIDS, the CD4 protein could be used against viruses such as mononucleosis or even against the common cold. (Source: Chemical Marketing Reporter, 28 December 1987)

AIDS virus cultured in India

Human immunodeficiency virus (HIV) has been isolated for the first time from patients in India with AIDS. Dr. Pradeep Seth, a microbiologist at the All India Institute of Medical Sciences in New Delhi says it is not possible to say at present whether the virus is HIV-1, HIV-2, or a new strain.

The virus was isolated from the lymphocytes of three asymptomatic prostitutes by co-cultivation with phytohaemagglutinnin-stimulated normal human lymphocytes. The presence of the virus was confirmed by indirect immunofluorescence using mouse monoclonal antibodies against HIV antigens p24 and p17, and by a reverse transcriptase assay with the culture supernatants.

Because of a lack of virus typing and containment facilities, the Indian isolates have not been further characterized. Typing and characterization of Indian HIV has acquired a new urgency in the light of the peculiar HIV-antibody distribution in the country. Although there are 145 known cases of positive antibody infection, only one full-blown AIDS case has surfaced. (Source: Nature, Vol. 330, 19 November 1987)

Function of AIDS virus gene clarified

The so-called tat gene of human immunodeficiency virus (HIV), the virus that causes AIDS, appears to encode a protein that acts as a transcriptional antiterminator, according to researchers at the San Francisco and Davis campuses of the University of California. The tat protein, acting in concert with the protein encoded by another HIV regulatory gene, art/trs, is known to act to increase the expression of the HIV genome in infected cells. Working with three plasmids that contained the HIV long terminal repeat (LTR) attached to a marker gene, the intact HIV tat gene, and a mutant tat gene that could not encode a functional protein, the California researchers, led by UCSF assisant professor of medicine B. Matija Peterlin and Davis assistant professor of medical pathology Paul A. Luciw, showed that, in the absence of tat protein, transcription of the viral genome proceeds only through 59 nucleotides of the LTR. In the presence of tat, 99 per cent of the messenger RNA transcripts were the full length of the LTR/marker gene construct. The scientists conclude that an intrinsic transcriptional terminator exists in the HIV LTR and that tat acts to inactivate this block. The finding may have implications for how a latent HIV infection becomes active. (Reprinted with permission from Chemical and Engineering News, 14 December 1987. Copyright (1987) American Chemical Society)

Cattle's link with AIDS

American scientists will soon begin testing people who work with cattle for infection with an animal retrovirus that is a distant cousin of the AIDS retrovirus.

The US National Institutes of Health and the Department of Agriculture announced last week that they are perfecting assays to screen the blood of humans and of cows for bovine immunodeficiency-like virus (BIV). The cattle virus is not thought to infect humans. None the less, because BIV shares about 35 per cent of its genetic make-up with HIV, scientists are concerned about its prevalence. (Extracted from New Scientist, 8 October 1987)

Research instrumentation

Computer aided molecular design

Computer aided molecular design allows biotechnology and drug companies to gain a better understanding of basic molecular structures, in addition to saving R&D time and money. Computerized molecular modeling and molecular mechanics techniques lower the randomness of the initial screening process, gets rid of the need for ball-and-stick models, and enables research only of new molecular structures that have the most potential. The researcher can run the molecular modeling software on computationally intensive scientific computers to predict what molecular or protein reaction might result if a specific atom within the molecule were changed.

Novo Industri (Copenhagen, Denmark), a leading supplier of insulin products, used computer aided molecular design and molecular modeling hardware and software tools to develop an insulin that acts more like the basal insulin secreted by nondiabetics. Novo's challenge was to modify the synthetic insulin molecule to act as a normal insulin when injected. The next step in broadening the use of computer aided molecular design is expected to be putting the computer power on or near the researcher's desk - e.g. Sun Microsystems' 10 Mips RISC-based Sun 4 workstations. Also, by putting added power in the hands of more users, new workstations like the Dana and Stellar systems promise to improve productivity and by linking graphics and high-speed computing on a single system they may also solve the present bandwidth limitations. (Extracted from Datamation, 15 November 1987)

A fast gene amplifier

The joint venture of instrument maker Perkin-Elmer and biotechnology company Cetus has launched its first product: an automated gene amplification system for performing rapid gene multiplication. The system, called the DNA Thermal Cycler, is based on polymerase chain reaction (PCR) technology, which consists of a series of repetitive replication cycles; it relies on the use of DNA polymerase to make as many as a million copies of a target gene sequence.

The DNA Thermal Cycler, which lists for $8,500, is a microprocessor-controlled temperature-cycling instrument designed to perform rapid temperature changes and incubations necessary for PCR gene amplification. It must be used with a $395 Gene Amp research reagent kit that includes the organism Thermus aquaticus (Taq), which supplies a heat-stable DNA polymerase. With the kit and the cycler, a target DNA sequence can be amplified in hours rather than days or weeks typically required by conventional methods. In addition, PCR technology is useful for research into genetic diseases such as sickle cell anaemia and cystic fibrosis, research into genetic predisposition to diseases such as diabetes, and research into gene mutations involved in the development of cancer.

It is also useful for forensic analysis of tissue samples such as hair and blood stains, and for tissue typing associated with organ transplantation and paternity determination.

Scientists at Cetus believe CPR technology has broad potential in the field of diagnostics and are applying the techniques to the development of diagnostic tests for such infectious diseases as AIDS and leukemia, among others. (Source: Chemical Week, 16 December 1987)

Computer programmes will speed new drug design

There are two Canadian companies combining their expertise in computer programming and protein engineering, to access the tremendous power of a new "breed" of computers. This will speed the drug design process to improve on current drugs and help find drugs to treat what are now incurable diseases.

Allelix biochemicals, a division of Allelix Inc., and Hypercube Inc., a Cambridge, Ontario computer software company will work together to design programmes for computers that are moving chemistry.

As Neil Ostlund, chairman of Hypercube explains, "it should be possible for chemists to do all their experiments on a computer, but until now, all but the simplest chemical reactions exceeded the capacity of even the most powerful supercomputers. However, a type of computer just being introduced links together tens or even thousands of small computer processors into one functioning giant 'parallel' computer that can cope with the huge numbers of calculations required. The only problem is, there is no software to run them. Allelix have the practical experience in drug design to help develop the programmes - while Hypercube have the parallel computer programming skills that will make computer-aided drug design possible".

Allelix Biochemicals uses its knowledge of complex chemical reactions in the body to develop new therapeutic drugs. A process known as "rational drug design", it helps scientists predict, at a molecular level, how drugs affect the body. It takes a lot of guesswork out of the traditional trial-and-error method of finding new drugs, resulting in more specific drugs with fewer side-effects. The process is also a lot faster - and cheaper - than traditional drug design. (Extracted from Company News Release, 10 November 1987)

DNA sequencers

The DNA sequencer market among genetic researchers is worth $250 million/year, but will increase to $1 billion/year by 1997, according to R.E. Snamel, President of Consulting Resources (Lexington, MA). Applied Biosystems (Foster City, CA) introduced its sequence DNA decoder in 1986, and has sold 50 of the $90,000 devices. Du Pont introduced a sequencer in October 1987 which is twice as fast for the same price. The sequencers use laser scanners to read the order of nucleotides stained with fluorescent dyes. The sequencers are vital for conducting genetic research into genetic diseases and to finding vaccines and medications to prevent or cure them. Pharmacia (Sweden) is collaborating with the European Molecular Biology Laboratory to develop a sequencer. Hitachi (Japan) also plans to introduce a sequencer. (Extracted from Business Week, 9 November 1987)

New machine sequences DNA strands

An automated instrument to determine the order of bases in DNA strands has been introduced by the medical products department of Du Pont. Deliveries of the $90,000 instrument will begin in February 1988. A user begins by incubating a DNA primer, template nucleic acid, a reverse transcriptase, and the four deoxyribonucleotides. This results in a mixture of DNA strands that have been elongated by one to 300 nucleotides. The mixture is next divided into four parts, and each part is incubated with one of four dideoxyribonucleotides, each tagged with one of four fluorescent labels to distinguish it. Dideoxynucleotides add to those strands where the template calls for them, but prevent further addition of nucleotides. The operator subjects each mixture to gel electrophoresis in four "lanes" of the instrument. There are 12 lanes for three simultaneous six-hour runs. The xanthine fluorescent tags are chemically similar, yielding similar mobilities of tagged DNAs in the gel. Each tag fluoresces characteristically at 505, 512, 519, or 526 nm. The instrument plots fluorescence intensity versus time as tagged components migrate along the gel and reconstructs the order of nucleotides according to the order of appearance of each fluorescence signal. (Reprinted with permission from Chemical and Engineering News, 26 October 1987. Copyright (1987) American Chemical Society)

Closing the biosensor gap

There is a rush of activity, both in the United States and in Japan, to develop biosensors. One of the aims of this research is to devise more sensitive marriages between biologically active substances and electronic materials - since a sensor must be able to translate minute changes in glucose level, pH or other biological signals into electronic signals that are strong enough to be read by a meter, computer or alarm.

Researchers at Massachusetts Institute of Technology have taken a big step down this road with a molecular-based transistor. Unlike silicon transistors, which use three metal contacts - one to the gate, which turns the device on and off, and the others to the source and the drain, between which the output current flows - the molecular-based transistor consists of source and drain electrodes made of gold, spanned by a polymer that can become conductive when it interacts with the environment, which essentially acts as the gate.

The key to the new transistor, made by Wrighton, E. Tracy Turner Jones and Oliver M. Chyan, is its smallness. Using a technique from microelectronics fabrication called shadow deposition, the researchers have shrunk the distance between the source and drain from 1.5 microns in a previous version to 50 nanometers.

The smaller the source-drain gap, the lower is the electrical resistance of the material in the gap and the greater is the output current. At 50 nm spacing it becomes possible to bridge the electrodes with polymers that are biologically sensitive but are very poor conductors.

The polymers Wrighton has in mind can be oxidized and reduced depending on environmental conditions such as pH. These particular "redox" materials are most conductive when half their molecules are reduced and the other half are oxidized. Any more or less oxidation turns the polymer into an insulator, shutting down the current and switching off the device.

The attractive property of these polymers is that they possess a very narrow band of oxidation states that will cause a current to flow. As a result, polymer transistors can, in principle, be designed to respond - with sensitivity and speed superior to that of other biosensor approaches - to specific chemicals or environmental changes while ignoring stronger oxidants and reductants. This enables the researchers to use biology as a starting point, to choose biologically interesting molecules and to make these into polymers that can be incorporated in their transistor.

According to Larry R. Faulkner at the University of Illinois in Urbana-Champaign, Wrighton's work is part of a larger drive among chemists to learn how to build molecular assemblies that are smaller than the several-thousand-angstrom régime of microelectronics and are larger than 20 angstroms - a size that encompasses most single molecules and that has been the traditional focus of chemists. (Source: Science News, Vol. 132, 3 October 1987)

General

Faulty genes lead to old age

The process by which we age is an undeniable part of life, yet scientists still know little about it. The theory most accept is that aging results when an organism fails to maintain or repair itself.

Several factors have been implicated in the aging process. The earliest suggestion was that toxic products accumulated in the small intestine. Other ideas include the Ames free radical theory - which holds that aging is the result of destructive moieties called free radicals, the immunological theory of aging, and the "error catastrophe" theory.

Recent research suggests that a new mechanism must be added to the list: the accumulation of epigenetic errors, that is, errors in the control of gene expression.

Biologists now know that methyl groups ($-CH_3$) attached to a cell's DNA can in some way control whether or not a particular gene is expressed. Any change in methylation results in a corresponding change in control of gene expression. Not all genes are sensitive to methylation in this way, however. From birth, around 4 to 5 per cent of mammalian DNA is methylated. The methyl groups are attached to particular cytosine residues of the DNA in a pattern that appears to be inherited.

At a meeting of the International Association of Gerontology held in Brighton last September, Sebastian Fairweather of the Radcliffe Infirmary in Oxford suggested that the loss of methyl groups by a cell's nucleic acid is a normal part of aging. This is because genes will remain "silent", or unexpressed, so long as specific cytosine bases within that gene remain methylated. A gradual loss of methyl groups early in development is therefore necessary to allow the normal pattern of gene expression to follow. Fairweather said there is now strong evidence that the rate at which methyl groups are lost from an animal's cellular DNA is directly related to that animal's lifespan. DNA from human cells loses methyl groups slowly as the cells age. The loss of methyl groups is faster in shortlived hamster cells and faster still in mouse cells, which have an even shorter lifespan. Immortal cells, such as those that have been "transformed" by certain viruses, exhibit a constant degree of DNA methylation. This is probably because they possess enzymes that can methylate DNA de novo. Conversely, it is possible to reduce the lifespan of cell culture by 25 per cent by adding a cytosine analogue, 5-azacytidine. This substance prevents the methylation that would normally occur during cell division.

Why should the loss of DNA methylation shorten a cell's life? The theory is that, as cells age, some methyl groups are lost, perhaps because the enzyme methylase is less active or because there is damage to the DNA. This allows the expression of genes that previously were silent. The result is that cells may produce proteins that are harmful to them, perhaps activating oncogenes or inhibiting synthesis of DNA. There is evidence for such changes in gene expression in animals.

Convincing evidence for the importance of the control of genes in aging animals comes from scientists at the University of Wales College of Medicine in Cardiff. They reported that a normal inactive X-chromosome in female mice was reactivated in aging animals. The study was the first to document an age-related failure of the genetic control that normally maintains one of paired X-chromosomes in an active state. Moreover, the researchers showed that the reactivation of the X-chromosome accelerated with age.

According to Robin Holliday, head of genetics at the National Institute for Medical Research in London, these findings can be explained by the loss of methylation at critical sites.

He suggests that the reduction of lifespan associated with irradiation of the whole body might be caused by introducing a large number of defects in gene expression of cells of the body rather than by causing fewer, but more severe, mutations in the sequence of bases in the DNA itself.

In a review of the inheritance of epigenetic defects Holliday says that defects in the cell would tend to appear after the loss of several methyl groups, rather than just one, because genes tend to have a cluster of methylated cytosine residues and not just one. (Source: New Scientist, 29 October 1987)

Jumping louse hits "wonder tree"

In recent years leucaena - a fast-growing, drought-resistant, nitrogen-fixing tree - has leapt from weedy insignificance to worldwide status as a "wonder tree". Governments and small farmers alike recognize its value in reforestation and the reclamation of marginal lands. At the same time, the tree supplies a veritable supermarket of products including fuel, fodder, timber and green manure. Throughout the tropics and subtropics leucaena has been planted on a massive scale.

Suddenly, however, thousands of leucaena trees are diseased and dying. Once considered to be almost free of pests, leucaena has fallen victim to the jumping plant louse, Heteropsylla cubana.

Resembling a miniature cicada, the tiny psyllid insect was first noticed in Florida late in 1983. It then began to leapfrog westward perhaps riding the high air currents, reaching Hawaii in April 1984, Western Samoa in February 1985, then moving through the Pacific islands until it reached the Philippines in October 1985. In 1986 the psyllid was reported from Indonesia, Papua New Guinea, Australia, Malaysia and Thailand. Burma and India may be next, and after that Africa.

Everywhere the psyllid has devastated stands of leucaena trees. Although adults feed on both old and new growth, the nymphs do most damage. Nymphs eat only the young shoots, but they excrete a sticky honeydew which prevents the development of the remaining growth. They might also inject toxins with their saliva. Trees infested with psyllids, especially those that are frequently lopped, appear to be much more susceptible to disease.

So far, no one has found an effective way to control the jumping plant louse. Chemical pesticides have little effect, and are expensive and hazardous to both users and to the environment. Biologists are looking for more natural methods of control. Options include introducing exotic predators but these carry their own risks, so scientists in several countries are experimenting with local predators and other possible controls such as fungi.

In the long run, the substitution of varieties of leucaena that are resistant to attack and of other nitrogen-fixing trees such as Calliandra, Sesbania and Gliricidia will probably prove to be the most effective solution. The leucaena infestation should be seen as a warning; as the natural forest diminishes and is replaced with "artificial" forests and plantations - many of them monocultures of exotic species - other pests are waiting in the wings. (Source: New Scientist, 5 November 1987)

D. APPLICATIONS

Pharmaceutical and medical applications

Cancer vaccine

Experiments to find a cure for cancer in cows may pave the way for a vaccine against cervical cancer.

Bovine papillomaviruses (BPVs) are the biggest killers of beef cattle in Britain and cause epidemics of cancer. Three to four per cent of cows in the country are infected, but on some farms almost 25 per cent of the herd have this cancer.

BPVs do not always cause lethal cancers; in many cows they may cause benign tumours or papillomas. Only a small number of animals go on to develop carcinomas. In this respect, BPV cancer is similar to human cervical cancer: only 1 per cent of human papillomas develop into potentially dangerous carcinomas.

Bill Jarrett and his research team at the University of Glasgow are trying to develop a therapeutic vaccine for BPV cancer. Their technique is to make tissue extracts from induced carcinomas. So far such tissue extracts have successfully caused rejection of the benign papillomas but, as yet, they are not effective against carcinomas.

Jarrett's group wants to find out which part of the viral genome codes for the antigenic proteins inducing rejection.

The viruses linked with cervical cancer are human papillomaviruses 16 and 18. Jarrett believes that the human genes are "read" in the same way as the bovine genes and that the bovine system can be used as a model for a human vaccine made from cell cultures. This may lead to a vaccine for cervical cancer. (Source: New Scientist, 5 November 1987)

Cancer blocker synthesized

National Institutes of Health researchers have formulated an amino acid that, the agency claims, is able to block the spread of cancer through the body.

The compound, a peptide synthesized with five amino acids, proved in laboratory tests that it can keep cancer cells confined to blood vessels where they eventually die or are killed by the body's immune system.

The peptide was able to prevent the formation of lung cancer tumours in laboratory rats and was effective against Karposi's sarcoma in test-tube experiments. It is now being tested on other types of tumours.

NIH has applied for a patent on the peptide they have developed, but it will require years of laboratory animal experiments before the compound is approved for tests on human cancer patients. (Extracted from Chemical Marketing Reporter, 30 November 1987)

Antimelanoma vaccines under development

Antimelanoma vaccines are being developed to prevent the spread of malignant cells, according to D.S. Rigel of New York University and M.S. Mitchell of the University of Southern California. Animal studies have already demonstrated the safety and effectiveness of the vaccines. The Skin Cancer Foundation says the chance of developing melanoma is one in 150. The cancer is the fastest-growing in the US, with the exception of lung cancer in women, with some 26,000 cases/year diagnosed. Only about 20 per cent of malignant melanomas first appear on sun-exposed areas such as the face and hands, but ultraviolet radiation from the sun might be the triggering factor. Thus, intense exposure rather than chronic exposure may be the key factor. Malignant melanoma is considered curable if detected early. The incidence of the disease has risen 83 per cent in the past seven years, but mortality has grown more slowly because of early treatment.

The new vaccine is made from melanoma cells grown in culture. About 100 cell surface antigens are used as innoculants to stimulate the production of killer T cells. The vaccine is in phase II clinical trials to test its efficacy. The vaccine might also be used in conjunction with cyclophosphamide, which inhibits suppressor T lymphocytes. Despite the initial results, the researchers caution that there still is no firm evidence that the vaccine will improve survival. Some researchers are also trying to develop vaccines to prevent the cancer from developing in the first place. This is made difficult by the fact that no one knows exactly what causes malignant melanoma. (Extracted from Science News, 24 October 1987)

Marine organisms may provide cancer treatment

Compounds isolated from marine organisms might be effective against cancer. Researchers at the University of Illinois (Urbana-Champaign) have synthesized didemnin B, which naturally occurs in the sea squirt (Trididemnun solidum). Phase II trials are already under way using isolates of the drug to determine its effectiveness against various cancers. Synthetic production of the compound will be needed to support larger trials, however.

