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Genetic Engineering and Biotechnology Monitor

Issue No. 23 1988/II

This publication is distributed free of charge

Compiled by Development and Transfer of Technology Division, Department for Industrial Promotion, Consultations and Technology, UNIDO, P.O. Box 300, A-1400 Vienna, Austria.

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ICGEB affiliated centres' news

During 1988 several significant activities were carried out in regard to the ICGEB, which is currently implemented as a project by UNIDO. In March 1988, a Forum of Scientists of the member countries was held. It was attended by scientists from 21 member countries and it helped to promote mutual interaction between the ICGEB management and the member countries' scientists and it clarified in particular the research and training needs of those countries. Based on this interaction, requests were also sent out to national focal points asking for their training needs.

The New Delhi Component of the ICGEB started functioning from May 1988. Between the two Components five research groups have been initiated. The project management is giving particular attention to strengthening these groups and also creating another group on lignocellulose in Trieste. Currently, besides administrative staff, five scientists and nine technicians are working in Trieste and four scientists and seven technicians in New Delhi. All major equipment required for the interim programme has been procured.

Visits to affiliated centres of the ICGEB were completed in the course of 1988. In all, visits have been made to 12 affiliated centres. This has helped to ascertain the needs of these centres and their possible co-operation with the ICGEB.

In response to the request of the project management, requests for training courses from member countries have been made as also requests from affiliated centres for research co-operation. These proposals which have been received very recently will be evaluated. The training facilities available in affiliated centres and in the host and other member countries will also be utilized, while the conduct of courses in the ICGEB premises requires further development of facilities and staff in the ICGEB. In March 1988 a workshop on protein engineering was held in Trieste. Training courses in Argentina and Nigeria were also assisted by grants from the ICGEB.

The number of member countries of the ICGEB now stands at 41, and more countries are showing interest in joining it. The number of countries which have ratified the Statutes of the ICGEB is 14. Once 24 ratifications have been made and it is agreed that the ICGEB shall become an autonomous entity, the project will be transferred from UNIDO to that autonomous entity.

First five-year interim work programme rescheduled

A rescheduled interim programme for the International Centre for Genetic Engineering and Biotechnology's (ICGEB) first five years of operation was the main focus of the Centre's Preparatory Committee, held from 6-8 July under the auspices of the United Nations Industrial Development Organization. The 41-nation body also considered the progress on the work programme at the ICGEB's two components in New Delhi and Trieste; recommendations of the Panel of Scientific Advisers (PSA); financial resources; affiliated centres; and intellectual property rights.

According to the latest PSA report, space limitations at both component sites have not allowed speedier development of the Centre and it urges completion of the new buildings, as well as suitable housing for scientists, which remains "an unresolved problem of urgency" essential to attracting high-quality scientists.

Recruitment of senior scientific staff is also subject to availability of space as well as to the longevity of the offered contracts. These are currently being offered for the duration of the interim programmes. Current commitments for the first five-year programme - amounting to some $30 million and representing a healthy financial outlook - are expected to provide adequate guarantees for the acquisition of a good scientific group, necessary to give the Centre the credibility to mobilize further funds.

The Committee therefore considered rescheduling the programme to begin next January, allowing for longer contracts to be offered while reinforcing the image of the ICGEB.

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

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UN and other organizations' news

New third world production initiative

One of the most frequently cited expectations for biotechnology is that its enormous potential will be used to alleviate the suffering in developing countries caused by a variety of infectious diseases. Often joined to this is the promise of effecting a real transfer of the relevant biomedical technologies to the disease-affected regions.

Ten years ago, the United Nations Development Programme, the World Bank, and the World Health Organization (WHO) addressed the first of these goals by establishing their Special Programme for Research and Training in Tropical Diseases (TDR). The significant progress made through TDR-sponsored research - particularly in the development of vaccines against malaria, schistosomiasis and leprosy - has now spurred a new component to the programme aimed at fulfilling the second pledge.

Termed the TDR Initiative for Biotechnology Implementation, the new undertaking will consist of a limited number of unique, technology-driven partnerships between scientists and institutions in the developed and developing world. There is an increasing need for a variety of reagents, such as monoclonal antibodies, recombinant and synthetic antigens, and DNA probes, many of which have been developed as a result of TDR-funded research, to be produced in sufficient quantities and formulated for use in tropical countries in simple and inexpensive ways.

Such reagents are essential for patient diagnosis, parasite identification and characterization, to supplement other methods used in evaluating candidate vaccines, and in a variety of epidemiological studies, including vector control and disease transmission. By carefully selecting both the projects and the collaborating institutions, a first-stage goal of creating a small number of self-sufficient, quality production facilities in the developing world can be realized.

The Initiative is thus designed more along the lines of contract-production than investigational research, and the reagents to be produced will, it is

hoped, quickly find their way into ongoing TDR projects. A rather rapid timetable for the Initiative which will be co-ordinated and overseen by the Programme's various steering committees is envisaged. Once a short list of specific projects is completed proposals for production projects will be solicited from institutions in the developing world that have already demonstrated ability to carry out technologically advanced research. (Source: Bio/Technology, Vol. 6, March 1988)

United front against AIDS

The World Health Organization's Special Programme on AIDS is to join forces with the United Nations Development Programme in the fight against AIDS. In recognition of the alliance, the Special Programme on AIDS is to become known as the Global Programme on AIDS.

Halfdan Mahler, the Director-General of WHO, announced the alliance in Geneva. The change will provide the WHO's expanding programme on AIDS with a ready-made administrative framework. The UNDP has set up 112 "field offices" in developing countries.

The resident representatives of the UNDP also co-ordinate assistance from all the agencies of the United Nations, so they are ideally placed to know everything about all development projects in a country. They can avoid duplication, and unite people tackling the same problem.

The WHO's Special Programme on AIDS, directed by Jonathan Mann, planned to have carried out initial visits to 127 countries by the end of 1987 to discuss programmes to control the spread of the disease.

Countries that take part set up their own national committees and design their own five-year plans to combat AIDS.

The UNDP has already allocated $3 million for the preparation of joint programmes with the WHO. The UNDP's guidelines to its representatives point out that the resources needed by the WHO's Programme on AIDS are expected to grow from $37 million in 1987 to $650 million in 1991, excluding direct costs of diagnosis, treatment and any future vaccine.

The guidelines assume that 50 to 100 million people around the world may be infected with the human immunodeficiency virus by 1991, and that a vaccine will not be available for use in large populations. (Source: New Scientist, 28 January 1988)

Advisers say the WHO must tackle ethics of vaccine trials

An advisory group of leading researchers in science and public health has held its first meeting in Geneva to advise the WHO on the role that it should play in biomedical research into AIDS. Its main conclusion is that the WHO has a vital function in co-ordinating research into vaccines and antiviral drugs.

The group is chaired by Sir James Gowans, former head of the Medical Research Council in Britain and, until recently, director of the Council's directed programme of research into AIDS.

The group agreed that WHO is in an ideal position to monitor research into AIDS throughout the world, identifying gaps that need to be filled. It can also ensure that the choice of what research is done is not entirely the prerogative of developed countries.

Roy Widdus, a co-ordinator with the WHO's Global Programme on AIDS and former director of the division of international health at the United States Institute of Medicine, said that WHO's global perspective makes it an ideal clearing house for information on AIDS research.

Widdus added that it is becoming increasingly difficult in the US to find volunteers to enter trials of vaccines who belong to a "high-risk" group but who are not yet infected with HIV. In San Francisco, for example, up to 70 per cent of male homosexuals are thought to be infected. This means that researchers, research institutions and pharmaceutical firms are beginning to look to developing countries for suitable trial populations.

Another problem is that "pharmacologically virgin" people who are infected with HIV are scarce in the US. "Many AIDS patients," Widdus said, "medicate themselves with so-called underground drugs that could interfere with a trial of a new compound."

The advisory group believes that the WHO should provide governments of countries where trials of vaccines or drugs against AIDS are taking place with advice and assistance to ensure that such trials meet acceptable scientific and ethical standards. Trials also need to be designed in such a way as to offer the best chances of producing scientifically valid and statistically significant results.

The advisory group believes that the Global Programme on AIDS might usefully address several issues concerning the conduct of vaccine trials. These include:

- How best should researchers conduct a trial to assess the protective efficacy in humans of a candidate vaccine against AIDS?

- If a vaccine has shown no protective effect in animals, should scientists go ahead with trials to test its protective efficacy in humans? (Two candidate vaccines which are currently undergoing initial tests in the US of their safety in humans fall into this category.)

The advisory group will circulate its recommendations to a wider circle of researchers and specialists in public health. The aim is that their suggestions will ultimately guide the direction of the research activities of the Global Programme on AIDS.

The other members of the advisory group include Nobel prizewinner Sune Bergstrom, Valentin Pokrovski, President of the Soviet Academy of Medical Sciences, Samuel Thier, head of the United States Institute of Medicine, Vulimiri Ramalingaswami, visiting professor at the Harvard School of Public Health in Boston, Massachusetts, and former Director-General of the Indian Council of Medical Research and Alain Pompidou, health advisor to the French Ministry of Health. (Source: New Scientist, 18 February 1988)

Number of infected children will increase substantially

The incidence of AIDS in children and women of child-bearing age now demands comprehensive surveillance because there are far more cases than those reported, says a group of international experts on AIDS. But they say that it would be neither cost-effective at the moment, nor ethical.

The 17 scientists, from Europe and the US, met last year under the auspices of the World Health Organization. The report of their meeting, AIDS and the Newborn, was published at the end of 1987. It

says that for every known case of AIDS there will also be many women and children infected with HIV. The group is concerned that current reporting of AIDS merely reflects transmission of the virus that took place five or more years ago.

The report says that only about 50 per cent of children infected with HIV who have symptoms fulfil the criteria for a diagnosis of AIDS, which are primarily for diagnosis of the disease in adults. Proposed revisions by the Centres for Disease Control in the US are still too complex for routine use, so Europe needs its own criteria for children.

Catherine Peckham, professor of paediatric epidemiology at the Institute of Child Health in London and rapporteur of the meeting, said that 16 European countries had reported 206 cases of AIDS in children up to September 1987. France was at the top of the list.

An analysis of the 182 cases of children with AIDS reported in Europe by June 1987 showed that about half have mothers who have AIDS or who belong to a high-risk category such as drug users. About 30 per cent of the 182 children became infected through blood transfusions. The implementation of rigorous screening of blood donors and treatment of blood products, however, means that the main source of HIV infection in children in future will be from mother to child. The numbers are likely to increase substantially over the next three to four years.

On immunization, the report recommends that HIV-infected children without symptoms should receive the combined diphtheria, pertussis and tetanus vaccine and live oral polio and measles vaccines. But health workers should not give live vaccines to children with symptoms, because of theoretical concerns about the competence of their immune systems. Children living in households with a person with AIDS should also be given inactivated, rather than live, polio vaccines because of the risk of transmitting polio infection to the person with AIDS.

The report calls for more widespread surveillance in order to detect any increase in heterosexual transmission and the resultant rise in infected infants. The experts say that comprehensive antenatal screening of all women would provide useful epidemiological information, but it would not be feasible or cost-effective at the moment - nor would it be ethical. (Source: New Scientist, 21 January 1988)

Turning back the guinea worm

Guinea-worm disease, an incapacitating parasitic infection that is widespread in parts of Africa, could be eradicated within the next few years. More than 100 representatives of countries where the condition is endemic attended a meeting on the disease, held in Accra, in Ghana, in early March 1988.

The World Health Organization wants to eradicate guinea worm by 1995. William Foege, executive director of an organization called the Task Force for Child Survival, which aims to improve child health, said he expected the disease to disappear within three years.

The eradication of guinea worm would lift a tremendous burden from millions of people in the third world. An estimated 10 million cases occur each year - most of them in Africa, in a band of 19 countries from Senegal in the West to Ethiopia in the East. India, Pakistan, Saudi Arabia and Yemen are also affected.

Representatives from 17 of the 19 African countries affected, as well as delegates from India and Pakistan, attended the meeting. The WHO's regional director, Ottlieb Monekosso, and Jimmy Carter, a former American president, were also present. (The Carter Presidential Centre, based in Atlanta, Georgia, is the umbrella organization for both the Task Force for Child Survival, and Global 2000, which has as one of its main aims the eradication of guinea-worm disease.)

At the meeting, Carter signed a memorandum of understanding between the Minister of Health in Nigeria, Global 2000 and the Bank of Credit and Commerce International. This London-based bank is one of the main sources of funds for Global 2000.

Nigeria is one of the countries most seriously affected by guinea worm. It has about 2.5 million cases a year. Global 2000 has recently agreed to provide funds for one year to help Nigeria establish a secretariat to focus the country's effort to eradicate the parasite.

In some parts of Nigeria, up to half of the people are incapacitated at one time. The parasite is in some places the principal reason why children miss school. In south-eastern Nigeria, aid agencies have estimated that guinea-worm disease is diminishing the annual rice crop by 11.6 per cent. The value of the rice crop in that area is about $20 million.

The most obvious way of combating the spread of guinea worm is to supply affected villages with safe drinking water. Donald Hopkins, a consultant with the Task Force for Child Survival and Global 2000, says that while this is the most expensive option, at $20 a head, it provides other benefits, over and above the elimination of guinea worm. Diarrhoeal diseases, for example, also spread via water.

Hopkins points out that we are now in the second half of the UN-backed International Drinking Water Supply and Sanitation Decade, which has as its goal the supply of safe drinking water to everyone by the end of 1990. Governments should give priority to villages with guinea worm when extending supplies of safe water, Hopkins says.

A second means of controlling the disease is to persuade people to filter their water through cotton cloth. It is also possible to kill the worm's larvae by putting a chemical, Abate, in ponds, for example. At a concentration of 1 part per million, Abate is colourless, tasteless and odourless, safe for human consumption, and does not kill other wildlife such as fish. (Source: New Scientist, 31 March 1988)

The Environment Liaison Centre

Throughout the world, thousands of non-governmental organizations (NGOs) are working in diverse ways to promote responsible human actions regarding the environment and development. The Environment Liaison Centre (ELC), itself an international NGO, was established in Nairobi, Kenya, in 1974, for the purpose of strengthening communication and co-operation between these NGOs. In addition, ELC serves as a link between NGOs and the United Nations Environment Programme (UNEP), headquartered in Nairobi.

With 232 member organizations in 94 countries and contact with over 7,000 other groups, ELC is part of the global effort to protect the Earth's eco-systems for human welfare, and for sustainable utilization and equitable distribution of resources.

To keep the NGO community informed of international, regional and national initiatives in the fields of environment and development, ELC publishes two bi-monthly periodicals.

- **ECOFORUM** is an environment and development journal, published in English, Spanish and French. The journal acts as a focal point for NGOs to share information, review the activities of UNEP and other United Nations agencies, and discuss emerging environmental and developmental problems.

- **NEWS ALERT** presents brief, current action-oriented news items regarding environment and development issues. English, Spanish and French versions are available.

Practical "How to" booklets, directories of NGO activities in various areas of environment and development and books and monographs dealing with specific sustainable development concerns are available in English, Spanish and French. A complete list of current publications is available from ELC.

Surveys conducted on a regular basis since 1976 have identified some 10,000 NGOs world-wide. ELC is continually seeking to update its information on NGOs everywhere, with a major new survey having been completed in 1985. This computerized data system is at the core of ELC's global efforts to expand NGO co-operation and networking.

ELC receives 826 periodicals, the majority produced by NGOs themselves. Together with other NGO publications, these form an unparalleled record of the development work of an expanding NGO community, especially in the third world.

ELC provides grants ranging from US$100 to $5,000 to third world NGOs, to support practical field project initiatives which pay particular attention to the environmental dimensions of development work. More information on the small grants fund is available from ELC.

The positive impact of environment and development NGOs is often constrained by problems of institutional development and the lack of necessary professional, administrative and management skills. ELC's Training and Support Services programme provides assistance to NGOs in the key areas of project design and fundraising accountancy and financial management and communications. The emphasis is on responding to practical needs and on facilitating processes whereby NGOs can learn from one another through networking and skills exchange.

The programme's primary objective is networking, the building and strengthening of links between NGOs from the developing countries of Africa, Asia and Latin America. The programme provides a unique opportunity for third world grassroot NGO staff members to gain and share experiences on environment and development issues and problems.

The programme provides on-the-job training at ELC in appropriate networking, writing, computer and administrative skills useful to third world NGOs on the return of the intern to his or her home country.

ELC provides a mechanism for NGO inputs to the United Nations and other international organizations and keeps NGOs informed of relevant international organizations' initiatives. This is facilitated by ELC's special working relationship with UNEP, consultative status with ECOSOC, UNESCO and the International Whaling Commission, and liaison status with FAO. Also, ELC has recently agreed to a new co-operation arrangement with IUCN.