Researchers at Arizona State University (Tempe) have characterized dolastatin 10, and will begin clinical trials in mid-1989. The compound is a 5-unit peptide found naturally in the sea hare (Dolabella auriculuria). ASU's G.R. Pettit started looking for anticancer compounds in marine organisms because cancer is not known in marine invertebrates. Dolostatin 10, the most effective of over 40 dolostatins isolated, has cured mice with melanoma and has doubled lifetimes of mice with leukaemia. (Extracted from Science News, 7 November 1987)

Green tea effective against tumours

Unfermented green tea can inhibit the growth of cancerous tumours, according to H. Fujiki of the National Cancer Center Research Institute. Tanning agents in the tea might be responsible for the effect. Researchers suspected green tea of some influence when it was noted that cancer rates are lower in the Shizouka area, where green tea is produced and consumed in large quantities. The main constituent of the tannin agents is epigallocatechin gallate (EGCG). Mice treated with tumour-inducing agents develop far fewer tumours if also treated with EGCG. EGCG is believed to alter receptors to which tumour promotors can bind. (Extracted from New Scientist, 12 November 1987)

New drug to treat inherited protein deficiency

Cutter Biological's new drug treats a rare, inherited protein deficiency that can lead to early development of a form of emphysema, alpha1-antitrypsin-deficiency-related emphysema. The US Food and Drug Administration approved Prolastin alpha1-proteinase inhibitor, an enzyme normally made by the liver, inhibits neutrophil elastase enzyme, which helps destroy bacteria in the lungs. When the enzyme is missing, neutrophil elastase may attack connective tissue in the lungs, reducing the elasticity needed for effective breathing and possibly leading to emphysema. Cutter derives the enzyme from

human plasma, which it heat-treats to reduce the risk of transmitting such infections as AIDS and hepatitis. Deficiency of the enzyme occurs in one in 5,000 people, generally when they are 30-40 years old. Prolastin will be administered to patients deficient in alphal-proteinase as weekly injections to help slow the progress of emphysema. (Extracted from Chemical Week, 16 December 1987)

Suppression factor of allergy to be developed

Quidel (US) will develop suppression factor of allergy, a treatment for allergies and asthma. SFA is targeted for treatment of immunoglobulin E mediated diseases. The firm's development of SFA to date includes cloning and expression in bacteria, purification, and testing in various animal models. SFA suppresses IgE synthesis, having the reverse effect to enhancing factor of allergy. In animal studies SFA reduced IgE levels 65-70 per cent, versus controls. The firm will begin toxicity studies in late 1987, and start phase one clinical trials in the first quarter of 1988. (Extracted from SCRIP, 25 November 1987)

New protein preparation facilitates allergy research

A new product that is claimed to simplify medical research in the body's immune defence system has been developed by Pharmacia, the Swedish pharmaceutical group, based in Uppsala. Designated Protein A Superose, the preparation will make it easier to purify the antibody IgG, a component of the immune defence believed to block allergic reactions.

Protein A Superose is made of special strains of bacteria and has gel consistency. It binds specifically to IgG, an antibody that has long interested Pharmacia Diagnostics researchers. The first test in a series of three, called Phadebas IgG RAST, will be launched in November.

The new protein is the first product that can be used in Pharmacia's high-speed system for biomolecules, FPLC. This also constitutes the beginning of a new product family within affinity chromatography, a technique whereby the ability of two substances to become a chemical compound is used in order to purify certain substances effectively, the company says in a recent issue of Pharmacia News. (Source: SIP, November 1987)

New diagnostic test for Down's syndrome

A blood test for estriol could provide early prenatal diagnosis of Down's syndrome, according to researchers at St. Bartholomew's Medical College, London. The currently available test for Down's syndrome is karyotyping, which requires amniocentesis and is expensive. Another test now available is to measure maternal levels of alphafetoprotein, which is produced by the foetus. Levels are unusually low in Down's syndrome pregnancies. Estriol is also produced by the foetus, and again, levels are unusually low in Down's syndrome pregnancies. Combining estriol, alphafetoprotein and maternal age will allow detection of 45 per cent of Down's syndrome foetuses. (Extracted from New Scientist, 31 December 1987)

Enzyme blocking drugs as possible therapy

Drugs that block an enzyme important in the progression of AIDS might provide a nontoxic therapy, according to researchers at the University of Amsterdam and the Netherlands Cancer Institute. The drugs inhibit glucosidase, reducing the virus' ability to infect human cells and preventing the formation of "giant" cells that form when an uninfected blood cell attaches to an HIV-infected cell. Castanospermine and 1-deoxynojirimycin both reduce HIV's infective ability in culture 100 times. The drugs block glucosidase, which removes sugars from HIV's gp120 during viral production in cells. The gp120 is needed to join the virus to the host cells. The drugs have very low toxicity. (Extracted from Science News, 7 November 1987)

Diagnostic test for gum diseases

BioTechnica has developed a test to detect bacteria that cause gum disease. The DNA of bacteria in a scraping from between the tooth and gum is analysed to determine if it belongs to one of the three major types of bacteria that cause gum disease. The test will be especially useful for monitoring the progress of patients who have already been treated for periodontal disease, to determine if the disease recurs. (Extracted from New York Times, 29 December 1987)

Human organs growth in laboratory

Typical biotechnology companies make single molecules that are useful as drugs, pesticides or chemicals. But Organogenesis (Cambridge, Mass.) aims to produce entire organs, including human skin, blood vessels, pancreas and bone. "We are spearheading a new industry devoted to rebuilding the human body."

Organogenesis's products will share a common technology that uses human cells and structural proteins to make organs that resemble their natural counterparts in structure and function. The company has an exclusive, world-wide license to the organ technology from the Massachusetts Institute of Technology (MIT) in Cambridge. In fact, Eugene Bell, Organogenesis's founder, chairman and president developed the technology while an MIT professor of biology. It is embodied in five US patents, but mainly in 4,485,096.

Organogenesis's first planned product - which it hopes to market within a year - is a toxicity assay that is actually identical to its "living skin equivalent". The assay will test the reaction of human skin to chemicals and pharmaceuticals, as well as to pesticides and cosmetics. Bell sees the product, the "biotest system", as generating a "substantial cash crop" in a multi-billion-dollar, world-wide market. Current toxicity assays depend on a variety of sources, including experimental animals like rodents and rabbits, cultures of human cells and cadaver organs. The company points out that all tests depending on those objects have shortcomings.

Biotest marketing. Despite its strategy of steering clear of marketing on its own, Organogenesis does plan to market the biotest system - which does not require Food and Drug Administration (FDA) approval - in the US. Initially, the company plans to manufacture the assay on a semiautomated, pilot-plant scale, but it aims to scale up to larger, automated facilities eventually. It may seek joint-venture partners to market and possibly manufacture the assay in Europe and the Far East.

Organogenesis hopes to have its living skin equivalent on the market in three to four years. It plans clinical trials for the material early next year at Western Pennsylvania Hospital (Pittsburgh).

Organogenesis foresees the skin equivalent becoming a universal wound dressing and skin replacement that a recipient will not reject. At the start, the company will market the product as a dressing and skin replacement for burn victims.

Skin deep. The skin equivalent, as does the biotest system, closely resembles human skin. Human

skin consists of two layers - the underlying dermis and the outer epidermis - that are bound together by a matrix called the basal lamina. The cells of the dermis, such as fibroblast cells, make structural proteins like collagen that give skin its strength. Epidermal cells provide an outer coating as protection against water and as partial protection against such pathogens as viruses and bacteria.

In the skin equivalent, the dermal layer is made from an acidic solution of fibroblasts and collagen. The fibroblasts are obtained from infant foreskin, while collagen is extracted from human placenta or from the skin of pigs or cows. As the acidic solution is neutralized, the collagen fibres precipitate, forming a lattice. The fibroblasts cause the lattice to contract into a tightly woven mat, a contraction that causes a 20- to 30-fold reduction in size. The lattice, Bell says, has strength and durability comparable to those of dermal tissue.

The dermal equivalent is seeded with human epidermal cells. As the cells grow over the dermal equivalent to form the epidermis, a basal lamina develops to hold the two layers together, forming the skin equivalent. The skin equivalent can be made in a wide range of sizes, shapes and thicknesses.

In animal trials, Bell says, the skin equivalent was not rejected by the recipient animal. That was so even when the fibroblast cells in the skin equivalent came from a donor animal rather than from the recipient animal, a donor animal whose skin the recipient animal had rejected. Organogenesis attributes such universal acceptance of its skin equivalent to the fact that fibroblast cells do not elicit an immune reaction. Fibroblasts do not express cell surface antigens that make it possible for the cells to be recognized as foreign, says Bell. And that universal acceptance is why Organogenesis believes that its product can succeed as a generic skin replacement.

Still, the product poses problems. It is colourless, hairless and does not generate sweat glands. Organogenesis is working on those obstacles. For example, it has developed a way to pigment the skin by adding melanocytes, the cells responsible for pigmentation, although the method requires testing.

Artificial artery. The same technology is used to make the blood vessel equivalent, which closely resembles a living artery. Animal trials are just gearing up for the blood vessel equivalent. In vitro, however, the vessel has withstood pressures of 300 mm of mercury without leaking or delaminating. Also, the flexibility of the vessel can be tailored to match the flexibility of the host blood vessel. That prevents such trauma as blood clotting where the vessels join.

Other organ equivalents now in early stages of development - such as pancreas and thyroid equivalents - are based on the blood vessel equivalent.

Organogenesis's bone equivalent technology, also in an early stage, is unusual because it involves the transformation of one cell type into another, a transformation that Organogenesis itself does not entirely understand. (Extracted from Chemical Week, 11 November 1987)

Biomaterial implants

In clinical medicine, artificial organs, extended-wear contact lenses, dental implants, and other biomaterials are being used with increasing frequency. These tissue substitutes integrate within host tissue; for the integration to succeed, available "dangling bonds" on the surface of the implanted biomaterials must be filled with cells of the host. With each implant, there is a race for surface sites between host cells and bacteria. Sometimes bacteria win the race, sabotage the "take" of the implant, and cause severe and even fatal infections. Anthony G. Gristina, Wake Forest University Medical Center, Winston-Salem, North Carolina describe the desirable surface features for implant materials, physical and chemical interactions that take place between surfaces and bacterial or host cells, host immune defences that affect implantation, types of bacteria that most often colonize implants, and ways in which the success rate of biomaterial implants can be increased. (Source: Science, Vol. 237, p. 1551, 25 September 1987. Copyright AAAS)

Promising results from FGF tests

California Biotechnology (US) has reported promising results from preclinical trials of its recombinant fibroblast growth factors. The firm has cloned and expressed the genes for basic and acidic forms of FGF, both of which have demonstrated angiogenetic properties. This gives them great potential for a range of applications including promotion of wound healing, as the blood vessel growth increases oxygen and nutrient supply to the site of the wound. The firm expects its FDFs to be suitable for burns, chronic bedsores, surgical wounds, lacerations, musculoskeletal injuries, ophthalmic uses and revascularisation of heart tissue. Delivery methods would include topical application and implantation. The firm has filed patent applications for the FDFs in the US and Western Europe. (Extracted from SCRIP, 25 September 1987)

New type of typhoid vaccine is safe and effective

A new typhoid fever vaccine - made from only the capsule that surrounds the disease-causing bacterial cell - is safer and possibly more effective than is the current typhoid vaccine made from whole bacteria cells. This is the conclusion of a pilot study carried out for 17 months in Nepal by an international team headed by researchers at NIH's National Institute of Child Health and Human Development. Part of a large ongoing clinical trial, the study showed that a single dose of the new vaccine protects against typhoid fever with virtually no side effects. The vaccine was made from a polysaccharide called Vi and found in Salmonella typhi's outer capsule. The two current vaccines for typhoid fever have limitations. One requires two injections and has a high rate of unpleasant side effects, discouraging its routine use. The second vaccine is taken in pill form and requires three or four doses to achieve protection similar to that of the new vaccine - a treatment programme difficult to carry out in developing countries. (Reprinted with permission from Chemical and Engineering News, 2 November 1987. Copyright (1987) American Chemical Society)

Possible vaccine against chlamydia

A chlamydia vaccine could be produced as a result of the recent cloning of a surface antigen found on three of the bacterium's 15 serotypes. An oral vaccine trial will be conducted in 1988, according to R. Stephens of the University of California (San Francisco). The vaccine will use purified proteins. The cloning might also allow development of assays or DNA probes to allow better diagnosis of chlamydia. (Extracted from Medical World, 9 November 1987)

Immunosuppressant used in organ transplants

Ortho Pharmaceutical's monoclonal antibody Orthoclone OKT3 can help prevent rejection of transplanted hearts and livers as well as kidneys, according to A.P. Monaco of Harvard University. OKT3 is already approved for use with kidney transplants.

The drug eliminates or inactivates killer T cells that would otherwise reject transplanted tissue. The US Food and Drug Administration is now reviewing an application to allow the use of OKT3 in heart and liver transplants. Over 60 heart transplant recipients have received OKT3 in trials at Utah Transplantation Affiliated Hospitals. The drug is used as a prophylactic and in response to rejection episodes. The drug has been used on 57 liver transplants at Massachusetts General Hospital.

Pancreas grafts, which could reduce complications from diabetes, may be aided by use of OKT3. The University of Iowa now gives OKT3 prophylactically for all pancreas transplant patients. So far results have been good in 20 pancreas transplant patients. (Extracted from Medical World, 29 September 1987)

Slow progress on malaria vaccine

Two independently developed malaria vaccines have shown an ability to induce immunity. The key element in each vaccine is a 4-amino acid peptide that is a primary immunogen of the malaria sporozoite. Researchers at Walter Reed Army Institute of Research produced a molecule consisting of 32 repeats of the sequence attached to an immune-enhancing carrier. It is made by genetically engineered Escherichia coli bacteria. Researchers at the University of Maryland produced a molecule with three linked copies of the amino acid sequence joined to tetanus toxoid as a carrier. Both groups challenged some patients who showed good antibody response with malaria-infected mosquitoes. One recipient of each vaccine was totally immune to infection, while two others receiving each vaccine took longer than normal to develop malaria. However, a commercial vaccine is still a long way off. (Extracted from Medical World, 14 September 1987)

Further development of TPA

Genentech is being challenged by as many as 30 firms in the development of tissue plasminogen activator, a hormone blood-clot dissolver and treatment for heart attack victims. Genentech lost its market lead when the US Food and Drug Administration put off approval of the firm's TPA by at least six months by requesting more test data. Competing firms hope to win a share of the market by modifying the TPA molecule so it lasts longer in the body. Genentech's TPA is quickly destroyed and must be injected for several hours to dissolve the clot and keep new ones from forming. Several biotechnology companies claim they have found ways to modify TPA so that it can retain its activity longer. The belief is that such versions would allow TPA to be used at lower doses that will diminish the risk of uncontrolled bleeding - a side-effect as TPA disables the body's clotting mechanism. Integrated Genetics (Framingham, MA) claims that its form of TPA lasts 10 times as long as the natural one in the body, and has greater clot-dissolving ability in animal tests. Eli Lilly is thought to be trying to design a version of TPA that pushes TPA past the enzymes in the body that inhibit it. Genentech argues that the short time its TPA remains active is beneficial because doctors can quickly stop administering it if bleeding develops. With this in mind, Upjohn is trying to develop a TPA that focuses in on clots without affecting the rest of the circulatory system. Verax (Lebanon, N.H.) says that it has developed the cheapest way to make commercial quantities of genetically engineered TPA. Verax cultures Chinese hamster ovary (CHO) cells engineered to make TPA in its mammalian cell culture system, known as the Verax System 2000. That system, says Verax, increases TPA production by the CHO cells sevenfold. In addition, the system eliminates the conventional need by CHO cells for a foetal-bovine-serum-medium supplement, thereby simplifying TPA purification. Verax ran its system continuously for 27 days and produced a daily average of 23 grams of TPA. Other firms are experimenting with monoclonal antibodies, copies of the immune system's own disease-fighters, that can be designed to affect specific targets in the body. (Extracted from Business Week, 26 October 1987 and Chemical Week, 9 December 1987)

MSF production

Integrated Genetics is jointly working to genetically engineer a compound to regulate blood platelet production with Ortho Pharmaceutical. Megakaryocyte-stimulating factor (MSF) helps regulate the number of red blood cells, white blood cells and platelets produced from stem cells in bone marrow. MSF may be used in patients undergoing chemotherapy and bone marrow transplants and in coronary bypass patients who require blood transfusions. (Extracted from Chemical Week, 28 October 1987)

Monoclonal purified Factor VIII on the market

A monoclonal-purified Factor VIII licensed last October by the US Food and Drug Administration promises virtual freedom from AIDS and hepatitis. Representatives of the Scripps Clinic, La Jolla, California, and Armour Pharmaceutical Co., Fort Washington, Pa. made the announcement at a joint press conference.

Armour has begun shipping the injectable Factor VIII product, trade-named Monoclate, to hospitals and haemophilia clinics throughout the USA.

The National Haemophilia Foundation estimates that 20,000 Americans are afflicted with haemophilia type A, the commonest form, and that two thirds of them have been exposed to the HIV, of which two to three per cent have contracted AIDS. Haemophilia affects populations world-wide in the same ratio as in the USA - some 80 cases per million.

When 17 juvenile haemophiliacs, who had never had the conventional extract, got injections of Monoclate for three months, none contracted hepatitis, reports Theodore S. Zimmerman, chief of Scripps' coagulation laboratory, and co-inventor of the monoclonal-antibody extraction process.

Conventional Factor VIII products provide one to three units of blood-clotting activity per milligram of protein. By comparison, the monoclonal-purified factor exhibits 3,200 activity units, and a genetically engineered molecule, still in the future, 4,500.

Monoclate will sell for 55 cents a unit, a mark-up of 20 per cent over the most expensive conventional Factor VIII now marketed, which costs 45 cents. Haemophiliacs consume an average of 60,000 units per year for maintenance and treatment of bleeding episodes. (Extracted from McGraw-Hill's Biotechnology Newswatch, 2 November 1987)

Vaccine against influenza being developed

Connaught Laboratories is developing a vaccine against Haemophilus influenzae type b, which causes meningitis and other serious diseases in children. Tests on the vaccine have been conducted on 700 infants in Finland, demonstrating an 87 per cent reduction in H. influenzae infection rates. L.K. Gordon of Connaught says the vaccine uses the carrier approach to vaccine development. Part of the Haemophilus bacterium that would ordinarily provoke only a mild immune system response is linked to a carrier that strongly stimulates immune response. The resulting antibody thus allows an amplified attack on the Haemophilus bacterium.

In the US, the only approved vaccine against Haemophilus influenzae fails to induce immunity in children under the age of two, but most cases occur in children under 24 months old. Some 18,000 cases/year occur in children under the age of five, and about 1,000 infants/year die from the infection. (Extracted from Science News, 26 September 1987)

New partnerships for commercializing EPO

A new team has formed to make commercial quantities of erythropoietin (EPO), a protein currently in clinical trials for the treatment of kidney failure. Ortho Pharmaceutical has awarded Celltech (Slough, UK) a two-year, "multi-million-dollar" contract to produce EPO from mammalian cell culture. Celltech expects to produce 200 g of EPO by the end of 1989. That would represent a significant proportion of world supply, which is expected to be on the order of 500-1,500 g/year, depending on the success of clinical trials. Current market estimates for EPO are $165 million/year for treating anaemia associated with renal failure and $160 million/year for other anaemias and for other blood-enrichment tasks.

Meanwhile, Boehringer Mannheim (FRG) will develop genetically engineered EPO which the firm will import from Genetics Institute (US) and be responsible for preclinical and clinical development. (Source: Chemical Week, 9 December 1987)

Genetic "B" vaccine approved

Following approval in over 30 countries, including most of Europe, the world's first commercially available genetically engineered human vaccine against hepatitis B has been approved for use in the UK.

The vaccine, Engerix B, was developed by Smith-Kline Biologicals, the vaccine division of Smith-Kline Beckman group, at Rixensart, Belgium, as a result of an eight-year programme.

Genetic engineering has provided a production method capable of producing a highly purified vaccine in large quantities, at half the cost of the currently available plasma-derived vaccine.

The immunization régime consists of three 20µg doses of vaccine at a total cost of £31.50. This should confer immunity for three to five years.

Hepatitis B is said to be one of the world's most serious viral diseases, claiming over two million lives per annum, according to the World Health Organization. (Source: Manufacturing Chemist, October 1987)

Merck's new drug free to WHO for river blindness programme

If a newly-launched programme to eradicate onchocerciasis, or river blindness, a parasitic infestation affecting as many as 20 million people in Africa, South and Central America and the Middle East, is successful, much of the credit will be due to Merck & Co., the New Jersey pharmaceutical company, which announced it will provide its antiparasitic drug Mectizan free of charge to countries that need it. The burden of distributing the drug and supervising medical care falls to the World Health Organization (WHO), but Merck was apparently the initiator of the idea and its driving force until WHO was persuaded of the potential effectiveness of the new treatment.

The parasitic worm Onchocerca volvulus is transmitted to man by the blackfly, which breeds in fast-flowing rivers and harbours immature worms, or microfilaria. In the human body, adult worms grow over a period of years, generating in turn more microfilaria which travel throughout the bloodstream. Infestation generally causes skin lesions and weight loss, but when the microfilaria travel to the eye, the resulting tissue damage causes blindness.