ELC works to reinforce thousands of grassroot and international NGO initiatives that respond directly to the basic needs of the people, which together contribute towards building a sustainable society. In doing so, the Centre strives to achieve two principal objectives.

1. To support, encourage and assist NGOs, particularly in the fields of environment and development, and especially in the South, in their efforts towards sustainable development.

2. To liaise with intergovernmental and other international bodies on behalf of its NGO constituency, in order to enhance the effectiveness of both NGOs and international organizations in the pursuit of sustainable development.

Always a major facet of the Centre's work, ELC encourages NGO linkages in all directions (South-South and North-South). The Centre tries to help in the understanding not only of local environment/development problems, but also of the global nature of sustainable development issues. ELC supports and promotes regional networks and regularly organizes meetings to encourage the emergence of links among NGOs.

ELC is a founder of many issue-oriented and regional networks such as the Pesticides Action Network (PAN), SEEDS Action Network (SAN), Kenya Energy Non-Governmental Organization (KENGO), and the African NGOs Environment Network (ANEN). The Centre's French and Spanish liaison staff also build links by establishing contacts with NGOs and all government representatives.

During the NGO forum marking the end of the United Nations Decade for Women (Nairobi, July 1985), ELC hosted a week-long series of workshops on the actual and potential importance of women and women's organizations in the struggle for sustainable development. ELC is committed to continue highlighting women's perspectives and activities in all programmes.

Development and the environment: ELC has consistently emphasized the crucial links between development and the environment. Member organizations include an increasing number from the development community. In 1985, over 100 NGOs attended an ELC-sponsored meeting on the subject in Nairobi. The meeting focused on the adoption of a Global NGO Programme of Action for Sustainable Development.

ELC continues to provide basic services to meet the needs of the NGOs, at the same time concentrating on four thematic issues during the 1985-1988 period:

- Deforestation/afforestation

- Water management

- Energy

- Sustainable agriculture.

An integrated programme of action for three years entitled "Working Together for Sustainable Development - Building NGO Networks and Capacities" has been drawn up.

The objective in each area will be to enhance the capacity of NGOs, especially in the developing countries to carry out effective and meaningful information and field project activities in pursuit of sustainable development. It will also increase the opportunities for NGOs to engage in productive

dialogues, on the basis of their own knowledge and experiences, with governments, research institutions and intergovernmental agencies, so that all parties are better able, and more willing, to pursue sustainable development initiatives.

This programme creates for the first time a systematic attempt to assist and mobilize NGOs in the third world to realize their full potential as key actors in the pursuit of sustainable development which can fulfil the basic needs of the poorest people for the long-term future.

ELC welcomes new members to this NGO community to work for sustainable development. Members are involved in making policy decisions and moulding the future of the Centre.

Further information may be obtained by writing to the Executive Director, Environment Liaison Centre, P.O. Box 72461, Nairobi, Kenya, Telex: 23240 "ENVICENTE", Telephone: 24770/340849/336989.

Social issues

Genetics and ethics

The ability to diagnose genetic diseases poses ethical problems that challenge the relationship between doctor and patient and threaten concepts of privacy.

At present very few genetic diseases can be detected directly. Those which can be detected directly, such as sickle cell anaemia, pose few ethical problems because the test says unequivocally whether a person with no symptoms carries the gene that causes sickle cell anaemia. Most tests - so-called linkage tests - are less unequivocal.

They detect portions of the genetic code very close to the defective gene. That means they can be used to trace the inheritance of disease genes in the children of two parents, but they give almost no information about individuals in isolation. A doctor has to examine all members of a family to make any decision about an unborn child; who, then, is the patient?

Diseases that do not become obvious until later in life also cause problems. Huntington's disease does not normally appear until the age of about 40, after people have had children. It is a dominant disease, so the child of someone with Huntington's has a 50 per cent chance of having the disease themselves. Often, the sufferer may be dead before his or her child has a child. In these circumstances, the best that genetic screening can do is to say either that the unborn child almost definitely does not have the disease, or that it has the same chance of carrying the disease as its parent. (Source: New Scientist, 18 February 1988)

Issues of embryo research

The great debate in Britain on test-tube babies and embryo research began in the House of Commons last February. The Government's White Paper on "Human Fertilization and Embryology", published last November, elicited a wide variety of views from MPs.

Tony Newton, the Minister for Health, reiterated the Government's position. It will ban all possibility of research aimed at creating animal-human hybrids and cloned people. It will give MPs a free vote on whether to ban all research on embryos, or to allow controlled research.

An independent statutory licencing authority (SLA), proposed by the White Paper, is the "keystone", says Newton. It would have the power to grant or revoke licences for doctors and scientists performing *in vitro* fertilization and embryo research.

Meanwhile, the anti-experiment lobby argued that the Government's proposals protected experimental animals better than human embryos. (Source: New Scientist, 11 February 1988)

Transplants of foetal tissue likely to increase ethical debate

Doctors in Mexico City have transplanted tissue from a spontaneously aborted foetus into the brains of two patients suffering from Parkinson's disease.

The dramatic development is likely to intensify the worldwide debate about the ethics of using foetal tissue to treat neurological and other diseases. Until now the question has been largely theoretical.

The operations took place last September and used tissue from both the brain and the adrenal gland of a 13-week-old foetus. The recipients, a 50-year-old man and a 35-year-old woman, experienced marked relief from symptoms of Parkinson's and had returned to their homes.

The procedure is a refinement of a technique that Dr. Madrazo of La Raza Medical Centre and his associates have been using for nearly two years on patients with severe cases of Parkinson's. In more than 20 operations, the medical team had taken tissue from the patients' own adrenal glands and implanted them deep in the brain in order to stimulate production of dopamine. Physicians in the United States and elsewhere also have used the procedure.

Foetal tissue is known to have been used on at least two previous occasions. Dr. Robert P. Gale transplanted foetal liver cells into six victims of the Chernobyl nuclear accident in an effort to generate bone marrow. All six died. Another American doctor has used foetal islet, or endocrine, cells that secrete insulin in treatment of diabetes patients.

Biomedical ethics experts said Dr. Madrazo's work would renew pressure on physicians and ethicists to confront new and complex issues.

Dr. Madrazo has said that he had been acutely aware of the ethical and moral issues the operation was likely to raise. In order to avoid controversy, he said, he used a foetus obtained by a spontaneous, rather than elective, abortion and followed procedures that went beyond those required by law.

The ethics and research committee of the hospital first considered and approved general objectives and guidelines for the use of the foetal tissue, specifying that each operation must be approved on a case-by-case basis. Officials at the Ministry of Health in Mexico also gave written approval to the procedure, Dr. Madrazo said.

In addition, written consent was obtained from the two patients who were to receive the foetal tissue. Both were admitted to the hospital knowing that they would not be operated upon until foetal tissue was available. (Extracted from International Herald Tribune, 8 January 1988)

Regulatory issues

Australia forms Genetic Manipulation Advisory Committee

Australia's newly formed Genetic Manipulation Advisory Committee (GMAC), which monitors and advises on all recombinant DNA and other genetic manipulation

work in Australia was set up last year to replace the Recombinant DNA Monitoring Committee, as part of a major effort to strengthen monitoring procedures in anticipation of an expected increase in the number of projects reaching the environmental release stage.

The GMAC aims to set up a uniform code to regulate genetic manipulation nationally, and to rationalize the maze of state and federal regulations currently affecting the biotechnology industry.

There has so far been only one other environmental release in Australia. This was of a micro-organism rather than a plant. In the middle of last year, Alan Kerr of the Waite Agricultural Research Institute in South Australia began field tests of a genetically altered bacterium to control crown gall disease, which stunts the growth of fruit trees. Before this there had been two releases in contained environments, including tests on a vaccine against gastroenteritis in piglets which went ahead in an isolated animal house.

Kerr's trials coincided with the introduction of voluntary guidelines for environmental release which involve a co-operative system of safety assessment between the GMAC and state and federal bodies. Final approval for release will rest with the federal or state body responsible for the relevant legislation, rather than with the GMAC.

The present regulations differ between states, and the GMAC will set out to rationalize them, and to alert the state governments to the need to update their rules to cope with new technology.

The Australian guidelines are much less stringent than those in the US. There have been fears that overseas biotechnology companies might move into Australia to take advantage of the less regulated environment, but this has not happened so far. The GMAC is understood not to have received any requests for release from multinational companies and organizations.

A number of other environmental releases are planned for the next year or two, including trials on a new high-yielding soya bean that is nitrogen-rich and super-nodulating. Researchers from the Australian National University in Canberra developed it in collaboration with a Queensland company, Pacific Seeds. (Source: New Scientist, 10 March 1988)

Argentinian scandal prompts new gene rules

International guidelines on the release into the environment of genetically engineered organisms are on the agenda of a meeting between the main Western nations. Scientists at the meeting will urge the developed countries of the West to issue strict controls over the release into the environment of novel organisms, engineered in the laboratory by recombinant-DNA technology.

The meeting of member States of the Organization for Economic Co-operation and Development (OECD), which comprise the developed countries of the West plus Japan, is an attempt to harmonize guidelines on the release of novel organisms into the environment. The scientists at the meeting want to ensure that researchers from one country do not exploit lax rules in another country by conducting field experiments abroad that would be forbidden, or severely controlled, at home.

The meeting heard of such an experiment that took place in 1986 in Argentina. An American research organization, the Wistar Institute of Philadelphia, commissioned the Pan-American Health Organization (PAHO) to conduct a secretive experiment with a genetically engineered rabies vaccine on a herd of 40 cattle on a research station in the province of Buenos Aires.

The rabies vaccine, based on the vaccinia virus (the cowpox virus), was allegedly smuggled into Argentina in a diplomatic bag, and the experiment took place without the knowledge or approval of the Argentinian authorities.

At the OCED meeting, John Beringer, professor of microbiology at the University of Bristol, called on the organization's members to establish an international set of rules for the deliberate release of novel organisms.

Nobody would have detected the experiment had an Argentinian scientist not heard about it and told the Argentinian Association of Research Scientists. Following this, the Argentinian Ministry of Health ordered the experiment to end. In November 1986, the Ministry destroyed the 40 cattle involved.

According to the experimental protocol, the plan was eventually to use live rabies virus.

Argentinian scientists were worried about the possible accidental release of the rabies virus. They were also concerned that there might be an uncontrolled release of the vaccinia virus. This could result in hybridization with naturally occurring pox viruses endemic to the area.

Beringer, who chairs a subcommittee of Britain's Advisory Committee on Genetic Manipulation, said last week that Wistar's experiment was ineptly handled. (Extracted from New Scientist, 14 April 1988)

Europe releases rules on microbes

The European Commission has approved regulations for handling genetically engineered organisms, in the laboratory and on the market. The proposed directives - one to govern laboratory tests on genetically modified micro-organisms, the other to govern the deliberate release outdoor of modified organisms - now go to environment ministers and the European Parliament for approval.

The rules are meant to give industry a safe legal footing for developing products based on biotechnology, and to reassure the public that the industry is under control.

The Commission prescribes a high degree of international supervision. The proposals require international consultation for commercial, but not for experimental releases of modified organisms, and for the contained use on an industrial scale only of dangerous micro-organisms.

The Commission wants all users to notify national authorities, such as Britain's Health and Safety Executive, of all plans to work with any micro-organisms, from viruses to cell cultures, that have been modified artificially. Users must disclose full details 60 days in advance.

Researchers must apply "good microbiological practice" to Group 1 organisms which are judged to be safe, such as the Lactobacillus that helps to produce yoghurt. Researchers using Group 2 organisms that are considered more dangerous (such as pathogens used in vaccine production), must tell authorities 15 days in advance what they plan to use, in what volumes, and for what purpose, with details of potential dangers, safety measures and local weather conditions.

Companies working with Group 2 organisms must produce a wider safety assessment, detailing changes in the behaviour of organisms outside their containment, the substances they can produce, details of hazards that could arise from wastes and how these will be treated and information needed by local authorities in case of accidents.

Staff at the Commission say it is impossible to regulate an industrial process without some idea of whether its proposed benefit warrants the risk. The real battle will arise over the proposals for the deliberate release of modified organisms. Members of the European Parliament are protesting that few benefits will warrant the largely immeasurable danger.

The Commission wants deliberate releases of genetically modified organisms to be assessed individually, with the aim of developing a "more organism-related approach", once the risks are better understood. (Source: New Scientist, 7 April 1988)

General

International Food Biotechnology Council formed in USA

The International Food Biotechnology Council has been formed to identify and develop scientific guidelines for the food biotechnology industry. The Council is a co-operative programme which brings together major food processors as well as companies using biotechnology to produce food and ingredients. Details from: Dr. Alan Goldhammer, Industrial Biotechnology Association, 1625 K Street, NW, Suite 1100, Washington DC 20006, USA. (Source: Biotechnology Bulletin, Vol. 7, No. 3, April 1988)

The valid way to quality biotechnology products

As more biologicals and rDNA-derived drugs begin to flow into the regulatory pipeline, more biotechnology companies are gearing up to bring these products - and the processes and facilities that will produce them - into compliance with the US Food and Drug Administration's (FDA) regulations. In fact, the difficulties of cloning and expressing a valuable gene product tend to pale beside the complicated, precise procedures necessary for compliance.

One company that has certainly been through the rigours of validating processes for manufacturing a pharmaceutical is Genentech (South San Francisco, CA).

To pass muster with FDA, a cell-cultured biological must have a demonstrated efficacy, potency, safety, purity, stability and identity. A number of basic steps must be taken to ensure that the final product has these qualities.

First, the company must prepare and characterize a master cell bank. Characterization involves searching for adventitious and endogenous agents, determining whether the cell line is tumorigenic, and confirming the identity of the cell line. According to Bruce Mackler, general counsel to the Association of Biotechnology Companies, FDA currently accepts the use of malignant, tumorigenic or abnormal cells to produce biologics.

Cell line characterization allows a company to identify putative risk factors that need to be considered in the second phase, risk assessment. Risk assessment involves identifying and quantifying the level of risk, as well as assessing safety levels. Additional risk factors, which may or may not prove important, include cellular proteins and nucleic acids, residual serum proteins and traces of compounds used to clean the cell culture equipment.

The third step is to design procedures to eliminate or inactivate the identified risk factors. This process also includes designing facilities and manufacturing procedures that prevent the re-introduction of these risk factors.

This procedure is followed by the actual process validation, which is in many ways the cornerstone of product safety. This fourth step is also required by regulations. According to Rebecca Devine, of FDA's office of biologics research and review, validation establishes a procedure for demonstrating that a method or system can be relied upon to consistently produce the intended result within defined limits. Validation has four basic elements: it must be documented; it must provide a high degree of assurance; it is specific for a given manufactured product; and it depends on predetermined specifications of quality attributes.

The fifth step, product testing, follows process validation. These tests should be rigorously run on each and every product lot to reconfirm purity, safety, potency, identity, and stability. Once the product has been licenced, each lot released for sale will have to be cleared by FDA's division of product quality control.

The sixth and final step necessary to assure product quality is compliance with Good Manufacturing Practices (GMPs). FDA expects Investigational New Drug (IND)-based products to be made "as much as possible" under GMP conditions.

The purpose of the GMPs is to improve the quality of a manufactured product - a quality standard FDA is bound to uphold. (Extracted from Bio/Technology, Vol. 6, February 1988)

$200 million a year for human genome

A US National Academy of Sciences (NAS) panel is recommending that the federal Government devote $200 million per year in new funds toward a large-scale effort to map and eventually sequence the 3 billion nucleotides within the human genome. Although the committee says the programme should be managed under a single federal agency, it shies away from recommending which of several contenders should take responsibility, insisting only that a scientific board guide the effort and "take it out of the political process". The entire project will require about 15 years and thus will cost a total of about $3 billion, according to the "Report of the Committee on Mapping and Sequencing the Human Genome", which was released in February.

The NAS committee says a comprehensive map of the human genome will help bring greater order to the many mapping and sequencing research projects now being done by individual laboratories, and it will be of "tremendous medical importance".

New facilities and technologies will be needed to exchange, store and analyse the biological materials and data that the project will generate, the NAS committee report notes. During the early stage however, the emphasis should be on decentralized small and mid-size projects because technology development is "still badly needed". Thus, the committee strongly recommends that much of the effort be funded under grants and contracts subject to peer review.

Although there was no consensus, a majority of panel members suggested designating a lead federal agency with "ultimate responsibility for funding and policy decisions" for the programme rather than setting up an interagency committee. The NAS report avoids recommending either NIH, the Department of

Energy (DOE), or the National Science Foundation, all of which are now involved in genetic research pertinent to the human genome programme. Implicitly, the committee seems to favour NIH, whose style and programmes are familiar to most members of the NAS panel. However, if several agencies can participate in a peer-reviewed spirit, their contributions will be welcomed.

Currently, Congress and the Administration are encouraging both NIH and DOE to expand their human genome efforts - providing them in fiscal year (FY) 1988 with about $17 million and $12 million respectively in new funds for such research. The President's budget request for FY 1989 recommends boosting this component of the NIH budget to about $29 million and of the DOE budget to $18 million.