Mectizan was developed by Merck in 1975 as a variant of ivermectin, a drug widely used against animal parasites. It kills microfilaria, and damages the reproductive system of the adult worms, putting a stop to infestation. Its great advantage is that it is effective in small doses given only once or twice a year, and has few side-effects. There may be adverse effects on pregnant and lactating women and small children, but Dr. Mohamed Aziz, who supervised the clinical development of Mectizan, says the doses necessary to control onchocerciasis are about one hundred times lower than the level at which reproductive problems are seen in mice.

The idea of developing ivermectin for human use originated with Dr. Bill Campbell, a veterinary doctor at Merck, Sharpe and Dohme who had lived in Ethiopia.

Although Mectizan, because of its potency and safety, could in principle command a high price, Merck could not necessarily make much profit from it because the only countries that need it have no money.

Until recently, US law would not have countenanced even the giveaway of Mectizan, as it has not been approved for human use by the Food and Drug Administration (FDA). But US law now permits export of unapproved drugs provided the recipient allows it, and in this case the countries concerned are unlikely to say no, especially as the French Directorate of Pharmacy and Drugs has approved Mectizan for human use.

Dr. Halfdan Mahler, Director-General of WHO, joined in the chorus of praise for Merck's "generous gesture", and hoped that it would help break down the "paranoia" that exists between WHO and the pharmaceutical industry. WHO has $4 million available to begin to set up the infrastructure for delivery, but will need more. Mahler hopes that the promise of a manifestly effective and relatively cheap programme such as this will persuade member countries that WHO is not the "bloated bureaucracy" that many think it. Mahler foresees visible reduction in the incidence of river blindness in a few years, and maintains that eradication of the disease by the end of the century is a reasonable goal. (Source: Nature, Vol. 329, 29 October 1987)

A blood test for osteoporosis

Osteoporosis is the result of an imbalance in bone turnover, the natural and continuous process of bone formation and breakdown. Currently, such imbalances are assessed by bone biopsies, which are invasive, or calcium radioisotope studies, which are expensive and can take three weeks to complete. Now a blood test has been developed that could quickly and non-invasively identify such a bone imbalance. The test assays for two bone specific markers, which "correlate well" with bone formation, according to the Endocrine Research Unit at the Mayo Clinic (Rochester, Minn.). Those markers include a bone protein known as Gla-protein and alkaline phosphatase, a bone enzyme. The test will be useful in determining the effects of experimental osteoporosis therapies. (Source: Chemical Week, 7 October 1987)

Immobilising cells may cut drug costs

Dr. Eric Robinson of QDM Laboratories, Derriaghy has developed a new method for cell immobilization which he claims overcomes many problems. It enables individual cells to be used as catalysts more

effectively and for longer periods than present methods and will therefore dramatically reduce costs. His system is also an entrapment technique but one which cells are held in the cavities between porous inorganic microspheres of an appropriate size. The process, which can be undertaken under conditions to suit the cell, cages the biocatalyst in a strong highly porous structure.

This ingenious concept depends upon the use of silica hydrogel microspheres prepared by a new procedure. Close packed, usually air or freeze dried, these produce a microscopic honeycomb structure, in which a tear-shaped pellet just 2 mm across contains over two million spheres. Every six microspheres enclose a cavity, accessed by eight pores. A single cell, entrapped in this cavity, is securely held, provided it is larger than the pores surrounding it.

The high porosity of the system eliminates the permeability barrier encountered in polymeric immobilization materials. It renders the silica chemically neutral, making it possible to mix the catalysts cells with the silica microspheres. The silica/catalyst mixture is then squeezed into pellets to compact the microspheres, trapping the cells. When dried the structure is claimed to be strong and porous. And, importantly the process is described as gentle and unlikely to damage the cells during immobilization. Because the process can be varied to make the spheres smaller or larger, virtually any size of cell can be trapped inside the honeycomb.

Dr. Eric Robinson established QDM Laboratories earlier this year with support from the Local Enterprise Development Unit. He has patented his invention. His discovery of this new silica for cell immobilization has already resulted in a large contract from a Canadian company to develop a special variant of the new technique for antibody production. Further contracts are expected in the near future. (Extracted from Technology Ireland, November 1987)

Clinical trials begin for promising antibiotic

Doctors in several countries have started trials with fusidic acid, an antibiotic normally used to treat bacterial infections, after the drug produced a dramatic improvement in the condition of a man with AIDS. The man had advanced tuberculosis and had lost a great deal of weight.

Vigo Faber, of the University Hospital in Copenhagen asked researchers at the Clinical Research Centre in Harrow to investigate the drug's antiviral activity.

Faber began a trial of fusidic acid in 12 patients with AIDS two months ago. He now has 20 patients on the drug and the number is rising all the time. Another trial of fusidic acid in people with AIDS or severe disease related to HIV infection began at St. Stephen's Hospital in London. Angus Dalgleish, of the Clinical Research Centre, says that doctors in the US and Canada have also begun tests.

Preliminary research by Dalgleish and his colleagues found that fusidic acid somehow inhibits the replication of HIV. They are now trying to discover how the drug acts against the virus.

Fusidic acid is known to disrupt protein synthesis in bacterial cells by inhibiting the normal association between transfer RNA and ribosomes, an important part of the process of protein synthesis. Whether a similar effect occurs during the synthesis of viral proteins is not known. Another possibility is that the drug may inhibit viral enzymes that split the large precursor proteins manufactured by the virus into smaller functional units.

Dalgleish says that it will take at least three months to come to any meaningful conclusions about the efficacy of fusidic acid in the treatment of AIDS. (Extracted from New Scientist, 29 October 1987)

Tests on DDC continue

American researchers are continuing trials of the experimental antiviral drug dideoxycytidine (DDC), despite earlier reports to the contrary.

Phase I tests of DDC on AIDS patients - to establish safety and toxicity of the drug - began last May at four university hospitals in the US. After a couple of months of treatment with those dosages, doctors found a condition called peripheral neuropathy in some of the patients taking DDC. The neuropathy manifested itself as pain in the patients' feet. The drug was withdrawn and the pains eventually stopped.

The four centres began a new series of tests last summer, with a new group of between 60 and 70 patients, using lower dosages of DDC. Doctors are now giving four new dosages, including 0.01 and 0.005 milligrams per kilogram for four hours. (Extracted from New Scientist, 29 October 1987)

Drug delivery takes the nasal route

Some researchers believe that nasal delivery of drugs can eliminate many of the problems associated with injections and pills. California Biotechnology (Mountain View, California), for example, has licensed its Nazdel nasal drug delivery system to Eli Lilly and Ayerst Laboratories for insulin administration, and both companies have begun clinical trials for nasal delivery of insulin. The firm has also licensed its Nazdel system to Jonnson & Jonnson's Ortho Division for delivery of contraceptives and of cancer drugs based on luteinizing hormone releasing hormone. Hoffmann-La Roche has licensed the Nazdel system for use with such appetite suppressants as serotonin and with growth hormone releasing factor. And such institutions as the University of Southern California (USC) in Los Angeles are developing nasal drug delivery systems of their own.

Traditionally, nasal delivery has been reserved for drugs that are small molecules, such as antihistamines, but the nasal delivery systems now being developed could allow delivery of larger molecules. The route could be particularly useful for protein drugs made by genetic engineering as such drugs are broken down in the gut, leaving injection as the only practical way of administering them.

Cal Bio's Nazdel system, like other nasal delivery systems, is based on a compound known as a penetration enhancer. A penetration enhancer is a small molecule that facilitates the movement of other molecules across a biological membrane. Cal Bio's enhancer - called sodium tauro-24,25-dihydrofusidate (STDF) - is derived from the antibiotic fusidic acid, produced by the fungus Fusidium coccineum.

STDF, which coats the drug to be delivered, seems to work by disrupting the so-called tight junction that holds together neighbouring cells of the nasal mucous membrane. Thus, STDF, along with its accompanying drug, slips through the resulting nasal membrane gap, then dissipates as the drug it is carrying enters the bloodstream. The tight junction reforms within 20 minutes preventing other substances, such as viruses and dirt, from entering the bloodstream.

Clinical trials with insulin have shown that the Nazdel system produces a "prompt" rise in blood levels of insulin, similar to the spurts of insulin that the pancreas itself releases into the blood. Injections, on the other hand, cause the insulin level to rise

only gradually, and they keep the level more constant. Moreover, the Nazdel system has proved effective in animal studies for delivering a variety of drugs, including growth hormone, reproductive hormones and calcitonin.

If the system passes the tests, it could prove a boon for people with Type I diabetes, also known as juvenile onset diabetes. Patients with Type II diabetes might also benefit. (Extracted from Chemical Week, 21 October 1987)

Booster shots for AIDS patients

Recipients of experimental AIDS vaccines might benefit from booster shots, according to D. Zagury of the Pierre and Marie Curie Institute (Paris). Zagury vaccinated volunteers in Zaire in April 1987. A group of 12 of the volunteers also received one of four possible 'booster' shots. A booster shot of whole autologous cells produced the most marked antibody response.

Studies in chimpanzees at the National Cancer Institute indicate that booster shots of an anti-AIDS vaccine provided improved protection when chimps were then innoculated with HIV.

Zagury also hopes to develop genetically engineered antibodies to protect developing foetuses in HIV-infected women in Africa. (Extracted from Science News, Vol. 132, 19 and 26 December 1987)

New drug to be tried against AIDS

Ethigen (US) will clinically test AL-721 for AIDS and cystic fibrosis. The firm will concentrate on these areas, but will also test the drug on alcohol and narcotic addiction, and age-related memory disorders. The firm has applied to the US Food and Drug Administration for an orphan drug indication for AL-721 in AIDS treatment. AL-721 is an apparently safe antiviral agent. It is believed to have a fluidising action on the rigid lipid membrane of HIV, thereby changing the attachment protein configuration to inhibit attachment to the T-cell receptor. (Extracted from SCRIP, 25 November 1987)

Egg yolk for AIDS victims

AL-721, a potential treatment for AIDS and HIV infection, is now available in Britain for doctors to prescribe on a compassionate basis. A trial of the substance, made from egg yolks, will soon begin at St. Mary's Hospital in Paddington, West London, to test its efficacy against the virus. The trial should take about three months to complete.

AL-721 contains three different lipids (fats) in the ratio three to two to one, hence its name. It is being made in Britain by a company called Penn Pharmaceuticals. Its mode of action is not clear, but it may work by fluidising the viral membrane, so that viral proteins important in binding to white blood cells sink into the membrane.

Whether AL-721 works in combating HIV is the subject of controversy. The Food and Drug Administration in the US has recently asked for further tests to take place to establish the toxicity of the mixture. Yet many people with AIDS and HIV infection have already taken quantities of food-grade lipids, said to be similar to AL-721. Ethigen Corporation, which holds world-wide licence for AL-721, says that these products contain impurities which could be dangerous for immunosuppressed people. (Source: New Scientist, 24/31 December 1987)

AIDS vaccine to be tested

Glasgow University (Scotland) may start human trials of an AIDS vaccine in 1988. The vaccine, based on AIDS virus cells and using quilla, a Brazilian oak bark extract, as a delivery vehicle, successfully produces antibodies to neutralize the AIDS virus in animals. The Glasgow University project has received over £1 million in Medical Research Council grants. Quilla is successfully used in a feline leukaemia vaccine. (Extracted from The Times, 11 September 1987)

FDA approves tests of AIDS vaccine

The US Food and Drug Administration has approved another AIDS vaccine for human testing, Bristol-Myers' innoculant based on vaccinia virus. The Bristol-Myers offering uses a vaccinia virus into which the genes for the surface proteins from the HIV virus have been inserted by recombinant DNA techniques. FDA says that studies of the new vaccine will be carried out at the Pacific Medical Center by Lawrence Corey, director of the virology division at the University of Washington School of Medicine. The vaccine will be tested in 30 to 60 healthy homosexual volunteers who are not infected with the AIDS virus. (Reprinted with permission from Chemical and Engineering News, 7 December 1987. Copyright (1987) American Chemical Society)

AIDS drug scale-up

Wellcome (UK) has raised zidovudine AIDS drug capacity in the UK and the US and has also improved scaling up of the 16-stage synthesizing process. It will expand clinical trials of zidovudine in combination with other drugs such as acyclovir, dideoxycytidine and interferons, although this is not guaranteed to raise efficacy. Ribavirin, for example, cuts zidovudine's effectiveness. Dideoxycytidine, DDC, causes peripheral neuropathy, but may lose this side-effect at lower doses, while retaining its anti-AIDS properties. Granulocyte macrophage colony stimulating factor increased AIDS patients' immune cell numbers in tests. (Extracted from European Chemical News, 21 September 1987)

New trial of peptide T begins

Twelve patients with AIDS begin treatment with peptide T in Los Angeles. The trials are the first on humans in the US and will determine whether the substance is toxic and, eventually, whether it can reverse the fatal progression of the human immunodeficiency virus (HIV).

Peptide T is a synthetic copy of eight amino acids from a naturally occurring neurotransmitter. It has been the subject of controversy since it was made last year by Candace Pert, a neuropharmacologist at the National Institute of Mental Health (NIMH) in Bethesda, Maryland.

The peptide has already been tested in four patients in Sweden. According to Lennart Wetterberg of the Karolinska Institute's Department of Psychiatry, who conducted this first trial of peptide T, three of the patients had since died. Another trial of the substance with 30 AIDS patients began in May. Results of this trial are expected in March 1988 and Wetterberg plans to give more details of the work at an AIDS meeting planned for June 1988 in Stockholm.

Whereas Wetterberg has given peptide T to patients in all stages of the disease, from mild to severe, Pert has laboratory evidence suggesting that

peptide T is most effective where the quantity of virus is relatively low and so has chosen to enter only patients with "early AIDS" in her trial. Wetterberg is cautious about extrapolating from laboratory experiments to human beings, however. (Extracted from New Scientist, 12 November 1987)

Further steps on AIDS vaccine trail

A team of Dutch workers has found that compounds previously used to control blood-glucose levels in people unable to process large sugar molecules may prevent those infected with HIV from developing AIDS.

The potential vaccine is based on antibodies which mimic the receptor molecule for HIV in human cells. In vitro, the antibodies bind to a glycoprotein in the envelope coating of the virus, preventing it from attaching itself to the cell and thus inactivating the virus.

Moreover, the researchers found that the antibodies neutralized three distinct isolates of HIV-1 and one isolate of the recently discovered HIV-2. Previously, antibodies raised against the glycoprotein of one HIV isolate have shown little or no activity against other isolates.

The Dutch team has found that, because sugar molecules from part of the HIV envelope glycoprotein, the glucosidase inhibitors castanospermine 1-deoxynojirimycin can reduce HIV infectivity in vitro. The inhibitors have shown no side effects when used to control blood sugar. (Source: Chemistry & Industry, 16 November 1987, p. 243)

Zidovudine in three dimensions

The only drug that has so far shown significant ability to prolong the lives of people with AIDS is zidovudine (formerly known as AZT). Scientists already know its molecular structure and roughly how it works. Now researchers at the University of Dundee in Scotland have worked out the drug's three-dimensional structure, too.

Zidovudine is a member of a group of drugs called nucleoside analogues, which resemble the molecules that make up the chain of DNA. When HIV enters a cell, the viral enzyme reverse transcriptase controls the production of DNA from the viral genetic material, RNA. The enzyme readily accepts zidovudine in place of the normal nucleoside thymidine. When the next nucleoside tries to add on to the growing strand of DNA, it finds that the hydroxyl group to which it would normally attach is missing.

Not all compounds where the hydroxyl group of thymidine has been replaced by another chemical group have antiviral activity, however. This suggests that the three-dimensional configuration of zidovudine may play an important role in determining the drug's effectiveness. Patrick Tollin, together with his colleagues John Low, also at Dundee, Herbert Wilson at Stirling, and Alan Howie at Aberdeen, set about crystallizing zidovudine. They then bombarded the crystal with X-rays in order to study its structure.

They found that the basic unit of the crystal was two molecules of zidovudine, paired together with weak hydrogen bonds. Nucleotides (and their analogues) are made up of a sugar, a base and a phosphate group. Normally, when these molecules make pairs joined by hydrogen bonds, they join up symmetrically.

In the zidovudine crystal, the pair is asymmetrical. Each molecule in the pair holds the bonds between the three component parts - sugar, base and phosphate - at different angles.

Tollin suggests very tentatively that the flexibility of zidovudine might imply that it fits in very easily with the growing molecule of DNA. The next step, he says, is to try to find features common to those nucleoside analogues with antiviral action, and determine which are crucial to this action. (Source: New Scientist, 26 November 1987)

AIDS drug price

Wellcome has decided to cut the price of its AIDS therapy Retrovir by 20 per cent in the US and the EEC. The company claims that it is passing on the benefit of savings it has achieved in production costs.

The new price will bring the cost in the UK down from £5,000 ($9,000) to £4,000. The original price was established in February 1987 before the drug had won marketing approvals and the manufacturing process was fully developed. Wellcome justified the original price on the grounds that it cost £80 million to bring the drug to market. (Source: European Chemical News, 21/28 December 1987, p. 244)

Livestock applications

Milk feed fights disease on the factory farm

At the Vienna University for Agricultural Science, researchers have developed a milk-based feed which has successfully kept factory-reared pigs and poultry free of disease. Heinrich Flossy, who is in charge of the project, says that the feed works by controlling the growth of pathological organisms in the intestinal tracts of the animals.

The active ingredient is a culture of symbiotic bacilli - the "milk acid" bacteria which occurs naturally in the stomachs and intestines of calves. These bacteria help digestion and control the reproduction of malignant micro-organisms.

The cultures are grown in ordinary cows' milk and dried at a temperature which does not destroy the organisms. The powder forms part of a feed to plant the useful bacteria in the animals. Tests so far show that the feed is cheaper and more successful than antibiotics. (Extracted from New Scientist, 24 September 1987)

Embryo transfer techniques

Farmers may be able to choose the sex of livestock babies as embryo transfer techniques are developed, according to J. Sreenan of the Agricultural Institute of Ireland. Many of the calves that are now raised for beef are really surplus dairy calves not totally suited to beef production. G. Anderson of the University of California (Davis) has developed a technique that allows determination of the sex of an embryo with an accuracy of over 80 per cent. The test relies on detection of the H-Y antigen, which is present only on male embryos. A second antibody is then added, which binds to the first antibody and fluoresces.

Researchers are also seeking a way to separate male-producing from female-producing sperm, but this may be far in the future. J. Morrell of the National Institute for Medical Research (London, UK) is attempting to separate sperm in a flow cytometer, but with little success. (Extracted from New Scientist, 17 September 1987)

The first test of a liposome-based vaccine

What is believed to be the first US-approved test of a vaccine that uses liposomes to enhance the immune response will be conducted by IGI (Vineland, N.J.).

The US Department of Agriculture has approved an IGI field test of a liposome-based vaccine for controlling Newcastle disease in chickens, an affliction that costs US growers more than $200 million/year. To stimulate the immune response, the liposome must persist in the body for at least several weeks. IGI's liposomes have the required stability because they are not made with the conventional phospholipids, which are destroyed by body enzymes. IGI believes its liposome technology could lead to multicomponent vaccine products that could eliminate up to two innoculation procedures for the nation's 50 million breeder hens. The company also is working on liposome-based vaccines for large animal and human applications. (Source: Chemical Week, 23 December 1987)

Agricultural applications

Biotechnology set for boom in agriculture

Biotechnology is poised to make a massive impact on agriculture. Short-term prospects for its use are already clearly evident as companies develop new ways to control pests and disease in plants. Pest and disease control is a priority target for agricultural biotechnology. Firms are currently developing products that provide plants with resistance to disease, insects and herbicides. Diseases can cause US production losses in corn, soybean, wheat and cotton to the value of $1.6 billion per year.

Agracetus, the first company to field test a genetically engineered plant, is trying to modify plants with resistance to crown gall disease. The US firm is using tobacco as its model, although the disease causes most problems with fruit and nut production, viniculture and certain nursery production.

Rohm & Haas, in collaboration with Belgium's Plant Genetic Systems has tested plants engineered to be resistant to caterpillar pests. The scientists have transferred the Bacillus thuringiensis toxin gene into tobacco. Many firms are now working to put this toxin gene into other major crops.

A third short-term target is the development of herbicide resistant plants. Firms are looking to develop resistance to the major herbicides such as atrazine, glyphosate and chlorsulfuron. Most of the advances have focused on tobacco as it is an easy plant to manipulate.

Du Pont's agricultural products division and US seed concern Northrup King Co. recently announced completion of field trials with herbicide-resistant genetically manipulated tobacco plants. Tests demonstrated that two of Northrup King's tobacco varieties had been made resistant to Du Pont's sulfonylures herbicides by the insertion of a proprietary Du Pont gene.