Meanwhile, the Congressional Office of Technology Assessment (OTA) also has been compiling a broad-based human genome report, scheduled for release in April. Said to be "complementary" to the NAS effort, the OTA report promises to more fully explore the ethical, social, and commercial implications of this research. (Source: Bio/Technology, Vol. 6, April 1988)

Cholera's relentless march

The seventh cholera pandemic, which began in Indonesia in 1961 and has been moving relentlessly westward ever since, is now present in some 93 countries of the world and shows no signs of abating.

However, treatment of cholera, which consists of the replacement of water, salts and alkalis, supported by antibiotic therapy, has been perfected to such an extent that nobody should die of the disease if treatment can begin before the heart stops beating. Oral rehydration alone has now been found to cure all but the most severe cases, and these can receive the oral solution by nasogastric tube if intravenous fluid is unavailable.

To prevent the spread of the disease, some countries in the past imposed excessive quarantine measures, erecting cordons sanitaires and restrictions on traffic and trade, which only resulted in severe economic loss and ultimately suppression of information or denial of the disease's existence. The ineffectiveness of currently available cholera vaccine is common knowledge; few countries now use it and certificates of vaccination for travellers have long ceased to be required by the International Health Regulations. Mass chemoprophylaxis has been used extensively by some countries but the effectiveness of this strategy has never been demonstrated.

Although the word "cholera" nowadays rarely invokes the terror or panic of years past, its control is still frequently hampered by logistical problems. The cholera biotype eltor often occurs in areas where treatment facilities are unavailable. Recognized clinical cases are usually few; more frequent are very mild cases and asymptomatic infections, which may play a role in spreading the disease. Eltor is also more resistant to environmental factors than the classical type and survives longer in the environment.

However, cholera may be introduced into any country, but it cannot gain a foothold in non-receptive areas, i.e. those with good sanitation and surveillance facilities. In contrast to unprepared communities where deaths often exceed 50 per cent, those communities with properly organized programmes for diarrhoeal disease control can reduce mortality rates to below 3 per cent. In such programmes, health workers are trained in treating all acute diarrhoeas, including cholera, and are provided with essential supplies, especially oral rehydration salts (ORS). They are also trained to keep case records enabling them to notice any change in the pattern of disease that might indicate the possibility of an epidemic.

Once an epidemic has been detected, the capability of facilities and health workers should be strengthened, firstly to recognize and treat cases, and secondly to implement other control measures through education of the community, such as improving personal hygiene, food safety, water supplies and excreta disposal, disinfection of the area and proper disposal of dead bodies.

The importance of a state of preparedness enabling health workers promptly to detect an epidemic, provide treatment and prevent panic and death is clear, as are the limitations of control measures such as the cordon sanitaire, vaccination and chemoprophylaxis. (Source: Development Forum, March-April 1988)

The malaria comeback

Malaria, already a significant cause of disease and death in the world, is increasing rapidly again, especially throughout Africa, the Indian subcontinent, Southeast Asia and South America, leaving in its wake two million dead and another 200 to 300 million afflicted each year.

The hitherto effective and relatively safe malaria combatant, chloroquine, is now proving useless in areas where the drug has been widely used and malaria parasites have become resistant to its effects. Moreover, the kind of malaria caused by this drug-resistant strain frequently kills its victims.

But new hope of fighting chloroquine-resistant malaria strains now comes from the United States where scientists have recently discovered that when such parasites are treated with certain heart or cancer drugs they can be destroyed.

According to a report in The New York Times, researchers at Washington University in St. Louis and the Walter Reed Army Institute of Research in Washington discovered that resistant malaria organisms do not accumulate chloroquine but quickly release it after it enters their cells. They also found that three drugs of the type known as calcium channel blockers, two of which are used as anti-cancer drugs and another which changes the ability of the heart to contract, prevent such a release.

The researchers believe the drugs' effect on heart or cancer cells may be unrelated to their effects in blocking chloroquine resistance. They therefore hope to be able to modify the drugs and to minimize adverse side-effects while retaining their effectiveness in preventing the malaria parasites from releasing chloroquine.

On a less hopeful note, children in Africa who have been receiving blood transfusions to combat malaria-induced anaemia are reported to be in danger of contracting AIDS.

Results of a study conducted in Zaire and published in the Journal of the American Medical Association indicate that as many as one in 15 children may be at risk from having received unscreened blood transfusions, now estimated to be the second most common source of AIDS infection in Africa next to heterosexual transmission. (Source: Development Forum, March-April 1988)

A welcome new tool against resurgent malaria has been achieved by Australian scientists. The government-owned Australian Industry Development Corporation hopes an Australian antimalaria vaccine

will be ready for commercial production in about five years. Already tested on monkeys it may soon be tested on humans. Scientists are cautious about the vaccine, pointing out that it would not be enough alone to eradicate malaria. They are eager to avoid a repeat of what occurred in the 1960s when the success of the drug chloroquine and the insecticide DDT produced a burst of optimism that malaria could be eradicated. High hopes waned as DDT side-effects appeared and mosquitoes developed chloroquine resistance. Nevertheless, the new Australian vaccine will be a welcome arm in the arsenal against the disease. (Source: Development Forum, March-April 1988)

Commercializing gene therapy

Viagene Inc. and Genetic Therapy Inc. are trying to turn molecular biology's dream of gene therapy into commercial reality. Their common goal is to use retroviral vectors to deliver genes into selected cells within the body, and then direct that genetic material to integrate into the host's genome and express appropriately. Thus, in theory, a patient's own cells could be jury-rigged to produce key enzymes or other proteins needed to correct his or her disease.

Viagene (San Diego, CA) will use gene transfer to treat viral infections, malignancies, and genetic diseases. The firm will initially address relatively nearer-term therapeutic opportunities, such as fighting cancer and AIDS. In cancer therapy, for example, products made by retrovirus-delivered genes could act as markers to aid in the targeting of other therapeutic agents. Similarly, transferred genes could be used to produce protein antigens that would act as vaccines.

Genetic Therapy Inc. (GTI, Gaithersburg, MD) will be collaborating with W. French Anderson at the National Heart, Lung, and Blood Institute of the National Institutes of Health (NIH, Bethesda, MD). (Extracted from Bio/Technology, Vol. 6, January 1988)

Global co-operation pledged after first AIDS summit

The spirit of unity and consensus achieved at the first AIDS (acquired immune deficiency syndrome) summit of health ministers held in London in February was undeniable. Agreement was unanimous on the need for a global programme of health education, backed by sufficient resources, to stem the transmission of the human immunodeficiency virus (HIV). The 15-clause declaration that officially concluded the three-day meeting, attended by delegates from 149 countries, including 114 health ministers, pledged absolute commitment to the global AIDS strategy of the World Health Organization (WHO), co-sponsor, with the British Government, of the summit. How the meeting's laudable conclusions will be translated into political reality within individual countries is less certain.

The summit clearly achieved its stated objective to provide health ministers and senior policy-makers with a forum for discussing strategies for AIDS prevention and control with particular emphasis on information and education. The international publicity surrounding the summit will also have been welcomed.

Dr. Jonathan Mann, director of WHO's AIDS programme, told the summit that between 5 and 10 million people are believed to be infected with HIV, with 75,000 fully developed cases of AIDS having been reported so far, although the true figure is likely to be nearer to 150,000. By 1991 it will rise to 1 million.

Different modes of HIV transmission in different populations pose problems for global strategy. In Western Europe, North America and Australia, the virus spreads mainly among homosexual and bisexual men and through intravenous drug abuse. In Africa and parts of the Caribbean, transmission is mainly through heterosexual contact.

The summit failed to make a recommendation on mandatory testing of individuals in high-risk groups. Attitudes towards compulsory testing vary greatly.

As of 12 January 1988, the Americas accounted for some 57,000 reported cases of AIDS (with 49,000 in the United States), Africa 8,693, Europe 8,775, Asia 224 and Oceania 742.

Undoubtedly the most important aspect of the summit was the exchange of information and ideas on different countries' handling of AIDS. Furthermore, the meeting demonstrated a greater willingness for many countries to concede that AIDS is a truly global issue, and that the threat it poses is real. (Extracted from Nature, Vol. 331, 4 February 1988)

Not so much a medical problem

The economic, social and political aspects of AIDS are as vital to our understanding of the spread of this disease as the intricate details of the genome of the human immunodeficiency virus. At the first international conference to discuss the disease in this light, more than 1,000 delegates gathered in London to discuss the global impact of AIDS.