The company said genetically engineered plants were protected despite herbicide application rates up to four times the norm whereas tobacco plants without the Du Pont gene were killed by the herbicide.

Within the next 12 to 24 months breakthroughs in putting useful genes into commercially important crops will be reported. Several firms have reported limited success inserting genes into corn.

In the longer term biotechnology will shift beyond pest control targets. Industries might employ new plant sources for pharmaceutical or industrial products such as biodegradable plastics from plant-based feedstocks.

Furthermore, the development of plants that can fix their own nitrogen will change production economics of current crop production. (Source: European Chemical News, 23 November 1987)

Environmental release data start to come in

There are now data to confirm that releasing genetically manipulated micro-organisms into the environment can be safe. Steven Lindow's "ice-minus" experiment, performed on potato tubers last summer, is over. The data on frost protection are still being analysed; the data on the environmental fate of the released Pseudomonas syringae are nearly complete. In a press release from the University of California (Berkeley), Lindow said that none of the genetically modified ice-minus bacteria have been detected beyond the experiment's 30-metre bare soil buffer zone. Even immediately after spraying, the number of bacteria deposited on the soil dropped off precipitously toward the perimeter; almost none were detected even 15 metres into the buffer zone. Tests will continue for several months, to look for evidence of survival and growth of bacteria within the experimental plot.

The US Environmental Protection Agency has approved the first field-test of a genetically engineered micro-organism under the Toxic Substances Control Act (ToSCA). The 18-month experiment will test the genetically engineered microbial tracking system developed by Monsanto (St. Louis, MO). The bacterium, Pseudomonas aurofaciens, contains two genes from Escherichia coli that allow it to metabolize lactose. This marker is readily picked up on Lac indicator plates by a colour change in the bacterial colony: thus the bacteria can be tracked easily once they are released. The test, which is being conducted by Clemson University (Clemson, SC) scientists at the Edisto Research and Education Centre, involves applying the root-colonizing bacteria to winter wheat in seed furrows. (Source: Biotechnology, Vol. 5, December 1987)

Sudan's magic tree

A series of comprehensive industrial feasibility studies are to be launched soon in some of the poorest parts of Africa where a common tree has been identified as a potentially lucrative new source of pharmaceuticals and food.

Perhaps even more important, it is about to produce a powerful economic incentive for stabilizing the deserts.

The United Nations Industrial Development Organization's (UNIDO) initial pilot study in the Sudan has confirmed the enormous economic potential of the indigenous balatines tree.

Canada, as well as the Federal Republic of Germany, are already backing the project. Further support is expected from various development aid funds, the World Bank and other sources.

The stem and branches of the balatines tree often end up as firewood under the kettles of Nilotic tribes. Less than 2 per cent of its inedible fruit reach the markets. Yet UNIDO's two-year pilot project in the Sudan has identified it as the potential basis of a $US 80 million pharmaceutical and food industry.

Experts from the Canadian Research and Productivity Council analysed the fruit and assessed the storage, transport and industrial processing capacities of the Sudan and the social aspects of harvesting and processing. They concluded that the

tree offers some of the world's poorest arid countries - including those of the Sahel - a rich new source of medicines, pesticides, edible oil, animal feed, nuts, soap and fuel as well as hard-currency export revenues.

A discussion paper published in Ceres, the journal of the UN's Food and Agriculture Organization (FAO), now places the tree - Balatines aegyptiaca, known vernacularly as heglig, loba, shashoba, tau, saronga and g-og-g-ogat - on top of the world's rapidly growing list of forest resources of great and hitherto unknown potential value to humanity.

The scientists have called for schemes to plant more balatines trees, especially in desert areas, as well as further research to maximize yields of diosgenin, ethanol and edible nuts.

UNIDO is to sponsor a series of detailed and comprehensive industrial feasibility studies on a case-by-case basis before investment in suitable areas.

The FAO paper adds that the managers of balatines processing plants will have no difficulty finding fuel for their operations. Every ton of whole fruit also yields a good half-ton of hard woody shells surrounding the kernel that are highly combustible and produce excellent charcoal.

The deep-rooting tree is commonplace in semi-arid regions. It lives for more than a century, producing an average of 125 kg of fruit a year.

To uncover the fruit's full potential, the study team left it standing overnight in water, stirred it vigorously with a wooden stick and then passed it through mesh to separate the seeds. Subsequent tests revealed that the pulp, making up about a third of the fruit's weight, contained up to 72 per cent carbohydrates, mainly sugars, plus crude proteins, steroidal saponins, vitamin C and some minerals.

Even more valuable is the fermented mash left after distillation of the ethanol and CO_2. It is rich in steroidal saponins which, upon hydrolysis, form diosgenin, an important source of steroid drugs such as corticosteroids, contraceptives and sex hormones.

"Diosgenin is the most valuable product from balatines fruit," the study concluded, although drug manufacturers now prefer cheaper substitutes.

But "it is still possible for diosgenin to make a comeback and dominate the world steroid market provided it is offered at a low price with constant supply". Experts calculate that the Sudan alone could produce 1,200 tons of diosgenin a year, enough to satisfy half the world demand and earn an export income of $36 million.

After opening the kernel's hard woody shell, research workers found an almond-shaped seed containing up to 30 per cent protein and 51 per cent fixed oil, proportions similar to those of sesame seeds and groundnuts. The seeds were processed into several edible products. The Sudan could produce from its existing trees an estimated 13,600 tons of edible oil and 24,000 tons of kernel cake. (Source: Development Forum, October 1987)

Cross-purpose crops

Crops engineered to tolerate modern herbicides could seed a new race of farm weeds that resists attack by chemicals.

George Marshall, an agronomist from the West of Scotland Agricultural College, says that herbicide-resistant plants could one day become weeds themselves. They may also spread their genetic trait of tolerance to closely-related weed species or to plants that then develop cross-resistance to more than one herbicide.

Marshall identified chemicals called sulphonylureas and imidazolinones as the herbicides likely to be in greatest demand for the development of herbicide-tolerant crops. They combine a specific mode of action with good weed control. They are not highly toxic to mammals. However, their increased use in crop production is undesirable says Marshall, because the two herbicide families share a similar mode of action. They would exert a heavy selection pressure on weed flora which would probably respond by producing resistant versions of themselves.

Instead further research should be made on the longer-term effects of herbicides on the abundance and diversity of the weed flora. (Source: New Scientist, 10 December 1987)

Bacterial weed killers?

Root-dwelling bacteria that attack weed seedlings could replace some chemical weed killers.

The bacteria - called rhizobacteria - multiply in microscopic "crevices" between the root cells of weeds, says Robert J. Kremer, a microbiologist with US Department of Agriculture's agricultural research service.

Mr. Kremer has identified several strains of rhizobacteria that attack velvetleaf, cocklebur, jimsonweed, pigweed and morning glory. They break down root-cell walls or deliver toxins to leaves, cutting production of the chlorophyll a weed needs to convert sunlight into food energy. Rainstorms washed out field tests last spring, but Mr. Kremer has more planned for 1988. Earlier this year Mr. Kremer reported that some strains of rhizobacteria cause weed seeds to rot. The seeds have tough coats and toxic chemicals to ward off enemy microbes, but some rhizobacteria can overcome these defences. New tests show that rhizobacteria could get a boost from some commercial pesticides, including the herbicide butylate and the insecticide carbofuran. (Extracted from Chemical Marketing Reporter, 7 December 1987)

Genetically engineered tobacco resist pests

By transferring a gene from cowpea plants, British scientists have engineered tobacco that can escape damage from tobacco budworm infestation. The cowpea gene responsible encodes for an inhibitor of trypsin, an enzyme found in the gut of insects, according to Vaughan A. Hilder, Angharad M.R. Gatehouse, and Donald Boulter of the University of Durham's botany department and Suzanne E. Sheerman and Richard F. Barker of the Plant Breeding Institute in Cambridge. The trypsin inhibitor presumably is a part of the cowpea's natural defence system against pests. In laboratory tests, expression of the gene in tobacco plants gave them enhanced resistance to tobacco budworm attack. The scientists note that the same gene could

be incorporated into other important crops such as cotton or rice. (Reprinted with permission from Chemical and Engineering News, 16 November 1987. Copyright (1987) American Chemical Society)

Field test approved for new biological crop protection

Crop Genetics International Corp. has filed an application with the US Environmental Protection Agency and Department of Agriculture to field test its new delivery system for biological crop protection.

The tests will evaluate CGI's genetically engineered micro-organisms in the environment.

Under an agreement signed by CGI and USDA's Agricultural Research Service (HXS), a test will be conducted on federal land at ARS's Beltsville, Md. facility in co-operation with OSUM scientists.

CGI's InCide Division uses recombinant DNA technology to genetically alter plant-dwelling micro-organisms called endophytes so that they produce the naturally occurring pesticide of Bacillus thuringiensis (Bt). Agricultural crops and seeds can be vaccinated with the altered endophytes to protect them from plant pests. After inoculation, biopesticide-producing endophytes are carried throughout the plant in sap flowing in the plant's vascular system and, in effect, confer immunity against specific pests.

The first "InCide" product based on this technology will be used to control the European corn borer. According to an ARS publication, the new "InCide" system should give farmers a safer, easier to use, less expensive and more effective product than conventional pesticides. (Source: Chemical Marketing Reporter, 28 December 1987)

Field test for bacteria to go ahead

The US Environmental Protection Agency (EPA) has approved the first field test of a recombinant organism to fall under the Toxic Substances Control Act (TSCA). A unanimous vote by EPA's biotechnology advisory committee has cleared the way for Monsanto to field test a strain of fluorescent Pseudomonas aureofaciens containing lacZY marker genes that will allow the strain to be tracked in the environment. Monsanto plans to introduce genes for agriculturally beneficial proteins into the strain, and the marker genes will be used to assess the movement of the engineered bacteria. The field test is scheduled to begin in late 1987, in Blackville, South Carolina. (Extracted from Nature, Vol. 329, 29 October 1987)

Food production and processing

Toxicity tests for food enzymes

British toxicologists are about to embark on a research project to develop a non-specific test for ensuring that there are no unknown toxins produced in food enzyme preparations, provided they can persuade the enzyme producers and other food companies to present some of the funding.

In 1982, the UK Committee on Toxicity concluded that there was no doubt that some micro-organisms used to make food enzymes could, under certain conditions, produce toxins.

In the absence of sufficient data, most of the enzymes not rejected entirely were consigned to group B, a toxicological category indicating provisional acceptability for use in food. Now, five years later, scientists at the toxicology research association BIBRA and the Leatherhead Food Research Association have put forward proposals for research on tests that might form the basis of a battery of assays.

These tests, which involve cell cultures, protozoa, brine shrimps and germinating seedlings, would provide a cheap and quick way to determine whether any unidentified toxins are produced along with enzymes. They would be used to evaluate an enzyme for regulatory approval, but not, it seems to test different batches of enzymes on a regular basis. (Source: Chemistry and Industry, 19 October 1987)

Oxoid's aflatoxin test kits

Oxoid Ltd. has launched a series of aflatoxin testing kits in response to the growing awareness of the threat posed to health by the presence of potentially carcinogenic aflatoxins in all types of food. Based on monoclonal antibody technology, using immunoaffinity columns, the extraction process removes the full range of aflatoxins. After concentration, the aflatoxins are eluted from the columns for analysis by fluorescence. (Source: Biotechnology Bulletin, Vol. 6, No. 10, November 1987)

New method to hold renin

Bioprotein Canada, the University of Guelph and the Canadian National Research Council have developed Biobone, a matrix made from waste chicken bones, to hold enzymes. One application will be to hold renin used in cheese making. Renin is usually just poured into the vat, and thus can only be used once, but Biobone could hold renin in place for its reuse. It is still not clear whether Biobone could be used for cheesemaking on a commercial scale. (Extracted from New Scientist, 24 September 1987)

New chymosin approved for production

Pfizer's new chymosin is the first food additive involving a fermentation process using a genetically engineered organism to get FDA approval. The milk-clotting enzyme is the active component of calf rennet, which has long been the main milk coagulant used in the production of high quality cheese. Calf rennet is traditionally obtained by extraction from calf stomachs, and fluctuates in availability and price.

Development of the fermentation-produced chymosin involved developing a commercially practical process, and the synthesis of the "nature-identical" prochymosin gene, a major feat because of its complexity. Pfizer then used rDNA techniques to insert the prochymosin gene into a host micro-organism used in the fermentation process. The micro-organism is not present in the final product. Pfizer will produce chymosin under the appropriate NIH guidelines for rDNA research in a new facility in Terre Haute, IN. (Extracted from Chemical Marketing Reporter, 7 December 1987)

Developing superior edible oils

The application of biotechnology to crop plants to develop edible oils with improved fatty-acid composition and superior processing and formulation characteristics is the aim of a broad agreement between Du Pont and DNA Plant Technology (Cinnaminson, N.J.). Initial emphasis will focus on development of superior varieties of rapeseed, an emerging major source of edible oil. The companies plan eventually to form a marketing joint venture. (Source: Chemical Week, 16 December 1987)

Synergen announces first commercial product

Synergen, Inc., of Boulder, Co., announced the opening of a plant by Coors Biotech Products Company for the commercial production of riboflavin using an improved micro-organism developed by Synergen. The vitamin will be for human use and for use in animal feed as a nutritional supplement. This new commercial production process for riboflavin results from a joint research effort between Synergen and Coors Biotech.

Synergen applied its proprietary techniques of genetic strain improvement to significantly increase production levels of riboflavin over existing processes, making this the best micro-organism available for commercial production of the vitamin. Coors Biotech developed the fermentation and scale-up techniques and will be responsible for production and marketing activities.

Commercial quantities of the vitamin will be manufactured in early 1988 in the Coors Biotech-owned fermentation plant in Winchester, Kentucky. Synergen will receive a percentage of revenues generated by the sale of this product with first commercial sales expected by the end of the first quarter of 1988.

Synergen and Coors Biotech are also nearing completion of a second project in which they are developing a natural food colouring agent. This product, which should begin commercial production in mid-1988, would also be produced at the Kentucky plant. (Source: Company News Release, 1 December 1987)

Protein from Antarctic krill

A technology for obtaining protein from Antarctic krill has been developed at the Institute of Experimental Biology, Warsaw (Polish Patent No. 135946). The protein thus obtained is suitable for use as animal feed and also for human consumption purposes. The technology developed features the following advantages: the preparation of relatively unchanged, native proteins and the elimination of a considerable amount of non-protein components of the raw material (both those soluble and insoluble in water) and easy process control. The technology is applicable both for fresh and frozen raw materials.

Disintegrated fresh or frozen raw material is mixed with water or an aqueous solution of a salt (potassium or sodium chloride) for a period of up to four hours. A proteinases inhibitor may be added to that solution in order to protect the protein against decomposition, so that it does not lose its biological properties. The insoluble parts of the raw material are then separated, including the chitin, whereupon the protein is separated out and precipitated.

In order to precipitate the protein, the solution is acidified up to a pH value of 2.5 to 6.0 by means of a non-toxic acid, heated up to a temperature of 320 to 370 K or treated with organic solvents. Acetic, citric, hydrochloric or lactic acids are used in the former case, while ethanol or acetone are the organic solvents employed in the latter case. The precipitated protein is separated by a standard technique i.e. by filtration or centrifuging.

Process yield figures: dissolution of some 60 to 70 per cent of the protein contained in the raw material; precipitation of about 70 to 80 per cent of the dissolved protein. (Source: Polish Technical Review, No. 5/1987)

Complex utilization of whey

The Dairy Industry Institute, Warsaw, has developed a complex technology of whey utilization by a micro-biological technique. A patent application is being filed with the Polish Patent Office. This method gives the possibility of processing whey into such valuable products as neutral spirits, fodder yeast, edible fat and animal feed. In comparison with the whey processing methods employed at present, the new technology exhibits a number of significant advantages, including the following: (a) considerably reduced plant equipment investment outlays; (b) whey concentration to increase the lactose content is unnecessary (considerable energy savings are attained); (c) the lactose fermentation yield to alcohol excees 80 per cent; (d) highly economical alcohol separation process and most effective prevention of foaming, thanks to the application of distillation columns of special construction (Polish Patent pending). The alcohol obtained after a single-stage rectifying process conforms to the superior grade requirements.

The overall energy balance of the process is positive. A whey utilization plant based on the new technology is now being erected at the Dairy Co-operative at Szczebrzeszyn. This plant will be processing 100,000 litres of whey daily to yield about 2,000 litres of neutral spirits, 500 litres of whey fat, 10,000 litres of a protein concentrate containing 4 per cent proteins and 8 per cent dry matter as well as some 500 kg feed yeasts.

The dairy plant effluents will contain a whey decoction in the form of water with a small amount of mineral salts (chemical oxygen demand of that decoction is equal to about 10 per cent of the whey demand). (Source: Polish Technical Review, No. 5/1987)

Simultaneous utilization of shark meat and skins

Industrial methods applied hitherto for utilizing the sharks caught make it possible to obtain either edible meat or shark skins only. The new technology for processing sharks (Polish Patent No. 132211), developed at the Marine Fisheries Institute of Gdynia makes possible the simultaneous recovery of both those valuable raw materials.

It offers a simple and efficient separation of edible meat from other elements of the body used as raw materials for other processing stages (e.g. skins, livers, etc.) met with aboard medium-sized fishing vessels.

Other advantages of this technology are as follows:

(a) Simple mechanical transport of the fish onto the deck and then into the deep freezing section; the transport can be arranged using the transport facilities and equipment existing aboard the fishing vessel, and

(b) Possibility of deep-freezing the final fillets in refrigerating plant equipment.

The new technology consists of a suitable technique of slitting the sharks that are divided into two segments from which the fillets are cut out. The division into segments is done by means of a lateral cut in a plane perpendicular to the spine. The fillets thus obtained, the final product of

processing, do not require any further cleaning and are easy to store prior to the final processing on land.

The obtained skins are first fleshed, washed in outboard water and subjected to successive preservation steps.

This technology has been applied successfully aboard the WIECZNO vessel owned by the Marine Fisheries Institute. The freezer trawler KULBIN is now being reconstructed in order to utilize that new technology (the KULBIN is designed for large fish catching). (Source: Polish Technical Review, No. 5/1987)

Better preservation of fish

Fish should be bathed in water at 90° C for five seconds before being chilled in ice and salt, extending storage life from three to five weeks. The hot water bath kills bacteria on the fish, making the chilling more effective at preserving fish. In most tropical areas, where refrigeration is lacking, huge amounts of fish must be thrown away because it spoils. The hot bath might be replaced by immersion of the fish in a 5 per cent potassium sorbate solution or chloride dioxide. Quality and taste of the treated fish are unaffected. (Extracted from New Scientist, 17 September 1987)

Fish biosensor

Pegasus Industrial Specialties (Toronto, ON) and Canpolar (St. John's, NF) are developing machines that quickly show if fish is fit to eat. If either firm is successful, the result may be Canada's first commercially marketed "biosensor". Both firms plan to market probes that use enzyme-coated electrodes to measure small amounts of foul-smelling substances accumulating in fish. Pegasus said it is nearly ready to begin producing a probe developed by the National Research Council that will perform tests in under six minutes. The firm plans to make improvements to NRC's basic design. M. Thompson, co-director of the University of Toronto's biosensor research group, said most work so far has been done in the laboratory. The emerging technology may have uses in medicine, environmental quality control and defence. (Source: Financial Post, 15 November 1987)

New fruit and vegetables

RJR Nabisco will jointly develop bioengineered fruits and vegetables with Bio-Technica International (Cambridge, MA). The new plants will purportedly be more nutritious, tastier and disease resistant. Neither firm will reveal full details or the financial considerations of the venture, but Bio-Technica says the collaboration could yield new varieties of crops such as seedless green peppers, supersweet peas and dry-roasted nuts that would have a nuttier flavour. In addition, it plans to develop vegetables with higher protein content. For example, broccoli would contain the same protein as eggs minus the cholesterol. (Extracted from Business Week, 5 October 1987)

Energy and environmental applications

Useful bacteria

Bacteria are in great demand these days in the battle against environmental poisons. The Kraftwerk Union (KWU) has developed a new purifying plant for a factory producing potato starch. It transforms 2,060 cubic metres of sewage every day into, for the most part, gas which then provides almost all the required energy which the factory needs for production. The University of Hohenheim in Stuttgart also thinks very highly of the voracious bacteria where thousands of millions of these minute microbes hunt a poison which until today was impervious to all attempts to destroy it: nitrate, which is found in fertilizers. First trials were very promising. The microbes can also deal with extremely high concentrations of nitrate; they break it down into harmless nitrogen. If nitrate enters the human body it is transformed there by bacteria into nitrite. Nitrite is highly suspect as a cause of cancer. (Source: Scala, January/February 1988)

Algae fuel petrol research

Research is under way to produce algae for conversion to petrol. Scientists at the Solar Energy Research Institute (SERI), in Golden, Colorado, are screening species of algae for their ability to produce large amounts of fats and oils. Algae produce these compounds as food reserves, and in some cases between 50 and 70 per cent of the biomass of these plants may be oils. When produced in large quantities, these can be converted into fuels by chemical conversion processes such as cracking or transesterification.