The conference heard about the problems of groups as diverse as migrant labourers in South Africa and prostitutes in London. Papers presented discussed the consequences for health services around the world and the impact on families and individuals.

Governments will have to assess that impact in order to be able to provide services and contingency plans to cope with the consequences of AIDS. Predictions are hard to come by, mainly because AIDS is a new disease. Many questions about the spread of HIV have no answer at present, yet such information is vital to statisticians who wish to model the future pattern of infection.

The spread of AIDS will eventually slow down the rapid rates of population growth in those developing countries in which the disease is affecting the general population. This is the prediction of a model constructed by Roy Anderson of the Department of Pure and Applied Biology at Imperial College, London.

Anderson's model leads to three main forecasts: the first is that AIDS may or may not turn the rate of population growth in developing countries from positive to negative. It is more likely to do so if a high fraction of infected people eventually develop AIDS and die, and if a high proportion of babies born to infected women are also infected and die.

Secondly, if AIDS does reverse the trend of population growth, Anderson's model predicts that it will take a long time for the population to begin to decline after the invasion of HIV - perhaps several decades.

The third prediction relates to the value of the "dependency ratio". This ratio is defined as the number of children below the age of 15 years plus the number of people over 64 years old, divided by the number of adults between the ages of 15 and 65. In many countries, the dependency ratio is around 1:0. In Britain, by contrast, the ratio is 0:5.

Clearly, if the number of dependent individuals is much greater than the number of adults aged 15 to 55, there will be severe repercussions. Anderson says that whether AIDS increases or decreases the dependency ratio of an infected population will depend on parameters to which we cannot at the moment attach values. But, he adds, "for plausible values, the disease is predicted to have little impact".

Anderson warned that his conclusions must be accepted only with great caution because of the great simplification involved in modelling, and the lack of appropriate data.

In order to improve the accuracy of models such as this one, statisticians and epidemiologists need more data to fill in what Anderson calls a "depressing catalogue of ignorance". (Source: New Scientist, 17 March 1988)

How Africa must live with AIDS

If sheer effort is any indicator of future success, medical science should one day have a lot to offer people who are infected with the human immunodeficiency virus. But that day is not yet near.

Since HIV first began its silent spread around the globe, the World Health Organization (WHO) estimates that five to ten million people have become infected with it. Doctors now believe that up to three quarters of people infected will develop either AIDS or other severe symptoms of infection within nine years. Once AIDS develops, most people die within a few years.

The truth is that although AIDS is seen primarily as a problem for medical science to solve, medicine has little to offer infected people, particularly in parts of the world where health services are already severely stretched.

Unless there is an immediate and dramatic breakthrough, many countries will lose an increasing number of their citizens to AIDS over the next decade. This prospect raises questions about the social and economic impact of AIDS in countries where a significant proportion of the population is infected.

In Europe and the US, high rates of infection have so far been confined to high-risk groups such as homosexuals and drug addicts. In the US, AIDS appears to have struck especially hard among actors, artists, dancers and designers. In Africa, it could be farmers.

In many African countries, infection with the virus is not confined to well-defined high-risk groups, but is spreading among young sexually active people. Sexually active in most cases also means economically active.

At present in Africa, the highest rates of infection with HIV are found in some towns and cities. In many areas, the virus has yet to spread significantly into the countryside. Should the virus become common throughout Africa, it is hard to predict how severely AIDS will alter existing death rates.

Many other infectious diseases, such as malaria, measles, diarrhoea and tuberculosis, already kill extensively in Africa. In Ethiopia, the average life expectancy is just over 40. AIDS may not have a significant impact on the population there - at least, not until AIDS becomes apparent in children born to infected mothers.

In other parts of Africa, current rates of infection suggest that there will, within 10 years or so, be significant loss of life. This could seriously influence the amount of food produced in Africa.

Even in relatively industrialized countries such as Kenya and Zimbabwe, agriculture accounts for 30 per cent of gross domestic product. In many African countries, the health of the economy is closely related to the successful production of food by subsistence farmers.

Researchers at the School of Development Studies at the University of East Anglia in Britain believe that governments, relief organizations and international agencies should already be thinking about the impact of AIDS on the future supply of food in such countries. They are looking for ways of predicting which agricultural systems will be more sensitive to the loss of labour that might occur in an area severely affected by AIDS. They are looking particularly at those systems involving small-scale subsistence farming.

Even in normal circumstances, many people in Africa have a seriously inadequate diet. Africa is the only region of the world where food production per head has declined over the past 20 years.

The School of Development Studies' model will include information on cultural and social factors that might affect the spread of AIDS, as well as on the existing population structure. The ultimate aim is to produce a map of those parts of Africa most severely affected by the virus, indicating where aid workers will need to concentrate their efforts in order to prevent food shortages.

Sholto Cross, a rural development planner at East Anglia, explains that the starting point for such a model would be the land-use map showing crops. At this stage, it would also be possible to show the different types of work carried out by the members of a household, and the amount of labour needed for each agricultural task.

Such a model would need to take into account such characteristics as the size of the family, the extent to which men migrate to find other work, the traditions of inheritance and kinship, the extent to which households exchange labour and other resources, and the organization of land tenure. Some societies put constraints on the ways in which labour is allocated.

Next comes life expectancy and the age and sex structure of the population. This data will help the team to predict how changes in death rates might influence the sizes of households and their composition.

Piers Blaikie, the environmentalist in the team, says that one possible outcome of a sudden increase in deaths could be that household units become fragmented and unable to cope with the range of work.

One important factor which the model will have to incorporate is the system of kinship. Different systems of kinship in otherwise similar societies can influence the consequences of a shortage of labour.

Some characteristics of a society may make it more susceptible to the spread of AIDS. In Uganda and Kenya, for instance, long-distance lorry drivers may be one of the main carriers of the virus, forming an "AIDS corridor" across the continent. Some rural areas will have greater exposure to the virus than others, because they have more contact with the towns.

Local cultural practices will also come into play. In some parts of Kenya, for example, lactating mothers pass their babies around when they need feeding. As there is some evidence that infected women can pass the virus on through their breast milk, this system, known as "milk pooling", could accelerate the spread of the virus among infants.

Nick Abel, the team's ecologist, warns that if AIDS causes real falls in population in rural areas and the abandonment of farming areas, the resulting encroachment of the bush could lead to an increase in tsetse fly and an epidemic of sleeping sickness in humans and animals.

The team's ultimate aim, apart from prediction, is to train local people to help farmers cope. The researchers estimate that the whole scheme would cost about £500,000 to carry out. Initially, however, the team is seeking £60,000 to carry out a pilot study.

By the end of the main study, the team would hope to have identified which areas will be most vulnerable to shortages of labour. This would, it hopes, enable the team to provide a kind of early-warning system that would alert governments and aid agencies to an impending problem. They could then begin to develop strategies to avert disaster.

The working assumption is that Africa - along with the rest of the world - cannot rely on medicine to provide a solution to the inexorable spread of AIDS in the next 10 years. (Source: New Scientist, 14 January 1988)

Progress on vaccines against a variety of diarrhoeal diseases

The prospects of another breakthrough in genetically engineered vaccines in 1988 look slim. Two years ago scientists using new technologies produced the first such vaccine for hepatitis B. Although several others have since been tested on humans, none are considered ripe for a commercial launch.

More than 200 years after Edward Jenner discovered a vaccination against smallpox, only 10 other vaccines are commonly in use worldwide. They include the Pasteur vaccine against rabies, the Salk and Sabin polio vaccines and vaccines against yellow fever, whooping cough, measles, tetanus and diphtheria. But as Kenneth Warren of the Rockefeller Foundation in the US points out: "There are no vaccines for the great protozoan diseases of mankind such as malaria, amoebiasis, sleeping sickness or the worm diseases of the developing world, which include hookworm, river blindness and schistosomiasis.

"With respect to the two greatest killers of children in the developing world, diarrhoeal and respiratory diseases, vaccines are either unavailable at present or grossly deficient." Warren cites cholera vaccine, which is only 40 per cent effective for a period of less than four months and causes fever and other problems.

Work on new or improved ways of providing protection against these diseases is proceeding rapidly. Scientists working on malaria and schistosomiasis reported important advances last year.

Progress on diarrhoeal and respiratory diseases has been slow but there may yet be surprises in 1988. Diarrhoeas kill an estimated 500,000 children a year. Several techniques being used by scientists rely on advances in biology and biochemistry.

The vaccines of the new era can be made up of the tiniest portion of the offending micro-organism. These can be isolated and reproduced using the new technologies, giving scientists total control. This is a great improvement over the former more random and imperfect method of producing vaccines from among dead molecules, live but weakened ones or a combination of both.

Some of these methods are being used in the search for a safe and effective diarrhoea vaccine. There has been significant progress on four of the five vaccines against agents which cause diarrhoea, and these have been given the highest priority by the World Health Organization's diarrhoeal diseases control programme.

Research groups are working on rotaviruses, which are responsible for up to 40 per cent of the life-threatening diarrhoeas in children under two. Dr. Albert Kapikian of the US National Institute of Health is using a rotavirus that causes immunity in rhesus monkeys.

Preliminary tests on umans show that it produces immunity in infants in both developed and developing countries, though about a quarter of those tested suffered a mild fever. The snag is that it is effective against only one of the four types of rotavirus. Kapikian has produced a new version offering protection against all four types. It combines human and rhesus rotaviruses through genetic engineering.

The first human tests are under way in Finland, Venezuela and Peru. The results for the first two are expected in six months. Preliminary trials reveal that the vaccine causes slight fever on the third and fourth day of use, a small price to pay for the protection it offers.

Dr. Bruce Stocker of Stanford University, US, and scientists at Wellcome Research Laboratories in the UK are also using new technologies to engineer a more efficient vaccine against Salmonella typhi, the agent of typhoid fever. It consists of the offending bacterium, which has been deprived through genetic engineering of its capacity to produce the amino acids it needs to survive in human tissue. Once the relevant genes have been deleted, the Salmonella typhi multiplies two or three times, enough to unleash the body's defences, and then dies.

Cholera is the third diarrhoeal disease on the WHO's short-list. A vaccine produced by conventional methods is showing encouraging results in trials on more than 60,000 people in Bangladesh. But this has not deterred those working on a genetically engineered version. Such vaccines would require a small dose and would protect for years rather than months.

For inexplicable reasons, early trials with a genetically engineered cholera vaccine developed by Dr. Richard Finkelstein in the US produced diarrhoea in between 25 and 30 per cent of those treated. US doctors James Kaper and John Mekalones have experienced similar difficulties with their version and are now trying to identify the causes.

A fourth organism which causes diarrhoea is shigella. One of the serotypes, S. dysenteriae type 1, causes severe dysentery in thousands of children in developing countries. Dr. Samuel Formal of the Walter Reed Army Institute for Research in the US has been transferring genes from shigella into benign bacteria carriers such as safe E. coli bacteria, or into the typhoid vaccine, creating hybrid vaccines. One of these has proved to be safe and effective in volunteers and it could undergo further human tests in Thailand, Israel and Chile later this year. The trials will proceed if researchers are able to solve last-minute problems, including producing sufficient quantities of a vaccine as effective as it is under laboratory conditions.

There have been only minor advances towards a vaccine for enterotoxigenic E. coli, the fifth cause of diarrhoea in children on WHO's list. (Source: South, January 1988)

Biotechnology firms are threatened in 1988 climate

Survival may be the watchword for many companies in the biotechnology industry in 1988, according to Consulting Resources Corporation (Lexington, Mass.), a management consulting firm that follows the biotechnology industry.

They say that 1988 will not be a banner year for product introductions; rather, acquisitions and mergers will emerge as the key news events.

Since last October's stock market crash, which sent biotechnology stock plummeting 40 to 50 per cent, few issues have been able to recover fully. Most prominent biotechnology stocks remain well below their 1987 highs.

The lowered valuation of biotechnology stocks has created an unprecedented opportunity for firms that have been contemplating biotechnology acquisitions or mergers.

Potential suitors in this year's acquisition scenario will not only include pharmaceutical giants and diversified conglomerates, but the larger, more established biotechnology companies as well.

Japanese and European companies will also try to take advantage of the weak dollar to acquire a stake in this industry.

Mergers between smaller firms can also be expected this year. For many biotechnology entrepreneurs, this option may be more agreeable than a takeover, as a merger with another biotechnology company will allow both firms to expand, while allowing each to retain a degree of their independence and corporate culture.

Better days are ahead for the industry though, as more products begin to make their way out of the pipeline and into the marketplace in 1989/1990. Amgen's erythropoietin will probably be the only major product to be approved by FDA this year.

On the bright side, as many as 10 product licence applications for new therapeutics are expected to be submitted for review. Most of these will be long-awaited, flagship products, such as Cetus' interleukin-2, Chiron's epidermal growth factor, Centocor's cardiac imaging agent "Myoscint", Genetics Institute's TPA and colony stimulating factor, and Genzyme's glucocerebrosidase. (Source: Chemical Marketing Reporter, 1 February 1988)

World agricultural markets

Worldwide, more than 480 companies and 125 other research organizations are actively pursuing, through biological means, improvements in seeds, plant diagnostic tests, and plants used to feed people and animals. Though more than half of these research groups are in the United States, competition from companies in other countries is intensifying rapidly. At the same time, large agrichemical firms have started acquiring smaller seed companies to establish a foothold in evolving markets. By the mid-1990s, these players should be competing in a world market producing trillions of tons of foodstuffs worth trillions of dollars. Many are looking to technological advantages to give them the edge in this game.

Seed improvement is perhaps the most visible strategy for agricultural improvement, but is certainly not the only entree into the world agricultural markets, though.

Some are established. Monoclonal-antibody tests for viral diseases are already on the market, though there are formidable obstacles to further development in several areas: the logistics of field sampling may limit a test's usefulness to the farmer, and a test that identifies a condition for which there is no remedy has decidedly limited appeal. The emphasis is on inexpensive, easy-to-use diagnostics that can detect fungal, bacterial, and viral diseases, warn of spoilage (or the presence of such harmful micro-organismal products as mycotoxins), or signal the build-up of unwanted toxic chemical residues (from pesticides, for example).

Other, longer-term projects include non-traditional protein sources - bacteria, filamentous fungi, and algae among them. These alternative sources could be used to feed the human population, but their most likely use will be in animal feed.

While the US undoubtedly dominates the world market for biotechnology agricultural products (and will probably continue to do so), substantial markets do exist in other developed countries. And huge market opportunities are opening up in China, India, the Middle East, Africa, and most other parts of the developing world.

By the year 2000 the world's population should increase from its present 5 billion to some 6.2 billion - with most of that growth, and hence most of the new demand for food, concentrated in developing areas.

Genetically manipulated crop plants
Probable year of commercialization

Rice	1991
Wheat	1992
Corn	1992
Soybeans	1992
Rapeseed	1991
Sunflower	1991
Barley	1992
Sorghum	1992
Alfalfa	1992
Fruit	1990
Tomatoes	1988
Potatoes	1989
Other vegetables	1989
Sugar cane	1989

The world will need to produce 40 per cent more food than it now does. Biotechnology could obviously provide an important means of meeting that need; the challenge facing industry is how to introduce these products - especially into these developing markets.

Until now, few of the fruits of industrial and academic research have found their way to the farm. While sales in developed countries should grow quickly through the early 1990s, biotechnology products should achieve major penetration of developing-country markets in the middle and end of the decade.

By 1992, developed countries should see their agricultural yields increase 20 to 40 per cent from 1986 levels. Yields in developing countries should be at least 40 per cent higher than today's. By that year, Asia (for example) may be producing three times as much wheat as the US - and substantially more sugar cane. The now-developing nations combined may, in fact, produce some three fifths of all the world's crops by then. (Source: Bio/Technology, Vol. 6, March 1988)

B. COUNTRY NEWS

Australia

Regulatory guidelines adopted

Australia's National Health and Medical Research Council has adopted guidelines to regulate the practice of gene therapy, clearing the way for research that may eventually cure haemophilia and other inherited diseases. (Source: European Chemical News, 9 November 1988)

Brazil

New biotechnology centre in Rio de Janeiro

The Rio City Hall will take the occasion, in April, when the First National Biotechnology Fair and Congress are held at the Riocentro, to initiate the Rio Biotechnology Enclave, to be established on Ilha do Fundão, on an area of 200,000 square metres, with a capacity to accommodate 40 business firms. The enterprise will cost nearly $24 million (1.27 billion cruzados), and participating in it jointly will be the Federal University of Rio de Janeiro, the Oswaldo Cruz Foundation, the Rio City Hall, the Ministry of Science and Technology, and the private sector, represented by the Brazilian Association of Biotechnology Enterprises (ABRABI).