The research institute is developing the technology in conjunction with Microbial Products, a company based in Connecticut. The institute is concentrating its efforts on screening thousands of strains of algae, while the Connecticut company is developing culture techniques. The researchers believe the technology is most likely to be commercially successful in the southwestern US, where land and sunlight are plentiful, and temperatures favourable.

Most of the promising algae are diatoms and the most useful species come from puddles or larger bodies of fresh water in the southern US. The SERI scientists are searching for strains of species that not only produce large amounts of oils, but are also tolerant of high salt concentrations and wide fluctuations in temperature.

Little research has so far been directed towards the chemical conversion process needed to turn the algae into fuel. However, it is estimated that petrol prices have to reach $1.6 per gallon in the US, only about £1.20 per UK gallon, to make the whole programme economic. SERI are currently investigating the genetics of the algae to produce even better strains. However, the scheme is long-term and it is not expected that the process will be ready for industry to take over until the year 2010. (Extracted from New Scientist, 24 September 1987)

Machine processes organic waste to cattle feed

MI Techno Sales' new Biomate machine uses biotechnology to process various organic waste materials into odourless cattle feed. Designed to cope with the huge amount of industrial garbage discharged by restaurants and processed food companies, the machine has a built-in fermenting vat capable of holding 200-2,000 litres of waste and special ceramic granules treated with 23 different fermentative aerobic germs. The machine dissolves protein and fat in kitchen refuse, wood chips, cattle dung and other wastes into feed substances such as nitrogen and other substances such as carbonic-acid gas and water. Processing takes 8-24 hours and is accomplished without generating offensive odours. (Extracted from Asian Wall Street Journal, 31 August 1987)

Hazardous waste treatment

Bioremediation for hazardous waste treatment is gaining commercial acceptance due to its cost effectiveness. Acceptance should increase as more waste treatment firms incorporate bioremediation as one of several technologies they offer clients, rather than as a solution for all problems. Critics have downplayed the practicality of bioremediation, arguing that its application is limited, and point out that the waste stream at a particular site may consist of various compounds from several sources, only some of which may be vulnerable to biodegradation. However, proponents tout bioremediation as only one component in a larger treatment approach. G. Brubaker of International Technology's ARE Group notes that waste treatment companies can blend technologies and make them work together synergistically. The most obvious way of combining different treatments is to physically remove as much material as possible from a site, and stimulate micro-organisms to consume the rest.

One aspect of biodegradation that is sometimes exaggerated is that laboratories breed microbe superstrains. In fact, most waste management firms that offer the service do not breed microbe 'Rambos', preferring instead to stimulate organisms in the soil by feeding them the right nutrients, strengthening their natural ability to digest the contaminants. Ecova recently found a site where the soil was not permeable enough for in-situ treatment, so it first air-stripped the volatile organics, then biodegraded the semi- and nonvolatile organics by removing the soil to a closed greenhouse-like facility in a process called solid phase treatment. (Extracted from Chemical Marketing Reporter, 23 November 1987)

Bioremediation techniques

ERT has successfully tested a biological method of treating hydrocarbon hazardous wastes. Bioremediation techniques could dispose of an estimated 80,000 cubic yards of sludges and 70,000 cubic yards of soil and sand in a test lagoon laced with toxic petrochemicals. The waste hauler that dumped wastes at the site went out of business and deeded the site to the permanent school fund of the state of Texas. Laboratory and tank tests did not provide sufficient information about how to clean up the site, so part of the lagoon itself was partitioned off for testing. Compressors were installed to aerate the water and sludge, and fertilizer was added to encourage micro-organisms in the pond to grow. No hazardous volatile emissions were generated by these processes. The microbes converted organic compounds to harmless by-products, water and carbon dioxide. A suction dredge sucked up sediments and released them so that they could settle out slowly while microbes worked them over. (Extracted from Chemical Week, 11 November 1987)

Microbes to track organisms

Monsanto will release a genetically-altered microbe to help scientists track other genetically engineered organisms in the environment, with the approval of the US Environmental Protection Agency, as part of President Reagan's plan to regulate biotechnology. Clemson University scientists are helping Monsanto. Pseudomonas aureofaciens was altered by inserting two genes from E. coli to produce lactose, a natural sugar. The Pseudomonas microbes were sprinkled on a gel mixture containing lactose as the sole nutrient. Those that accepted the new genes thrived on the gel and appeared as tiny white dots. Monsanto then refined the system by adding a chemical dye to the gel, turning altered microbes able to synthesize the dye blue. The system may be used in other microbial products. The microbe is the third gene-altered micro-organism the EPA has allowed to be released into the environment in 1987. (Extracted from New York Times, 21 October 1987)

Coal desulphurization

A coal desulphurization process in which inorganic and organic sulphur are oxidized by micro- organisms is under development at the Idaho National Engineering Laboratory (INEL) in Idaho Falls. Pyritic sulphur is removed by introducing Thiobacillus ferrooxidans bacilli to an aqueous slurry of crushed coal. The bacteria oxidize the sulphur from the insoluble sulphide to soluble sulphate. Removing the organic sulphur is a more difficult problem. Researchers have been working with various micro- organisms that break the chemical bonds so that the sulphur can be dissolved. (Extracted from Chemical Week, 18 November 1987)

Bioreactor to degrade DMF

Toyo Polymers has developed a bioreactor that degrades dimethylformamide (DMF), which is generated during the production of acrylic fabrics, synthetic leather and paints. The core of the bioreactor contains a resin in which a special strain of aerobic bacterium is immobilized. The bacteria convert DMF to carbon dioxide and nitrogen gas, reducing concentrations to 3 per cent. Current decontamination techniques using distillation cannot economically reduce DMF concentrations to under 10 per cent, so that liquids containing DMF are released to the environment after being diluted. Small amounts of DMF are not thought to be harmful, but chronic exposure can cause liver damage. Toyo Polymers is conducting a market survey to assess demand for the bioreactor. (Extracted from Bio/Technology, Vol. 5, December 1987)

Extraction industry applications

Microbial metal recovery expanding rapidly

Virtually all major copper producers now use micro-organisms to some extent to extract and concentrate the metal, accounting for approximately 20 per cent of world production. Microbial metal recovery is currently a $450 million business in the US and is growing at a rate of 12-15 per cent annually.

Continuous processes for bioextraction of gold, silver, cobalt, and manganese are nearing commercialization, promising a rapid expansion of the field. Genetic engineering work now under way with T. ferroxidans and other microbes promises to improve the efficiency of bioextraction processes at low temperatures and high concentrations. (Source: Advanced Materials & Processes Inc. Metal Progress, November 1987)

Coal purification and liquification

Scientists are researching the use of microbes and fungi for the removal of pollutants from coal. D. Spencer of the Electric Power Research Institute (EPRI) predicts that such organisms can make coal deposits as valuable as oil deposits. The US Energy Department has spent $5.7 million over the past four years for research into biological techniques to purify and liquefy coal, while EPRI is spending $500,000 per year on biological coal-treatment projects. Some scientists also foresee using micro-organisms to turn coal into natural gas. Houston Lighting & Power, for instance, is converting coal into methane gas with the use of bacteria. (Source: Business Week, 16 November 1987)

Biological gold recovery

Carolin Mines may produce gold from its property near Hope, British Columbia. Giant Bay Resources and Wright Engineers (both of Vancouver, BC) have agreed to carry out a six-month metallurgical test and study of Carolin's mine. The mine, that closed in 1984 after operating briefly, had several technical problems. Giant Bay believes its bio-leaching technology might improve gold recoveries, while Wright will tackle the mine's effluent control trouble. (Extracted from Financial Post, 8 November 1987)

Chemical applications

Lavender pigment bioreactor

A bioreactor that can continuously produce the blue pigment of lavender flowers for up to three months has been developed by Kyoto University researchers. The lavender plant cells remain viable because they are immobilized in a special hydrophilic PVA resin polymerized by exposure to light. The immobilized cells are then immersed in culture medium supplemented with cysteine, an amino acid. Since few blue or purple dyes can be used as food additives, lavender pigment is in demand as a food colouring. (Extracted from Bio/Technology, Vol. 5, December 1987)

Industrial microbiology

Biotechnology potential in aromas and flavourings

The food sector's consumption of natural flavourings and aromas is rising by about 10 per cent per year, although the cosmetics, detergents and toiletries sector holds the lion's share of the market. The availability of trees and flowers for perfume production is falling, and increasing emphasis is being laid on using micro-organisms such as yeasts, bacteria and fungi to produce natural flavourings and aromas. As they can be grown in the laboratory supply is not subject to seasonal variation as with higher plants. However, methods need to be optimized before they can become competitive. (Extracted from Chemical Rundschau, 25 September 1987)

Further uses for algae

Algae could be cultured to produce organic chemicals, according to researchers at Queen Elizabeth College (London). Large banks of tubes can produce algae very efficiently even in low levels of sunlight. The photo-bioreactors can produce 200 times as much algae as a comparable area of pond. Temperature, salinity, acidity, and nutrient and CO_2 concentrations can all be carefully controlled. Some species of algae might be used to produce ecosapentanoic acid, gamalinolenic acid, betacarotene or phycoerythrin (an extremely expensive red dye). (Extracted from New Scientist, 1 October 1987).

A dry microbiocide

Mogul (Chagrin Falls, Ohio), a division of Dexter Corp., has developed a dry microbiocide for controlling algae, bacteria and fungi in commercial and industrial recirculating cooling-water systems and air washer systems that use mist eliminators. The product, Mogul A-482, is a nondusting powder sealed in porous, premeasured packets; it is effective over a wide pH range and has a stable shelf life. Use of the microbiocide requires no elaborate feed systems and avoids direct exposure to the chemical. The US Department of Agriculture has authorized the use of the new product in cooling water that does not contact food products. (Source: Chemical Week, 14 October 1987)

E. PATENTS AND INTELLECTUAL PROPERTY ISSUES

EPO patent infringement dispute

Amgen and Genetics Institute have filed lawsuits against each other over patents on erythropoietin. Genetics Institute claims that Amgen has infringed its patent for the compound, for purifying the compound and for resultant pharmaceutical preparations. Amgen's countersuit also charges patent infringement. EPO could be given to kidney dialysis patients to reduce the need for blood transfusions. Amgen's patent covers intermediates used in the production of EPO. The dispute could be settled through a cross licensing agreement. (Extracted from Chemical Marketing Reporter, 2 November 1987)

New proposal

The US Patent & Trademark Office has proposed that those seeking to patent a biological substance submit a sample of the material along with the patent application. The proposed rule will include formal requirements on type and quantity of the biological materials that must be submitted. It would require samples of materials capable of self-replication to be submitted. The proposed rules would cover bacteria, fungi, yeast, algae, plant cells, cell lines and seeds. Substances such as proteins and enzymes will be excluded from the requirements. (Abstracted with permission from Chemical and Engineering News, 14 September 1987. Copyright (1987) American Chemical Society)

A patent for protein-design system

Genex (Gaithersburg, Md.) has won a patent (US 4,704,692) for a computer-based system for the design of single-chain proteins that are engineered to function like monoclonal antibodies. The proteins are simple antigen-binding molecules that are much smaller than monoclonals and can be more quickly cleared from the body. Compared with monoclonals the proteins provide reduced toxicity and immunogenicity, greater stability, improved attachment of imaging or therapeutic agents, and improved binding performance when immobilized. Because the Genex-designed proteins can be produced in microbial fermentation systems, they are expected to be cheaper to produce than monoclonals. (Extracted from Chemical Week, 18 November 1987)

Biogen receives hepatitis-B antigens patent

The US Patent & Trademark Office has issued Biogen US Patent No. 4,710,463 covering the manufacture of all hepatitis-B surface and core antigens produced by genetic engineering techniques. The recombinant antigens are necessary to produce vaccines and diagnostic kits for hepatitis-B. Biogen claims that the patent grants the company the right to exclude other companies from manufacturing or marketing hepatitis-B vaccines and diagnostics produced in the US by recombinant DNA technology. The company received a patent covering recombinant hepatitis-B surface and core antigens from the European Patent Office in London earlier in 1987.

This strengthening of patents is likely to have "a favourable impact on the company's financial position", according to a company spokeswoman. Biogen has no intention of making products itself with the technology covered by the patent but has licensed to Wellcome and Green Cross.

Other products to be covered by the US patent, according to Biogen, include the recombinant vaccines made by Merck and Co. and SmithKline Beckman.

Biogen expects to apply for a broader application for its European patent. The company also hopes that the US Congress will close a loophole in process patent legislation. Current legislation allows companies to make products, covered by a US process patent outside the US for import.

Legislation is now pending in Congress proposing to prohibit violation of process patents. There is no clear indication when this bill will be passed as it is part of a larger bill covering trade issues.

Clearly the tightening of the process patent legislation would boost Biogen's claims for royalties. Royalty revenues would give the biotechnology firm a much needed boost. Biogen is still reporting losses from its operations. Total revenues for the third quarter rose by almost $1 million to $2.69 million and losses were pegged back slightly to $6.99 million from $7.52 million in the same period last year.

Similar fortunes were reported for the nine-month period. Revenues stood at $9.34 million compared with $8.37 million last year, with losses of $19.21 million compared with a $20.46 million deficit for the nine-month period last year. Continuing losses were the main reason for selling Biogen's Geneva operation to Glaxo Holdings during the quarter. (Source: Chemical and Engineering News, 7 December 1987, p.6 and European Chemical News, 14 December 1987)

Genentech's "industry-encompassing patent"

Genentech Inc. has finally been awarded a broad patent covering the basic techniques used in the biotechnology industry. The company first filed its claims in 1979, but its application got caught up in the whole issue of whether or not it was possible to patent new life-forms.

The patent includes 15 claims; some exceedingly specific, and others sweepingly broad. The first and broadest claim establishes Genentech's proprietary right over any "recombinant DNA cloning vehicle suitable for the transformation of a microbial host" that consists of a control region regulating the expression of a structural gene, where the gene coding for the polypeptide is in the correct reading frame for expression, and the polypeptide is in recoverable form. The other 14 claims cover specific plasmids used as cloning vehicles, including those containing the Escherichia coli lac and tryptophan operon-promoter systems. Genentech also lays claim to plasmids that produce mammalian hormones or polypeptides in general, and specifically ones that produce proinsulin, growth hormone, and the A and B chains of human insulin.

Already issued in 20 countries, the Genentech patent is the industrial counterpart of the landmark Cohen-Boyer patent issued to Stanley Cohen of Stanford University and Genentech co-founder Herbert Boyer of the University of California. The Cohen-Boyer patent covered the splicing of genes from one organism to another. The latest patent, issued to co-inventors Drs. Keichi Itakura and Arthur Riggs of the City of Hope research institution, Los Angeles, covers methods of producing useful commercial products, via fermentation, from the resulting recombinant organisms. The original City of Hope work was carried out with Genentech sponsorship.

Licences could cost 1 per cent of sales

Competing companies are still unclear about the implications of the Itakura-Riggs patent. Genentech must now steer a middle course between setting a licensing royalty rate high enough to generate useful income, while avoiding a rate so high that it forces potential licencees to challenge the patent. The usual rate for non-exclusive licences of this kind ranges between 0.5 per cent and 1 per cent. (Extracted from Biotechnology Bulletin, Vol. 6, No. 10, November 1987 and Nature, Vol. 330, 12 November 1987)

Genentech loses hgH case

A legal dispute between Genentech and Eli Lilly over recombinant human growth hormone has prompted a review by US Congress of the Orphan Drug Act, the law intended to give commercial protection to companies making treatments for rare diseases.

Genentech filed a case against the Food and Drug Administration (FDA) in March, after the FDA approved Eli Lilly's form of recombinant human growth hormone, Humatrope, under the Orphan Drug Act. Humatrope differs from Protropin by one amino acid, so it was considered a new drug by the FDA. Humatrope is also used to treat dwarfism, and Genentech claimed that its marketing exclusivity for Protropin was being infringed.

Genentech sought to void both its own and Lilly's protection under the Orphan Drug Act, claiming that neither Protropin nor Humatrope was a "new drug", and that neither should be protected by the act, but a US Federal circuit court judge dismissed that argument, upholding the rights of Eli Lilly to market their drug. (Extracted from Nature, Vol. 329, 1 October 1987)

Unigene gets patent

Unigene Laboratories, Inc., Fairfield, N.J., has been issued a US patent on its proprietary enzymatic process for production of a broad class of hormones. The two-step process, employing recombinant DNA methods along with Unigene's amidating enzyme, can be used to produce hormones that are structurally identical and equally potent when compared with their natural counterparts, the company says. Research indicates the substances have an important role in regulation of metabolic processes and transmission of nerve impulses. (Source: Chemical Marketing Reporter, 7 December 1987)

Diagnostics patent

Enzo Biochem has secured the exclusive rights from Yale University of a patent that is essential to the development of non-radioactive DNA probe diagnostics. The patent, US No. 4,711,955, protects all lengths of nucleic acids, both RNA and DNA, linked to biotin at specific positions, says the company. Biotin serves to anchor detection systems to nucleic acids, making them visible. The company claims that their proprietary biotinylated probes have a much longer shelf life, are less expensive to produce, and present no health hazard or licensing and waste disposal problems relative to their radioactive counterparts. (Abstracted with permission from Chemical and Engineering News, 21 December 1987. Copyright (1987) American Chemical Society)

Computerized proteins

Gene has been granted a US patent on its computerized system for designing novel proteins. Proteins designed so far are single-chain antigen-binding molecules that act like monoclonal antibodies, but with reduced toxicity and immunogenicity. (Source: Chemical Marketing Reporting, 16 November 1987)

F. BIO-INFORMATICS

Rapid growth of US biotechnology predicted

US sales of biotechnology products will grow by more than 30 per cent annually in the next decade, according to Consulting Resources Corporation. The market analysts predict, in a new study, that sales will rocket from this year's $660 million to $10,200 million in 1997. The study "The coming profit opportunities in biotechnology: a new assessment" is available from Consulting Resources Corp., 6 Northbrook Park, Lexington, MA 02173, USA.

The study acknowledges that industrial development is slower than initially expected by some people, and that the financial performance of biotechnology companies has generally been disappointing.

The greatest growth, according to the study, will take place in human therapeutics, led by tissue plasminogen activator (tPA). This area, followed by human diagnostics and specialty products, is expected to be the most profitable market segment.

One of the interesting aspects of the future of US biotechnology is the influence that contaminant monitoring tests will have on society, despite the relatively low profitability of the business segment. Off-the-shelf kits for detecting very low levels of pesticide residues in food and water, or hazardous chemicals in the home or workplace, are going to become widely available at prices the individual consumer or employee can afford. (Extracted from Chemistry and Industry, 10 October 1987)

Basic biotechnology

Academic Press has published a new introductory text which elucidates both the fundamental principles and applications of biotechnology. Under the title Basic Biotechnology, it is aimed at advanced undergraduates of applied biology, microbiology, biochemical and chemical engineering, together with graduates in pure science and general engineering who are involved in biotechnology products. It would also be useful for research and industrial staff who desire to broaden their knowledge of the subject.

The book is edited by John Bu'Lock of the Weizmann Microbial Laboratory of the Department of Chemistry in the University of Manchester, and Bjorn Kristiansen of the Department of BioScience and Biotechnology at the University of Strathclyde.

The book is well produced and covers all areas of biotechnology from the biochemistry of growth and metabolism, through microbial process kinetics to bioreactor design and downstream processing. There is ample coverage of sterilization and instrumentation, together with microbial screening, selection and strain improvement.

The latter half of the text is devoted to practical applications, such as microbial biomass as a protein source, enzymes as bulk products and the production of antibiotics. There are sections on biotransformation, genetic engineering and products derived from cultured animal and plant cells. There are good reading lists after every chapter.

The Biotechnology Revolution is in its infancy and will obviously become increasingly important for the ultimate survival of mankind. Available from Academic Press (Inc), 24-28 Oval Road, London NW1 7DX. Price £20 paperback, £57 hardback. Telephone number 01-267-4466.

Biotechnology in Western Europe by Robert T. Yuan

If a leading US company sent a top scientist/entrepreneur on a 16-month tour to survey the Western European involvement in biotechnology, his resulting in-depth report might resemble this compendium. Its author is professor of microbiology at the University of Maryland, College Park. In each country, Yuan met with key figures in industry, academia and Government, to compile an analytical anatomy of biotechnology research, development, funding, regulation and over-all policy. Charts and tables enhance the content; a 153-word glossary at the end does not. Not least of the work's virtues is its taxpayer-subsidized price; had this been a private think-tank's client study, the tag might well have run to five digits - and worth it. The book is available from International Trade Administration, US Department of Commerce, Washington, D. C., (1987) 264+v pages, $13.00.

Locating software for molecular biologists

Software Directory for Molecular Biologists: A Complete Guide to the Selection of Computer Software for the Analysis and Management of Molecular Sequences. By Christopher J. Rawlings. ISBN 0-943818-37-0. $80.00. (MacMillan, London/Stockton, New York: 1986).

Most molecular biology and biochemistry laboratories spend a great deal of their time collecting and analysing DNA and protein sequences. Government-funded agencies such as Genbank, the Protein Identification Resource and the European Molecular Biology Laboratory search the literature for new sequences and enter these sequences into large databases. All this activity, both in the laboratory and in the database facilities, requires a great deal of skill in preparing computer software. Considerable effort has been put into the development of commercial software packages designed to provide most of the necessary computer programmes and databases to individual research groups. In addition, many laboratories have developed software for their own purposes and have made such software available at a modest cost or no cost to others.

There are two questions which arise, however, in obtaining and using either commercial or non-commercial software. First, how does a laboratory pick one or more sets of programmes really suitable for their purposes? Second, is the analysis performed correctly and are the provided data, such as sequence databases, accurate? This book will assist laboratories in solving the first of these two problems. It gives a very complete list of the commercial and non-commercial software available, including price, target computer on which it will run, where to obtain the programme, types of sequence analysis performed and sequence databases provided.

The first part of the book contains a description of general purpose computer methods and software, including information on building and using DNA sequence databases, selecting hardware and using file transfer programmes such as KERMIT. The second part is a software directory listed in alphabetical order by name of author or vendor. The final part contains several cross-indexes by author, program function, target computer system or programming language used in the software. A list of author and vendor addresses is also given.

New laboratory directory from ASTM

ASTM, the world's largest developer of standard test methods, has announced the publication of the 1988 ASTM Directory of Testing Laboratories. This new

edition features 1,000 laboratories, the majority located in the US and 40 in Canada. Searching is aided by detailed subject and alphabetical indexes.

The laboratories are in the business of performing services for a fee. They are not certified or endorsed by ASTM. The Directory price is $50.00 ($40.00 to ASTM members). Contact: ASTM Customer Service, 1916 Race Street, Philadelphia, PA 19103, (215) 299-5585.

NBST publishers directory of Ireland's diagnostic research

Diagnostics has been selected as one of the priority areas for the biotechnology programme developed by Ireland's National Board for Science and Technology (NBST). Since 1983, researchers in this field have been assisted by the NBST through its grant schemes for research, equipment and travel. Now the NBST has published a Directory of Irish Researchers, Manufacturers and Distributors of Diagnostic Products 1987. The directory lists 25 diagnostic research groups and details their research interests, numbers of personnel and contact names. It also lists 23 Irish companies involved in diagnostic manufacture or distribution.

Copies of the directory are available from the NBST, price £20.00. Details from: Brendan Finucane, Manager, Biotechnology Group, National Board for Science and Technology, Shelbourne House, Shelbourne Road, Dublin 4, Ireland or on (01) 683311.

Economic aspects of biotechnology by A.J. Hacking

This invaluable book explains from first principles the economic factors, commercial reasoning and accounting procedures vital to scientists involved in practical biotechnology.

300 pp. 1987 0 521 25893 6 Hc £35.00 net
0 521 34681 9 Pb £12.95 net

For further information please write to Shelby Howe at the address below:

Cambridge University Press, The Edinburgh Building, Shaftesbury Road, Cambridge CB2 2RU

Annuaire des Biotechnologies et des Bioindustries 1987

The above book, containing over 2,000 addresses, aims to give a complete picture of French biotechnology. It costs 650 francs. Details from: Biofutur SA, 29 rue Buffon 75005, Paris, France.

Biotechnology information

The proceedings of Biotechnology Information 86 are now available, price £32. The conference, held in September 1986 at the University of Sussex, looked at the complete spectrum of biotechnology information services. Details from: IRL Press Ltd., P.O. Box 1, Eynsham, Oxford OX8 1JJ.

Open University. Three new biotechnology titles

The Open University Press is producing a number of volumes in a series on biotechnology in association with the Institute of Biology. The first three titles are now available.

(1) Biotechnology, the Biological Principles by M.D. Trevan, S. Boffey, K.H. Goulding and P. Stanbury, each author contributing a complete section on his own specialized subject area, e.g. microbial growth, culturing micro-organisms for production, genetic engineering and enzyme technology. It is an intermediate level book to assist students and industrial people to understand the new applications of biotechnology. Price £14.50, £30 Hardback.

The authors have worked together as Senior Lecturers at Hatfield Polytechnic, teaching an M.Sc. course in Biotechnology and a B.Sc. in Applied Biology, from which the book is derived.

(2) Enzyme Technology by P. Gacesa, who is a Lecturer in Biochemistry at University College, Cardiff, and J. Hubble, Lecturer in Biochemical Engineering at the University of Bath. Their book is aimed at senior undergraduates, post-graduates and industrial practitioners with a range of backgrounds, from chemical engineering to biology, who have a common interest in enzymes. The development of enzyme immobilization techniques since the 1950s has led to a boom in the industrial use of enzymes which has created a demand for scientists from a wide range of academic backgrounds to work in enzyme technology. The engineer is provided with an appreciation of the subtleties of enzymes and the potential techniques in molecular genetics for tailoring these catalysts to specific needs. Price £14.95. £32.50 Hardback.

(3) Fermentation kinetics and modelling by C.G. Sinclair and B. Kristiansen, edited by J.D. Bu'Lock. This book gives a straightforward introduction to the subject of modelling fermentation kinetics for the microbiologist, biotechnologist or chemical engineer. There are examples of how to construct simple mathematical descriptions of processes and how to combine, manipulate and check appropriate modules with confidence.

Editing the series are Professor John Kennedy of the University of Birmingham, Chief Editor; Professor J.A. Bryant of Exeter University, Dr. R.N. Greenshields of G.B. Biotechnology Limited and Dr. C.H. Self at Hammersmith Hospital. Price £14.95. £30 Hardback.

NSF issues biotechnology report

US National Science Federation has published its report on "Biotechnology R&D Activities in Industry: 1984 and 1985", which includes data on funding, methods, and resources. It is available from the US Government Printing Office, Washington, DC 20402; report number NSF 87-311.

Handbook of practical biotechnology

The Bioindustrial Group at Novo Industri A/S has published an easy to follow Handbook of Practical Biotechnology based on their experience in using enzymes, written by their technical experts. In the introductory section they consider the use of enzymes, their industrial reactions and immobilized enzymes. This is followed by a strategy for development which includes planning experiences and comparing enzymes. Industrial profiles are considered next and cover such headings as "Brewing with Barley", "Making Sweeteners from Starch" and "Enzyme-modified Dairy Products".

They deal with all six industrial enzyme classes: proteases, amylases, cellulases, isomerases and lipases, redox enzymes and their regulatory status.

The concluding chapter deals with monitoring enzyme reactions and covers safety aspects. There is a list of the most important references at the end of each chapter, each of which is colour-coded for ease of reference. The handbook can be obtained from Novo Enzyme Products Limited of Lion and Lamb Yard, West Street, Farnham, Surrey, GU9 7LL. Telephone number 0252 711212.

Brief reports on significant emerging technologies within the field of biotechnology

For nearly two years, futuretech, a service of Technical Insights, Inc., has been monitoring emerging technologies across major industrial fronts: Advanced Materials, Biotechnology, Computers/Electronics, and Manufacturing/Automation.

These emerging technologies have largely escaped notice by even the most avid technology watchers. Therefore, they offer meaningful opportunities for aggressive companies seeking investment, co-venturing, licensing, acquisitions, and strategic partnerships.

We have heard from many of you saying you are interested primarily in certain focused areas of technology. Now, you can purchase just those reports in the Biotechnology field.

Every futuretch report (running 12 to 20 pages) identifies clearly the strategic technology uncovered; presents the state of the technology on industry segments, company groups, products or processes and countries; contains a comprehensive description of the technology and how to exploit it - via licenses, acquisition possibilities, joint ventures, etc.; describes new companies in the field and their activites; lists key research groups to watch; profiles the key developer (group, person, or firm) and contains a resource file for further details in the technical literature, patent literature and government reports.

In the area of biotechnology, the following titles are available:

Report No.	Technology
FT4	**Electroacoustics: Advances in Dewatering.** Interacts electrical currents with acoustic waves. Result is faster, more complete dewatering of food, coal, paper pulp, yeast, ceramic, clay suspensions, other items. Licenses offered; joint ventures considered.
FT19	**Supported-Liquid Membranes: Enhanced Separation Technology.** Organometallic compounds are converted rapidly to lightweight ceramic materials at relatively low temperatures. They are used to coat parts that must withstand high temperature, excessive wear, and corrosive environments. Other uses: as binders for ceramic powders and as reinforcing fibres in carbon composites. Available for licence.
FT24	**Enzymatic Processing in Organic Solvents: Catalyzing New Reactions.** Organic media gives enzymes ability to catalyze reactions not possible in water. Can make optically active polymers, sugar, flavours, pharmaceuticals, chemicals. Researchers looking for joint ventures or co-operative R&D.
FT26	**Photomagnetic Catalysis: Innovative Curing Technology.** Researchers combine a magnetic field and electromagnetic radiation to catalyze chemical reactions. Cures cross-linkable materials quicker, more economically, and more reliably than current ultraviolet and thermal processes. Initial applications could be one to two years away. Financial support sought.
FT29	**Magnetic Biosorbents: Yielding Improvements in Waste Cleanup and Bioreactors.** Polymer-based magnetic beads that support micro-organisms which immobilize, modify, or produce materials. Potential applications in substrate modification, bioreactors, and waste cleanup. Technology can be licensed and commercialized within a year.
FT36	**Carbohydrate Synthesis.** Exploiting the potential of complex carbohydrates. Capability to synthesize these compounds providing a valuable tool for biotechnology and pharmaceuticals. Human and animal tumour cells produce their own carbonydrate types not found in normal tissue. Can be used to produce monoclonal antibodies that are more specific, detect cancer at an earlier stage, and diagnose and treat bacterial and viral infections. Researchers develop and sell specific processes to interested companies.
FT37	**Supercritical Fluid Synthesis.** Using carbon dioxide in its supercritical state as a nontoxic substitute for solvents such as chloroform and methylene chloride. Supercritical CO_2 is already employed in extraction processes; use in synthesis is new. Technology can make peptides for pharmaceuticals less expensive to produce. But the technology is broad and could potentially be applied to any process that involves organic solvents: polymers, gasoline additives, pesticides, growth hormones. Licenses being considered.

The price of the first report is $100 (plus $15 for airmail delivery outside North America), $55 for each additional report. Further information is available from Technical Insights, Inc., Dept. IDG127, P.O. Box 1304, Ft. Lee, NJ 07024, USA. Intl. Telex: 230199 SWIFT UR TII; Domestic Telex: 960127 SWIFT NYK TII. (Source: INSIDE R&D, 12 August 1987)

US Presidential Commission's AIDS report

Despite controversy and ideological clashes, the US "Presidential Commission on the HIV Epidemic", named after the virus that causes AIDS, put out its preliminary report in December 1987. The report identifies four key areas that the commission will focus on in the coming months: the accumulation of realistic data on the spread of the HIV virus in the United States, more home health care for AIDS patients, increased development of drugs to treat AIDS and the expansion of drug abuse treatment programmes.

The commission's final report and recommendations on the legal, ethical, social, medical and economic implications of AIDS is due next September. A series of interim reports on the four most critical topics will be issued in February 1988.

Meanwhile promoted both by the success and the failure of its first effort, the US Institute of Medicine (IOM) has begun work on a second edition of its report Confronting AIDS: Directions for Public Health, Health Care, and Research. When released in 1986, the report generated massive press coverage, and its conclusions were widely embraced, but not put into practice by the federal Government.

A small panel will assemble the report, aided by some 70 correspondents writing about different aspects of the AIDS problem. The updated edition of the report is due early next summer. (Source: Nature, Vol. 330, December 1987)

AIDS and the third world

AIDS is not confined to the epidemics in the United States, Europe and Central Africa; it is already a serious problem in Caribbean countries, Latin America, parts of West Africa and Australia. Moreover, there are increasing signs that it is beginning to grow alarmingly in some Asian countries such as India, Japan and the Philippines. New material contained in AIDS and the Third World, a report from the Panos Institute, confirms that the AIDS virus has now reached more than 127 of the world's 159 countries. Most of those already carrying the virus live in the third world.

An AIDS epidemic is like an iceberg: a few hundred proven cases of AIDS indicated that thousands of people are already carrying the virus, says the dossier. In Europe and North America, the numbers of AIDS cases have, until recently, been doubling every nine or 10 months.

In the United States, the worst-hit city is New York, where one in 15 people is now thought to carry the virus. But in some Central African capitals, up to one person in five is infected, most of them in their twenties and thirties, as many women as men. These are their nations' breadwinners, many of them educated professionals, whose deaths will scar Africa for a generation.

By 1991, the US Government estimates that 179,000 Americans will be dying of AIDS. The direct health costs will be over $8 billion in that year alone.

The far less well-equipped health services of those affected countries in Latin America, Africa and the Caribbean today contemplate a crisis which is several times worse. The cost of testing one person for the AIDS virus is more than the annual per capita health budget in many developing countries. The impact of AIDS on third world development will be profound.

AIDS and the Third World was first published in November 1986 by the Panos Institute in association with the Norwegian Red Cross and has now been updated to reflect the changing situation. A section on Latin America has been extended and the dossier also contains details of the new AIDS strategy developed by WHO.

Until an AIDS vaccine can be developed, the best protection is education. This report is a contribution toward that education.

Available from: The Panos Institute, 1405 King Street, Alexandria, VA 22314, USA or 8 Alfred Place, London WC1E 7EB, UK. (Source: Development Forum, October 1987)

Gene banks and the future of the world's food supply

Breakthroughs in genetic engineering are occurring with increasing speed, but the erosion of genetic diversity of crop plants and their wild relatives is foreclosing future options for food production, say the authors of a new book, Gene Banks and the World's Food.

On every continent, and even on small island nations, crop gene banks have emerged as linchpins in a global effort to conserve crop gene pools and to tap this reservoir for the benefit of mankind. The book chronicles the history of gene banks and their significance for world food production. It is targeted for interested citizens, policy-makers, researchers, and social scientists concerned with agriculture and rural development.

The global role of gene banks, the authors say, is increasing steadily, particularly with the escalation of the world population and the growing demand for food. Because expansion of good agricultural land is declining, much of the increase in food production will have to come from higher yields through the manipulation of plant germplasm. The source of this germplasm will need to be stored in gene banks.

With years of experience in germplasm conservation and utilization, the authors are well-placed to assess the rapid changes in this field. Senior author Donald L. Plucknett is a Scientific Adviser to the Secretariat of the Consultative Group on International Agricultural Research (CGIAR); Nigel J. H. Smith is Professor of Geography at the University of Florida; J. Trevor Williams is Director and N. Murthi Anishetty is Secretary of the International Board for Plant Genetic Resources (IBPGR).

Historically, unimproved germplasm has moved freely between nations and scientists. However, recently germplasm issues have become politicized. Some of the major issues are:

- Who should operate gene banks and who should own genes collected from the wild?
- Should companies or individuals have to pay for germplasm?
- Does the right of breeders to patent varieties threaten access for all to genetic materials?
- Can gene banks ensure the security of crop genetic resources?

The authors respond to these issues and clarify many misconceptions. They document that plant genetic resources are being used by breeders for the benefit of farmers and consumers in virtually all nations. They also cite critical areas of concern:

- Proper evaluation of materials being stored in gene banks so that germplasm can be used more effectively;
- Immediate conservation of wild species in natural reserves to ensure maximum genetic diversity for future generations; and
- Better understanding of long-term preservation techniques and storage conditions to protect existing germplasm.

Other related subjects covered in the book include genetic diversity and vulnerability, plant exploration, plant breeding, seed production, storage and conservation methods and biotechnology. An appendix includes a list of the locations and status of gene banks. Additional data are provided by country and institution on the number of accessions of cereals, pulses, roots and tubers and industrial crops.

The book (247 pages) is available from Princeton University Press at a cost of US$35. Journalists may request a complimentary copy by writing to Ms. Arlene Warren, Princeton University Press, 41 William Street, Princeton, NJ 08540, USA. (Source: Development Forum, October 1987)

Biosensors: sensing the potential for rapid growth

In monitoring or controlling any process, be it biological or industrial, chemical or physical, sensing is the obvious first step. Sensing is also an obvious bottleneck in many of today's monitoring and

control applications. Indeed the present state of the art is such that modern computers can often process data far more rapidly than sensing devices can obtain it. Biosensors provide one potential answer to this problem.

In applications where they are suitable, biosensors have the potential to provide sensing speeds many times greater than present devices, especially when the tiny biodetectors can be built into or onto silicon chips. Basically, what a biosensor does is to use (1) a biological reaction to detect a substance, then (2) a transducer to convert the output from the reaction into a signal which can be communicated to monitoring or control equipment.

Commercially, biosensors are approaching the take-off stage. A new Frost & Sullivan report, The Biosensor Market in the US, estimates the size of the US market at just $14.4 million in 1986, but forecasts a $29 million market in 1987 and a $365 million market by 1991. Thereafter, it suggests, growth will go into the "stratosphere". Health care applications are currently the primary end-use targets and will continue to be so through 1991. By then, however, products for other applications - in process industries, in environmental monitoring and control, or in agriculture - will be gaining larger shares of the overall market.

The enzyme electrode, which came on the market in the early 1970s, is still the most important biosensor in use. It incorporates enzymes as biodetectors. These are proteins which act to catalyze chemical or metabolic reactions. As detectors, enzymes have the advantage of being able to differentiate between even highly similar molecules. Any of various forms of electrode are used as transducers. Instruments employing enzyme electrodes, still mostly manual instruments, are used, for example, in blood and urine analysis. Enzyme electrode analysers are also used in the chemical, fermentation and food-processing industries.

Frost & Sullivan look forward to biosensors which promise to move way beyond today's instruments. Detecting and controlling crop and livestock disease, monitoring drinking water and air quality, providing a feedback control for more complete control of fuel combustion in engines, providing industrial robots with the ability to taste and smell - these are just some of the ways in which biosensors will be put to use. Eventually, they may also be used to measure and study neurochemical reactions in the brain.

The Japanese have committed themselves to becoming world leaders in biosensor technology. While organizations in Europe and the United States lead in basic science studies and are busy refining technologies, the Japanese are already finding ways to bring products to market.

Details of the report, priced at $1,975.00, 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., 106 Fulton Street, New York, NY 10038 or on (212) 233 1080. (Source: Biotechnology Bulletin, No. 6, Vol. 11, December 1987)

Free literature

A 79-page catalogue from American Type Culture Collection (Rockville, MD) lists probes/cloned genes sorted by chromosome and locus, gene name and locus, and depositor's name. Also included are human chromosome-specific genomic libraries, primate cDNA and genomic libraries, oncogene/transforming protein probes and clones, and bacterial hosts for transformation or plating libraries. Most materials were deposited as part of the "NIH Repository of Human DNA Probes and Libraries".

Sourcebook on Canadian Industrial Biotechnology 1987

The 1987 Sourcebook on Canadian Industrial Biotechnology activities will be available early in 1988. This compendium lists Canadian commercial organizations involved in biotechnology, their principal areas of research, development or manufacturing, contact information, details on size of staff and includes an overall analysis of the Canadian situation. Copies can be obtained, free of charge, by writing to: Biotechnology Unit, Strategic Technologies Branch, Ministry of State for Science and Technology, 8th Floor West, 240 Sparks Street, Ottawa, Ontario, K1A 1A1. Telex: 053-4123. Facsimile: (613) 996-7887.

Free 1988 standards catalogue from ASTM

A catalogue describing the 67 volumes in the 1988 Annual Book of ASTM Standards is available free from ASTM.

ASTM publishes over 8,500 standards in many technical fields, including ferrous and non-ferrous metals, energy, environmental analysis, coatings, construction, petroleum, textiles, plastics, medical devices and services, and consumer products.

ASTM standards include specifications, test methods, practices, and terminology. They are used worldwide to facilitate commerce, ensure the quality of commodities, and promote product safety.

The catalogue is available from Mrs. Jackie Nolden, ASTM, 1916 Race Street, Philadelphia, PA 19103 (215) 299-5594.

Protein sequence analysis software

HIBIO PROSIS is a software package for analysing protein sequences. It can predict secondary structures and perform amino acid conversions and homology searches. Also, it can determine the maximum homology between two amino acid sequences and plot homologies. Other capabilities include keyword searching, hydrophobicity analysis, and determination of amino acid composition and molecular weight. Data may be displayed on the screen or output to a printer or disk for storage. HIBIO PROSIS operates on IBM XT, AT, and compatible computers with 512 kilobytes of random-access memory, a hard-disk drive, and a colour and graphics adapter. HIBIO PROSIS is also available on optical disk along with HIBIO DNASIS, a DNA analysis programme. Hitachi America, Computer Division. (Source: Science, Vol. 238, 2 October 1987)

A data bank of DNA and RNA nucleotide sequences

Intelligenetics (Mountain View, California) will administer GenBank - a computerized data bank of the order of nucleotides in DNA and RNA - following an award from the US Department of Health and Human Services (HHS). GenBank already contains the order of some 14 million nucleotides from a variety of organisms, including people. That may increase 20-50-fold during the life of the contract, HHS says. Intelligenetics will distribute information to subscribing institutions and researchers. (Source: Chemical Week, 14 October 1987)

Genetic databases on optical disks

LASERGENE is an optical disk that contains the complete GenBank database and the National Biomedical Research Foundation's Protein Identification Resource database as well as molecular biology software. The disk, which is resistant to heat, moisture, magnetic fields, scratches, and X-rays, holds as much data as 1,444 floppy disks. Searching an entire database takes only a few seconds. Full updates of the databases are released four times a year. LASERGENE operates with IBM PC and compatible computers with an optical disk player.

Molecular modelling software

MicroChem is a software package for building, analysing, and displaying three-dimensional molecular structures. The programme is available in basic and advanced versions for organic molecules, inorganic molecules, and polymers. A format-conversion subprogramme allows molecule files to be transferred to and from a VAX computer. Structures may be displayed or laser-printed as stick, ball and stick, or space-filling representations. Other features include editing functions; x, y, and z rotations; automatic checking for missing bond angle and length values; hydrogen-suppressed drawing mode; and labelling by sequential atom number, atomic symbol, or type code. MicroChem operates on Macintosh Plus or SE computers with 1 megabyte of random-access memory and either a hard disk or an 800-kilobyte external disk drive. Intersoft.

Protein-structure prediction software

Surfaceplot is a software programme that predicts surface regions of proteins. The algorithm combines Janin's accessibility parameters, Karplus and Schultz's flexibility parameters, and a set of hydrophilicity parameters derived from high-performance liquid chromatography retention data of model synthetic peptides. The programme is written in MSBASIC and may be modified by the user. Surfaceplot operates on the IBM PC, XT, and compatible computers with 256 kilobytes of memory, two floppy-disk drives, and a monitor with graphics capability.

Faster toxicological data

Aiming to eliminate the cost and inconvenience of retrieving data from on-line systems, Du Pont has packaged toxicology information for thousands of chemicals in a compact disc form. Du Pont says that the product, called Dutox, will be available late next month. Dutox contains information from the Du Pont Haskell Laboratory for Toxicology and Industrial Medicine and from the National Library of Medicine. Users can access the disc data using any IBM-compatible personal computer and the disc reader that Du Pont supplies with the service. (Source: Chemical Week, 16 December 1987)

Three new packages from IRL Press

Computer simulation is an extremely important educational tool and may be used just as effectively to teach under-graduates scientific concepts as it can to teach pilots how to fly aircraft. These packages allow students to simulate actual laboratory experiments in order to improve their grasp of both theoretical principles and the logic of experimental procedures. This can substitute for actually carrying out the experiments, thus reducing the time and, more importantly, the money required to teach these concepts at university level.

Practical Genetics, by D. M. Hunt, contains programs which simulate breeding experiments with the fruit fly, Drosophila melanogaster, and the common mouse, Mus musculus.

The "fruit fly" program allows you to carry out monohybrid, dihybrid and three-point test crosses, illustrating recessive and dominant inheritance. Also covered is X-linkage, and students are encouraged to map the mutations on the chromosome by setting up the appropriate crosses. By calculating the coefficient of coincidence, they can also determine the degree of chiasma interference.

The "mouse" software simulates breeding experiments with mutations such as blotchy, belted and albino. Touching a button produces progeny, and up to 12 generations of mice can be generated in as many seconds! Included in this software package is a chi-squared calculation routine that provides a convenient method for analysing statistically segregation data.

Although developed with good intent, the programs do not force the student to strive for a complete understanding of the terms. The program asks multiple-choice questions so the student can guess the correct results. Practical Genetics runs on an IBM PC and BBC computer and costs £45.

Phil Cunningham's Protein Sequencing illustrates the strategies and procedures which can be used in the determination of the primary structure of a protein. A wide range of techniques (for example, Edman degradation, hydrolysis, N- and C-terminal analysis) are available to provide the necessary experimental data, and it is left up to the student to develop an appropriate strategy.

The program can provide a random sequence, or the student can enter a known sequence. A library of sequences can be maintained on disc. The student can identify polypeptide fragments produced during cleavage by a code number, allowing return to the fragment at any time and use of the overlap method. At the end of the sequencing "experiment", the program displays the correct sequence of the original peptide.

The package teaches the concepts in a professional manner, describing clearly what is happening in every part of the program. Progein Sequencing runs on a BBC computer and costs £50.

A more realistic approach to sequencing is adopted in the Protein Sequencing Apprentice, for the IBM PC. Because it includes a realistic simulation of experimental error, the student must come to terms with the uncertainty and complexity of laboratory work. Each experiment carried out consumes a specific number of nanomoles of the original sample, so that the number of operations on the sample is limited, just as in real life.

Generally, this is a well-designed package, with a comprehensive on-line help system available at every stage in the analysis. The program has been designed to aid the tutor as well as the pupil. For example, on completion of the analysis a file is saved on disc containing the results of all the work performed, along with the time taken for the analysis. A tutor can inspect this file and see where there are gaps in a student's understanding. Protein Sequencing Apprentice runs on an IBM PC and costs £65.

Further information may be had from IRL Press, P.O. Box 1, Eynsham, Oxford OX8 1JJ.

The Molecular Biology Series

The Molecular Biology Series from Elsevier-BIOSOFT is a software package designed for use in first-year university and college courses. The package explains, in animation and text, the four basic mechanisms that underly the maintenance of cells. The programs are very easy to use. They demonstrate transcription, translation (necessary for

the production of protein from DNA), DNA replication and repair. There is also the facility to construct and alter genes for subsequent animation.

The programs run in colour on an IBM PC or compatible machines, but in monochrome for the Apple II. The author, Robert Ransom, has supplied multiple-choice questions after each animation.

The DNAFILE program allows you to create your own genes for use in these animations, and this helps to emphasize the differences between prokaryotes and eukaryotes.

The translation program allows you to see the inhibitory action of six drugs. The replication program has a very useful help function, which replaces the animation with one of six explanatory pages at various points in the sequence. The benefit of this "on-screen" help is not extended to the other programs; when using these, the student must rely on the manual for extra information.

The DNA repair program is by far the most informative of the series. The program with its multiple choice questions illustrates well the distinctions between four repair mechanisms. Although endonuclease and ligase are included in the repair sequences, you cannot properly appreciate their function of nicking and reforming, respectively, the DNA backbone, because the program does not show the DNA sugar phosphate backbone.

The teaching material in the manual is both concise and precise, offering brief descriptions of the most definitive experimental work of the early days. The manual is a good introduction for the student with no previous knowledge of the subject.

The Molecular Biology Series is available from Elsevier-BIOSOFT, 68 Hills Road, Cambridge CB2 1LA; price £50. Also available from Elsevier-BIOSOFT (JIC), 52 Vanderbilt Avenue, New York, NY 10017, USA; price $99.

G. B. Biotechnology Ltd., has prepared an educational package for schools. Introduction to Enzymes comprises:

1. A series of five enzyme experiments approved for GCSE level with materials for over 100 pupils with each experiment.

2. A word processor package to enable individual worksheets to be printed. These can be modified by the teacher at will. (Acorn [BBC] - Wordwise/Wordwise+:RML-Write/Wordstar).

3. A Teacher/Technician booklet giving additional advice and information on the worksheets.

4. Pre-weighed packets of enzymes for ease of preparation for Teacher/Technician. Only essential substances (enzymes and substrates) are supplied.

5. Total cost of the kit is £19.55 inclusive of VAT, postage and packing.

More information may be obtained from Ms. Christine Roberts, G. B. Biotechnology Ltd., 4 Beaconsfield Court, Sketty, Swansea, West Glam. SA2 9JU. Tel. 0792 208190.

C. MEETINGS

1988

5-8 April 1988
Cardiff, Wales, UK. The First International Conference on the Release of Genetically Engineered Micro-organisms. Further information from Colin Griffiths, REGEM, P.O. Box 50, Lewis Road, Cardiff CF1 5XW, UK.

11-13 April 1988
Florence, Italy. Molecular Probes: Technology and Medical Applications. Further information from Fondazione Giovanni Lorenzini, Via Monte Napoleone 23, 20121 Milan, Italy.

12-14 April 1988
Montreal, Canada. CANBIOCON '88 biotechnology conference and exhibition. Further information from Biotech Canada Inc., 100 Alexis Nihon, Suite 870, Montreal, Quebec H4M 2P4, Canada.

13-16 April 1988
Brighton, UK. Fifth European Workshop on the Molecular and Cellular Endocrinology of the Testes. Further information from Ares-Serono Symposia, Via Ravenna 8, 00161 Rome, Italy.

14-15 April 1988
London, UK. Sixth Cell Surface Research Fund Meeting: Pores and Leaks across Membranes. Further information from Mrs. V. Marvell, Dept. of Biochemistry, St. George's Hospital Medical School, London SW17 ORE, UK.

16 April 1988
Imperial College, London, UK. Membrane Proteins of Photosynthetic Organisms. Further information from Prof. J. Barber, Dept. of Pure and Applied Biology, Imperial College of Science and Technology, London SW7 2BB, UK.

17-21 April 1988
Methybridge, UK. EMBO Workshop on Tumour Suppressor Genes. Further information from A. Balmain, Beatson Inst. for Cancer Research, Garscube Estate, Switchback Road, Bearsden, Glasgow G61 1BD, Scotland, UK.

18-22 April 1988
Loughborough, UK. Basic Microbiological Methods for the Analytical Chemist. Further information from Dr. R.K. Dart, Dept. of Chemistry, University of Technology, Loughborough LE11 3TU, UK.

22-23 April 1988
Arlington, Virginia, USA. Biotechnology Targets AIDS: A Clinical Perspective. Further information from Crystal City, Marriott, 1999 Jefferson Davis Highway, Arlington, Virginia 22202, USA.

23-30 April 1988
Keystone, USA. UCLA Symposium on Mechanisms of Action and Therapeutic Applications of Biologicals in Cancer and Immune Deficiency Disorders. Further information from UCLA Symposia, 103 Molecular Biology Institute, University of California, Los Angeles, CA 90024-1378, USA.

24-27 April 1988
Eynsham Hall, Oxford, UK. Second Harden Discussion Meeting on Biochemistry of Cell Walls and Membranes in Fungi. Further information from Dr. M. Goosey, Dow Chemical Co., Letcombe Laboratories, Letcombe Regis, Wantage, Oxon. OX12 9GT, UK.

25 April 1988
Royal College of Physicians, London, UK. International Research Symposium on Cytotoxic Drug Resistance in Leukaemia and other Malignancies. Further information from Leukaemia Research Fund, 43 Great Ormond Street, London WC1N 3JJ, UK.

25-26 April 1988
Rockville, Maryland, USA. Biotechnology Patent Conference. Further information from Doug Drabkovski, Workshop Coordinator, American Type Culture Collection, 12301 Parklawn Dr., Rockville, MD 20852, USA.

26-27 April 1988
Cambridge, Massachusetts, USA. The 1988 Conference on Commercial Biotechnology. Further information from Business Communications Co., 25 Van Zant St., Norwalk, CT 06855, USA.

27-28 April 1988
Reno, Nevada, USA. ASTM Committee Meeting (E-48 on Biotechnology). Further information from Teri McMasters, ASTM, 1916 Race Street, Philadelphia, PA 19103, USA.

1-6 May 1988
Las Vegas, Nevada, USA. Federation of American Societies for Experimental Biology Annual Meeting. Further information from Gary Kaganovich, Director, Office of Public Affairs, FASEB, 9650 Rockville Pike, Bethesda, MD 20814, USA.

4-8 May 1988
Cold Spring Harbor, New York, USA. Cell and Molecular Biology of Chlamydomonas. Further information from Meetings Co-ordinator, Cold Spring Harbor Laboratory, Bungtown Road, Cold Spring Harbor, New York 11724, USA.

10 May 1988
Grand Hyatt Hotel, New York City, New York. 1988 Bio/Technology Conference on Commercial Production, Coming into Compliance: Biotechnology Validation and Regulation. Further information from Diana Berger, Nature Publishing Company, 65 Bleecker Street, New York, NY 10012, USA.

8-13 May 1988
Miami Beach, Florida, USA. American Society for Microbiology 88th Annual Meeting. Further information from Robert D. Watkins, Director of Public Affairs, ASM, 1913 I St., N.W., Washington, DC 20006, USA.

9-11 May 1988
Beltsville Symposium in Agricultural Research - Biotic Diversity and Germplasm Preservation: Global Imperatives. Further information from Mrs. J. Weirman, ARS/USDA, Rm. 127, Bldg. 001, Beltsville Agricultural Research Center-West, Beltsville, MD 20705, USA.

10-12 May 1988
London, UK. Life Science Technologies '88. Further information from Online International Ltd., Pinner Green House, Ash Hill Dr., Pinner, Middlesex HA5 2AE, UK.

11-15 May 1988
Cold Spring Harbor, New York, USA RNA Processing. Further information from Meetings Co-ordinator, Cold Spring Harbor Laboratory, Bungtown Road, Cold Spring Harbor, New York 11724, USA.

15-21 May 1988
Aussois, France. Role of Glycoconjugates in Cell Recognition: Function of Endogenous Lectins. Further information from Michel Monsigny, Laboratoire de Biochimie Cellulaire et Moléculaire des Glycoconjugués, Centre de Biophysique Moléculaire, 1 rue Haute, 45071 Orléans, France.

16-19 May 1988
Minneapolis, Minnesota, USA. Short course on Animal Cell Reactor Engineering. Further information from Jan Becker, University of Minnesota, Department of Professional Development, Continuing Education and Extension. 315 Pillsbury Drive S.E., Minneapolis, MN 55455, USA.

16-20 May 1988
Gatlinburg, Tennessee, USA. 10th Symposium on Biotechnology for Fuels and Chemicals. Further information from Charles D. Scott, Chemical Technology Division, Oak Ridge National Laboratory, P.O. Box X, Oak Ridge, TN 37831, USA.

16-28 May 1988
Ann Arbor, Michigan, USA. Workshop on Morphometrics in Systematic Biology. Further information from Morphometrics Workshop, Museums of Paleontology and Zoology, University of Michigan, Ann Arbor, MI 48109, USA.

17-20 May 1988
Baltimore, Maryland, USA. 2nd Annual Seminar on Analytical Biotechnology. Further information from Janet Cunningham, Seminar Coordinator, Barr Enterprises, P.O. Box 279, Walkersville, MD 21793, USA.

17-22 May 1988
Cold Spring Harbor, New York, USA. RNA Tumour Viruses. Further information from Meetings Co-ordinator, Cold Spring Harbor Laboratory, Bungtown Road, Cold Spring Harbor, New York 11724, USA.

23-25 May 1988
Stony Brook, New York, USA. 7th Annual Stony Brook Symposium on Molecular Biology and Recent Advances in Inter-Cellular Communication. Further information from Janet Koenig, Department of Biochemistry, SUNY Stony Brook, Stony Brook, NY 11794, USA.

23-25 May 1988
Florence, Italy. Endocrinology under 35. Further information from Ares-Serono Symposia, Via Ravenna 8, 00161 Rome, Italy.

24 May 1988.
Westin St. Francis Hotel, San Francisco, USA. The 1988 Bio/Technology Conference on Commercial Production, Coming into Compliance: Biotechnology Process Validation and Regulation. Further information from Diana Berger, Nature Publishing Company, 65 Bleecker Street, New York, NY 10012, USA.

25-28 May 1988
Novi Sad, Jugoslavia. International Symposium on Heavy Metals and Pesticide Residues in Medicinal, Aromatic and Spice Plants. Further information from Dr. J. Kišgeci, Institute of Field and Vegetable Crops, Faculty of Agriculture, Novi Sad, YU-21470, Bački Petrovac.

25 May - 1 June 1988
Cold Spring Harbor, New York, USA. The Molecular Biology of Signal Transduction. Further information from Meetings Co-ordinator, Cold Spring Harbor Laboratory, Bungtown Road, Cold Spring Harbor, New York 11724, USA.

28 May - 1 June 1988
Palazzo dei Congressi, Bologna, Italy. XIV International Symposium on Cerebral Blood Flow and Metabolism. Further information from GIBI Studio Congressi, Via Marco Besso 40, 00191 Rome, Italy.

29 May - 1 June 1988
Florence, Italy. VII International Conference on Prostaglandins and Related Compounds. Further information from Fondazione Giovanni Lorenzini, Via Monte Napoleone 23, 20121 Milan, Italy.

30 May - 3 June 1988
Copenhagen, Denmark. Advances in Controlled Release Technology: Polymeric Delivery Systems for Pharmaceuticals and Other Bioactive Agents. Further information from Ms Pamela Brown, Massachusetts Institute of Technology, Cambridge, MA 02139, USA.

31 May - 2 June 1988
Avignon, France. Cucurbitaceae '88. Further information from G. Risser, INRA, Domaine St. Maurice-BP 94, F-84140 Montfavet, France.

1-3 June 1988
Rome, Italy. Platelets and Vascular Occlusion. Further information from Ares-Serono Symposia, Via Ravenna 8, 00161 Rome, Italy.

2-5 June 1988
Arlington, Virginia, USA. Third Annual ASM Conference on Biotechnology. Further information from Karen Johnson, ASM Meetings Dept., 1913 I Str., N.W., Washington DC 20006, USA.

6-11 June 1988
Lund, Sweden. Neuromuscular Junction. Further information from Eva Björkbom, Dept. Pharmacol., Sölveg. 10, S-223 62 Lund, Sweden.

9 June 1988
Cambridge, UK. Biological Engineering Society Meeting on Sensors for Biotechnology. Further information from E.A.H. Hall, The Biotechnology Centre, University of Cambridge, Downing St., Cambridge CB2 3EF, UK.

12-15 June 1988
Las Vegas, Nevada, USA. The Genetic and Biochemical Basis of Aging. Further information from Tissue Culture Association, 19110 Montgomery Village Avenue, Suite 300, Gaithersburg, MD 20879, USA.

12-16 June 1988
Buffalo, New York, USA. 11th International Convocation on Immunology: Immunology and Immunopathology of the Alimentary Canal. Further information from Dr. James F. Mohn, Director, 235 Sherman Hall, State University of New York, Buffalo, New York 14214, USA.

13-17 June 1988
Roscoff, France. Structure and Function of Membrane Proteins involved in Photosynthetic Election Transfer. Further information from Dr. Pierre Jolliot, Institut de Biologies Physico-Chimique, 13 rue Pierre et Marie Curie, 75005 Paris, France.

15-18 June 1988
Philadelphia, Pennsylvania, USA. Second International Conference on Molecular Biology and Pathology of Matrix. Further information from Dr. Darwin J. Prockop, Jefferson Institute of Molecular Medicine, Jefferson Medical College, Thomas Jefferson University, Philadelphia, Pennsylvania 19107, USA.

19-24 June 1988
Washington, DC, USA. 12th International Symposium on Column Liquid Chromatograph. Further information from Symposium Manager, Barr Enterprises, PO-Box 279, Walkersville, Maryland 21793, USA.

23-24 June 1988
Windsor, Ontario, Canada. Special Symposium on Microbial Surfaces. Further information from The CSM Secretariat, 20 Hobart Crescent, Nepean, Ontario K2H 5S4, Canada.

26-30 June 1988
Iowa City, Iowa, USA. International Symposium on Plant Nitrogen Metabolism. Further information from Dr. J. E. Poulton, Botany Department, University of Iowa, Iowa City, IA 52242, USA.

27 June - 1 July 1988
Canterbury, Kent, UK. Cell Culture Techniques for the Production of Monoclonal Antibodies and Recombinant Proteins. Further information from Dr. D. J. Hardman, Secretary, The Institute for Biotechnological Studies, Research and Development Centre, The University of Kent, Canterbury, Kent CR2 7PD, UK.

27 June - 2 July 1988
Nethybridge, UK. Genetic recombination. Further information from Dr. N. Symonds, School of Biological Sciences, University of Sussex, Falmer, Brighton BN1 9QG, UK.

3-8 July 1988
Girton College, Cambridge, UK. Sixth International Worksnop on the Molecular Genetics of the Mouse. Further information from Dr. Grahame Bulfield, AFRC Institute of Animal Physiology and Genetics Research, Roslin, Midlothian EH25 9PS, UK.

3-8 July 1988
West Berlin, FRG; Seventh International Conference on Methods in Protein Sequence Analysis. Further information from Dr. Brigitte Wittman-Liebold, Max-Planck Institut für Molekular Genetik, Ihnestr. 73, D-1000 Berlin (West), FRG.

4-8 July 1988
Cambrige, UK. Processes and Patterns of Molecular Evolution. Further information from Dr. G. A. Dover, Department of Genetics of the University, Downing Street, Cambridge CB2 3EH, UK.

4-8 July 1988
Salamanca, Spain. Gene Organization and Expression in Bacteriophages. Further information from Dr. M. Salas, Centro de Biologia Molecular, Universidad Autonoma, Canto Blanco, 28049 Madrid, Spain.

6-8 July 1988
Slusovice, Czechoslovakia. 21st Century Prospects for Biotechnology in Agriculture and the Environment. Further information from Ronald Cape, Chairman, Cetur Corp., 1400 Fifty-third St., Emeryville, CA 94608, USA. Tel. 415-420-3300.

10-15 July 1988
Prague, Czechoslovakia. Fourteenth International Congress of Biochemistry. Further information from The Meetings Officer, The Biochemical Society, 7 Warwick Court, London WC1R 5DP, UK.

16-19 July 1988
Prague, Czechoslovakia. Workshop on the Molecular Basis of Membrane-Associated Disease. Further information from Prof. A. Azzi, Institut für Biochemie und Molekular-biologie der Universität Bern, Bühlstrasse 28, CH-3012 Bern, Switzerland and Prof. Z. Drahota, Institute of Physiology, Academy of Sciences, Videnska 1083, CS-142 20 Prague 4-KRC, Czechoslovakia.

17-22 July 1988
Paris, France. Eighth International Biotechnology Symposium. Further information from Dr. C. Murphy, SFM/8th International Biotechnology Symposium, 28 rue du Dr. Roux, 75724 Paris, France.

18-23 July 1988
Renesse, The Netherlands. The Guanine Nucleotide-Binding Proteins, Common Structural and Functional Properties. Further information from Dr. L. Bosch, Department of Biochemistry, State University, Wassenaarseweg 64, 2333 Al Leiden, The Netherlands.

25-26 July 1988
Tokyo, Japan. The Adrenal and Hypertension: From Cloning to Clinic. Further information from Ares-Serono Symposia, Via Ravenna 8, 00161 Rome, Italy.

25 July - 5 August 1988
Plymouth, UK. Protozoa and Their Role in Marine Processes. Further information from Dr. P. H. Burkill, (ASI Sec.), Institute for Marine Environmental Research, Prospect Place, Plymouth PL1 3DH, UK.

27-29 July 1988
Pennsylvania State University, USA. Seventh Summer Symposium in Molecular Biology: Viruses; Pathogens and Model Systems. Further information from Dee Reeves, Symposium Programme Co-ordinator, Seventh Summer Symposium in Molecular Biology, 208 South Frear Lab., The Pennsylvania State University, University Park, PA 16802, USA.

31 July - 4 August 1988
Davis, California, USA. Conference on Risk Assessment in Agricultural Biotechnology. Further information from Donna Hyatt, Dean's Office, College of A and ES, University of California, Davis, CA 95616, USA.

1-5 August 1988
Perugia, Italy. 7th International Symposium on Yeasts. Further information from 7th ISY c/o Dipart, di Biologia Vegetale Borgo XX Giugno 74, I-06100 Perugia.

7-13 August 1988
Espar, Finland. 14th International Conference on Yeast. Further information from T. Koistenen, Res. Laboratories, ALKO Ltd., P.O. Box 350, SF-00101 Helsinki, Finland.

10-14 August 1988
Cold Spring Harbor, New York, USA. Molecular Biology of SV40, Polyoma and Adenoviruses. Further information from Meetings Co-ordinator, Cold Spring Harbor Laboratory, Bungtown Road, Cold Spring Harbor, New York 11724, USA.

13-17 August 1988
East Lansing, USA. 4th International Symposium on Vaccinium Culture. Further information from Dr. E. J. Stang, Department of Horticulture, 208C Hort. Bldg., 1575 Linden Drive, Madison, Wisconsin, 53706, USA.

14-19 August 1988
Montreal, Quebec, Canada. Fourth International Congress of Cell Biology. Further information from Congress Secretariat, Fourth International Congress of Cell Biology, National Research Council of Canada, Ottawa, Ontario, Canada K1A 0R6.

14-21 August 1988
Arolla, Switzerland. Mechanisms of Gene Regulation and Development. Further information from Dr. W. J. Gehring, Biozentrum der Universität, Klingelbergstrasse 70, 4056 Basel, Switzerland.

16-21 August 1988
Cold Spring Harbor, New York, USA. Molecular Biology of Bacteria and their Phages: Prokaryotic Gene Regulation. Further information from Meetings Co-ordinator, Cold Spring Harbor Laboratory, Bungtown Road, Cold Spring Harbor, New York 11724, USA.

21-24 August 1988
Norwich, UK. BIOAVAILABILITY '88 - Chemical and Biological Aspects of Nutrient Availability. Further information from AFCR Institute of Food Research, Colney Lane, Norwich, Norfolk NR4 7UA, UK.

20-27 August 1988
Toronto, Ontario, Canada. XVIth International Congress of Genetics. Further information from Genetics Congress Secretariat, National Research Council of Canada, Ottawa, Ontario, Canada K1A 0R6.

23-26 August 1988
Ghent, Belgium. 7th International Symposium on Mass Spectrometry in Life Sciences. Further information from Prof. Dr. A. De Leenheer, Laboratoria voor Medische Biochemie en voor Klinische Analyse, Harelbekestraat 72, B-9000 Ghent, Belgium.

24-28 August 1988
Cold Spring Harbor, New York, USA. Mouse Molecular Genetics. Further information from Meetings Co-ordinator, Cold Spring Harbor Laboratory, Bungtown Road, Cold Spring Harbor, New York 11724, USA.

28 August - 4 September 1988
Kolymbari, Crete, Greece. Molecular and Developmental Biology of Drosophila. Further information from Dr. S. Artavanis-Tsakonas, Dept. of Biology, Yale University, P.O. Box 6666-KBT, New Haven, CT 06511-8112, USA.

29 August - 2 September 1988
Roscoff, France. The Mitochondrial Genome of Higher Plants. Further information from Dr. Francis Quetier, Laboratoire de Biologie Moléculaire Végétale, Université de Paris-Sud, 91405 Orsay cedex, France.

31 August - 4 September 1988
Cold Spring Harbor, New York, USA. Intermediates in Genetic Recombination. Further information from Meetings Co-ordinator, Cold Spring Harbor Laboratory, Bungtown Road, Cold Spring Harbor, New York 11724, USA.

1-14 September 1988
Nsukka and Zaria, Nigeria. Training Worksnop in Genetic Engineering for African Scientists and 4th Meeting of the African Network on Microbiology. Further information from Prof. Nduka Okafor, Anambra State University of Technology, P.M.B. 1660, Enugu, Nigeria.

4-9 September 1988
York, UK. 9th European Congress on Electron Microscopy. Further information from The Administrator, Royal Microscopical Society, 37-38 St. Clements, Oxford OX4 1AJ, UK.

4-9 September 1988
Wye College, Ashford, Kent. Harden Conferences, No. 30: Nucleic Acids and their Interactions with Proteins. Further information from Meetings Officer, The Biochemical Society, 7 Warwick Court, London WC1R 5DP, UK.

5-9 September 1988
Roscoff, France. The Cell Cycle. Further information from Dr. Tim Hunt, University of Cambridge, Dept. of Biochemistry, Tennis Court Road, Cambridge CB2 1QW, UK.

6-9 September 1988
Norwich, UK. Protein Targeting - 8th John Innes Symposium. Further information from Symposium Secretary, John Innes Institute, Colney Lane, Norwich NR4 7UH, UK.

7-11 September 1988
Cold Spring Harbor, New York, USA. The Molecular Diagnostics of Human Cancer. Further information from Meetings Co-ordinator, Cold Spring Harbor Laboratory, Bungtown Road, Cold Spring Harbor, New York 11724, USA.

11-15 September 1988
Pitlochry, Scotland, UK. Sorting in Eukaryotic Cells. Further information from Dr. G. Warren, Dept. of Biochemistry, University of Dundee, Dundee DD1 4HN, Scotland, UK.

11-16 September 1988
Wye College, Ashford, Kent. Harden Conferences, No. 31: Microbes under Stress: Metabolic and Developmental Choices. Further information from Meetings Officer, The Biochemical Society, 7 Warwick Court, London WC1R 5DP, UK.

14-18 September 1988
Cold Spring Harbor, New York, USA. Modern Approaches to New Vaccines, including Prevention of AIDS. Further information from Meetings Co-ordinator, Cold Spring Harbor Laboratories, Bungtown Road, Cold Spring Harbor, New York 11724, USA.

18-23 September 1988
Weggis, Switzerland. Enzymology of DNA Replication. Further information from Dr. U. Hübscher, Institut für Pharmakologie und Biochemie, Universität Zürich-Irchel, Winterthurerstrasse 190, 8057 Zürich, Switzerland.

19-20 September 1988
L'Aquila, Italy. Advances in Biotechnology of Membrane Ion Transport. Further information from Ares-Serono Symposia, Via Ravenna 8, 00161 Rome, Italy.

19-24 September 1988
Shanghai, China. BIOTECH EXPO 88. 2nd International Exhibition and Conference. Further information from Biotech Expo 88, Suite 602, Harbour Crystal Centre, TST East, Kowloon, Hong Kong.

20-22 September 1988
Hannover, FRG. BIO'Technica '88. Further information from Deutsche Messe AG, Messegelände, D-3000 Hannover 82, FRG.

21-25 September 1988
Cold Spring Harbor, New York, USA. Ribosome Synthesis. Further information from Meetings Co-ordinator, Cold Spring Harbor Laboratory, Bungtown Road, Cold Spring Harbor, New York 11724, USA.

25-29 September 1988
Florence, Italy. 5th International Symposium on Bioluminescence and Chemiluminescence. Further information from O.I.C., Via G. Modena 19, 50121 Florence, Italy.

25-30 September 1988
Vienna, Austria. 17th International Symposium on Chromatography. Further information from Prof. Dr. J.F.K. Huber, Inst. f. Analyt. Chemie der Universität, Währinger Str. 38, 1090 Vienna, Austria.

25-29 September 1988
Cambridge, UK. Fourth International Congress on Computer Applications in Fermentation Technology - Modelling and Control of Biotechnological Processes. Further information from Conference Secretariat, Society of Chemical Industry, 14/15 Belgrave Square, London SW1X 8PS, UK.

26-29 September 1988
EMBO, Heidelberg, FRG. EMBO Annual Symposium: Organelle Genomes and the Nucleus. Further information from EMBO, Postfach 102240, 69 Heidelberg, FRG.

26-30 September 1988
Roscoff, France. Vessels and Vascular Pathology. Further information from Dr. Jacques Caen, 150 boulevard Magenta, 75010 Paris, France.

28 September - 1 October 1988
Orlando, Florida, USA. North American Cystic Fibrosis Conference. Further information from Cystic Fibrosis Foundation, 6931 Arlington Road, Bethesda, MD 20814, USA.

28 September - 2 October 1988
Cold Spring Harbor, New York, USA. Cell and Molecular Neurobiology of Aplysia. Further information from Meetings Co-ordinator, Cold Spring Harbor Laboratory, Bungtown Road, Cold Spring Harbor, New York 11724, USA.

2-5 October 1988
Rorschacherberg, Switzerland. Gene Transfer to Plants: A Critical Assessment. Further information from Dr. I. Potrykus, Institut für Pflanzenwissenschaften, ETH-Zentrum/LFV E.20, Universitätstrasse 2, 8092 Zürich, Switzerland.

3-6 October 1988
Roscoff, France. Cellular and Molecular Aspects of the Early Events in Neurogenesis. Further information from Dr. Anne-Marie Duprat, Centre de Biologie du Développement, 118 route de Narbonne - Bâtiment IV R3, 31062 Toulouse cedex, France.

6-8 October 1988
Villefranche-sur-Mer, France. Mechanisms of Immunoglobulin in Gene Diversification, Rearrangements and Expression. Further information from Dr. K. B. Marcu, Dept. of Biochemistry, Life Sciences Building, SUNY at Stony Brook, Stony Brook, NY 11794-5215, USA.

23-27 October 1988
Evian, France. VIth International Lymphokine Workshop on Lymphokine Receptor Interaction. Further information from Secretariat VIth International Lymphokine Workshop, Laboratoire d'Immunologie, Bâtiment Recherche 1, Institut Gustave Roussy, 94805 Villejuif cedex, France.

24-28 October 1988
Aussois, France. Animal Toxins. Further information from Dr. Hervé Rochat, Laboratoire de Biochimie, Faculté de Médecine, Secteur Nord, Boulevard Pierre Dramard, 13326 Marseille cedex 15, France.

8-10 November 1988
Paris, France. FILTRA 88 - European Congress and Exhibition of Filtration and Separation Technology. Further information from M. Michael Beaucourt, IDEXPO, 21 Ave. de Filtration, F-94 230 Cachan, France.

16-19 November 1988
Düsseldorf, FRG. MEDICA/BIOTEC. Diagnostica-Therapeutica-Technica. Further information from Gesell GesmbH & Co. KG, Kaasgrabengasse 37, 1190 Vienna, Austria. Tel. 32 50 37.

22 November - 1 December 1988
Moscow, USSR. NAUKA '88 - 4th International Exhibition on Scientific Instrumentation. Further information from v/o Expocentr, Sokolnitscheskij val, 1a, USSR-107, 113 Moscow.

1989

2-6 April 1989
University of Kent, UK. Comparing laboratory and Field Pesticide Performance. Further information from Dr. C. R. Merrict, International Centre for the Application of Pesticides, Cranfield Institute of Technology, Cranfield, Bedford MK43 0AL, UK.

20-25 August 1989.
Kobe, Japan. Protein Engineering '89. Further information from IRL Press Inc., P.O. Box Q, McLean, VA 22101-0850, USA, or IRL Press Ltd., P.O. Box 1, Eynsham, Oxford OX8 1JJ, UK.

21-24 August 1989
Utrecht, The Netherlands. 11th International Congress of the International Society of Developmental Biologists. Further information from Congress Secretariat, Congrex (Holland), Keizersgracht 792, 1017 EC Amsterdam, The Netherlands.

For new subscribers only

UNITED NATIONS INDUSTRIAL DEVELOPMENT ORGANIZATION

UNIDO MAILING LIST QUESTIONNAIRE

(Code 503)

The UNIDO Newsletter is sent free of charge to an approved list of readers

To be considered for inclusion on the UNIDO Newsletter mailing list, please complete questionnaire and return it to

UNIDO MAILING LIST, INDUSTRIAL INFORMATION SECTION.

P.O. BOX 300, A-1400 VIENNA, AUSTRIA

Type or print clearly (one letter per box) and leave a space between each word

NAME (underline family name)

TITLE OR POSITION

ORGANIZATION

STREET AND No. (or P.O. Box)

CITY AND STATE OR PROVINCE

COUNTRY

PLEASE DO NOT WRITE IN THESE SPACES

S/A DISP. CODE COUNTRY

CITY

T TYPE OF ORGANIZATION: Identify below the type of organization to which you belong, checking the box(es) as appropriate (e.g., for a research centre at a university, boxes 20 and 23 would be applicable).

01	UN, specialized agency or other UN body	12	Trade centre or association	23	Research centre/laboratory
02	Other intergovernmental organization	13	Professional association/learned society	24	Library/documentation centre
03	International non-governmental organization	14	Bank or financial institution	25	Information centre
04	UNIDO National Committee	15	Industrial enterprise	26	Publisher
05	Embassy or Mission to UNIDO	16	Public utility	27	Bookseller
06	Government body for development aid	17	Trading concern	28	News agency/press
07	Ministry for industry	18	Engineering organization	29	Radio and television
08	Other governmental department	19	Consultant		
09	Non-governmental aid agency	20	University		
10	Chamber of industry or commerce	21	Vocational or technical institute/school		
11	Manufacturers' association	22	Industrial training or productivity centre		

F FIELD OF INTEREST: Check the appropriate box(es) which reflect your *main* field(s) of interest

	MANUFACTURING INDUSTRIES – PLANTS, PROCESSES AND PRODUCTS	017	Electrical machinery	030	Industrial legislation
		018	Transport equipment	031	Industrial property
		019	Precision instruments	032	Transfer of technology (licensing)
001	Food processing	020	Agricultural machinery	033	Industrial research and development
002	Beverages			034	Standardization
003	Tobacco		NON MANUFACTURING INDUSTRIES AND PROJECTS	035	Industrial organization and administration
004	Textile and garment			036	Industrial co-operatives
005	Leather	021	Mining and quarrying	037	Industrial information and documentation
006	Wood processing	022	Utilities (including power plants)	038	Industrial promotion
007	Pulp and paper	023	Public services (transport, communications, tourism)	039	Industrial training
008	Petrochemical and plastics	024	Construction (civil engineering) projects	040	Industrial management
009	Industrial chemicals and fertilizers			041	Industrial consulting services
010	Pharmaceuticals and other chemical products		SUPPORTING INDUSTRIAL ACTIVITIES	042	Development of small-scale industries
011	Rubber			043	Industrial estates
012	Non-metallic mineral products and building materials	025	Industrial planning and programming	044	Appropriate technology
013	Iron and steel	026	Industrial policies		
014	Non-ferrous metal	027	Industrial financing and investment promotion		
015	Fabricated metal products	028	Promotion of export oriented industries		
016	Machinery	029	Industrial development surveys		

LANGUAGE Indicate below in which language you wish to receive the NEWSLETTER

ENGLISH FRENCH SPANISH RUSSIAN

UNIDO Form IPCI (12/85)

UNITED NATIONS INDUSTRIAL DEVELOPMENT ORGANIZATION

Price List for Advertisements in the Publication

Genetic Engineering and Biotechnology Monitor

General Provisions

1. UNIDO activities in the field of advertising are non-profit-making and are carried out to cover the cost of preparing, publishing and mailing its publications, which are sent to readers all over the world *free of charge*.
2. Requests for placing advertisements in the UNIDO *Genetic Engineering and Biotechnology Monitor* should be made in writing. They should be accompanied by a layout, illustrations and a text containing all necessary information.
3. Advertisements are printed in black and white and in English only.
4. UNIDO reserves the right to reject advertisements without giving reasons, to suggest amendments or to hold advertisements if space is not available.
5. UNIDO cannot guarantee to print advertisements on specific pages of the *Monitor*. Page proofs will not be provided to advertisers
6. Payment of invoices is due immediately after receipt and should be made within 30 days in United States dollars or Austrian schillings to the UNIDO bank account (see below) or to the Treasurer, UNIDO, Vienna International Centre, P.O. Box 300, A-1400 Vienna, Austria (telegrams UNIDO Vienna Austria; telex: 135612). Upon payment, please advise the Head Development and Transfer of Technology Division, at the same address

Bank accounts

For dollar payments

"UNIDO dollar account" No. 29-05115
Creditanstalt Bankverein
Schottengasse 6, A-1010 Vienna, Austria

"UNIDO general account" No. 949-2-416434
The Chase Manhattan Bank
International Agencies Banking
380 Madison Avenue, New York, New York 10017
United States of America

For schilling payments:

"UNIDO schilling account" No. 29-05107
Creditanstalt Bankverein
Schottengasse 6, A-1010 Vienna, Austria

Prices

Size	*Prices in Austrian schillings (AS) (or equivalent in US$)*
Full page (255 mm × 178 mm)	AS 5,000
½ page (125 mm × 178 mm or 255 mm × 86 mm)	AS 3,700
¼ (178 mm × 60 mm or 125 mm × 86 mm)	AS 2,500

The price for the publication of announcements of up to five lines under the rubric "Resources available" is AS 1,000. The text is subject to editing.