According to the president of ABRABI, Antonio Paes de Carvalho, the prospects for the return of business firms with investments in modern biotechnology are currently $1 billion (53 billion cruzados). The Rio municipal secretary of economic development, Jose Augusto Assumpcao Brito, said the City Hall will provide for the infrastructural work and administrative premises with an investment of $1 million (23 million cruzados). (Source: O Globo, 23 October 1987)

Brazil's UNICAMP to invest $14 million in biotechnology

Brazil's largest integrated programme for biotechnology is beginning to be implemented at Campinas State University (UNICAMP), with financing amounting to a million OTNs (nearly 463.5 million cruzados), released by FINEP (Funding Authority for Studies and Projects). At the beginning of 1985, UNICAMP is due to receive $8 million (nearly 440 million cruzados) from the International Development Bank, and, for apparatus alone, starting in 1988, will be investing $3 million in latest generation equipment.

According to the programme co-ordinator and director of the Institute of Biology, Antonio Celso Magalhaes, over the past 10 years UNICAMP has invested in isolated projects, which will now begin being treated in a multidisciplinary manner. The team of 60 scientists and an additional 150 persons, including specialized researchers and technicians, are working at the Molecular Biology Centre, on which construction has begun, and at the Integrated Research Centre, acquired from Monsanto.

Despite problems with the release of imported materials, in two years the co-ordinator expects to be showing the first results. The field of biotechnology applied to food should be one of the first to offer finished products, because it has a longer tradition. For example, projects are under way to develop biopolymers and enzymes used in food processing.

In the sector, which had already been carrying out projects, the production of pharmaceuticals will be accelerated, to meet the priorities for control of

Brazilian biotechnology: private enterprise

Company	Fields of Activity	R & D Areas	Principal Products
Biobras Bioquímica do Brasil S.A.	Chemicals and pharmaceuticals, diagnostics, human health	Medicines for human health, enzymes, diagnostic products	Enzymes; diagnostic products
Biobrás-Pesquisa e Desenvolvimento S.A. (related to Biobras)	Research and development of industrial technologies for chemical and pharmaceutical products and processes, services	Vaccines; diagnostic products; human and animal health; farming and livestock products	
Biofil-Industria e Comercio de Produtos Biotecnologicos	Bacterial cellulose by-products		Artificial skin
Biomatre S.A.	Plant micropropagation using tissue culture (grain, corn and cassava), plant genetic improvement using cell and molecular manipulation	Plant micropropagation using tissue culture	Disease-free and genetically selected seedlings of different species
Biotest S.A. Industria e Comercio	Diagnostics, human health	Diagnostics	Serums
Cantagalo S.A. Administradora e Participadora	Vaccines, veterinary pharmaceuticals		Vaccines
Cibrazi-Companhia Brasileira de Antibioticos	Antibiotics		Antibiotics
Companhia Florestal Monte Dourado	Forestry genetics		
Cultilab-Materiais para Cultura de Celulas Ltda	Diagnostics and human health, livestock (diagnosis and reproduction); basic materials for biotechnology (products, equipment and accessories)	Techniques for improvement of basic materials and creation of new products, new types of cell strains for virology, immunology, serology, new filtration equipment technologies, lyophilization of products used as basic materials	Culture media, sera and other materials for cell culture
Embrabio-Empresa Brasileira de Biotecnologia Ltda	Diagnostics, human health, livestock	Development of virus vaccine, quality control, development of virus vaccines, development of animal diagnostics	Vaccines, products and equipment for diagnosis
Laboratorios Simbiotica S.A.	Chemicals and pharmaceuticals, vaccines, human health, livestock		Pharmaceutical specialties
Leivas Leite S.A. Industrias Quimicas e Biologicas	Agriculture, vaccines, livestock, pharmaceutical chemistry	Fermentation technology, production of vaccines	Tissue culture vaccines, bacterial vaccines produced by fermentation, plant inoculants
Microbiologica Consultoria Analises e Produtos Biologicos	Chemicals and pharmaceuticals, vaccines, diagnostics, immunological, human health, agriculture		Plant hormones, culture media, sera
Nitral-Industria e Comercio de Inoculantes e Produtos Agropecuarios Ltda	Agricultural inoculants		Agricultural inoculants
Nortec Agroquimica S/A	Agrochemistry		
Quibasa-Quimica Basica	Pharmaceuticals, chemicals		
Quimbrasil Quimica Industrial Brasileira S/A	Pharmaceuticals, chemicals, vaccines, diagnostics, human health, enzyme production, agriculture, livestock	Extraction of sulphur from phosphogypsum by bacterial route, phosphorus solubilization using the bacterial route, nutrients for alcoholic fermentation	Vaccines, fertilizers
SBS-Sociedade Brasileira de Sementes	Agroindustry		Basic potato seed, strawberry, mulberry, pineapple, and banana seedlings
Sementes Agroceres S.A.	Agriculture, chemistry, livestock	Genetic improvement	Hybrid corn, vegetable and sorghum seeds
Vallee Nordeste S.A.	Vaccines, veterinary pharmaceuticals		Vaccines

This list only includes national private enterprises associated with ABRABI (Brazilian Association of Biotechnology Enterprises). SOURCE: ABRABI and other reports

medicines, developing technology for the manufacture of anti-inflammatory, analgesic and cardiotonic products. In the field of vaccines, without attempting to duplicate efforts or to compete with traditional institutions, UNICAMP is working on the procurement of vaccines for animals, such as the one to immunize pigs against bacteria. (Source: O Globo, 10 November 1987)

Synthetic skin: Brazilian biotechnological development

Brazil is beginning to export a treatment for burns to the United States. The product is a temporary substitute for skin, and was developed by Biofill. It has been used for three years with complete success by the Cajuri University Hospital in Curitiba, consisting of a permeable cellulose tissue that allows for the passage of water vapour, but prevents the entry of micro-organisms responsible for the infections commonly affecting burns patients. (Source: C&T Noticias, October 1988)

Canada

Allelix plans to reorganize

Despite today's trend toward consolidation in biotechnology, Allelix is planning on dividing into three separate operating entities, tentatively to be named Allelix Diagnostics Inc., Allelix Agriculture Inc., and Allelix Bio-pharmaceuticals Inc. (previously Allelix Biochemicals).

Allelix's founding shareholders - Polysar Energy and Chemical Corp. (formerly Canada Development Corp.), John Labatt Ltd., and Ontario Development Corp. - will own each of the three new ventures as separate investments.

Allelix Diagnostics will address two main markets with its immunological technology: over-the-counter kits (including tests for pregnancy, strep throat and ovulation) and doctor's office tests (also for pregnancy and strep throat, as well as for sexually transmitted diseases). Allelix is currently negotiating for some $8 million (Canadian) in funding for the venture, and it has leased a manufacturing facility in Toronto. The company is at the letter-of-intent stage with two or three organizations concerning distribution rights in various regions of the world.

Allelix's agricultural spin-off will continue the company's work on hybrid canola and soil innoculants to increase yield and provide herbicide resistance. The firm's hybrid spring canola has been in Canadian field trials for two years and could be licensed for sale in 1989.

In Allelix's third and newest area, biopharmaceuticals, the company is seeking strategic alliances totalling $10-15 million (Canadian) and is looking to raise another $5 million (Canadian) in a private placement. Allelix's pharmaceutical programme is a result of the firm's shift from producing industrial enzymes to developing drugs that act on the central nervous system, achieve tissue repair, and combat cancer. Allelix expects to take advantage of its proprietary expression systems as well as rational drug design.

For now, all three ventures will remain headquartered in Allelix's current facilities, although the diagnostic and agricultural operations may eventually move out. (Extracted from Bio/Technology, Vol. 6, April 1988)

European Economic Community

Biotechnology budget confirmed

Following the long-delayed approval of the European Community's framework research budget for 1987-1991, the budget for biotechnology research has been confirmed as $150 million, just over twice the previous allocation. Of this, $25 million will be added to the current Biotechnology Action Programme, which runs until the end of 1989. About $5 million is earmarked for risk-assessment research, and the same sum is targeted toward a feasibility study on sequencing and mapping the human genome. The $125 million programme for 1990-1995 will be known as BRIDGE (Biotechnology Research for Industrial Development and Growth in Europe) and is intended to be much more closely linked to industry than its predecessor. (Source: Bio/Technology, Vol. 6, January 1988)

EEC Court of Justice overturns ban on meat production hormones

In a surprise ruling late in February, the European Court of Justice overturned the European Community's directive banning the use of hormones in meat production. The challenge to the directive came from Britain, which believed that national sovereignty over consumer protection issues was at stake. However, with national legislation already in force, it is thought unlikely that the European Court of Justice's ruling will have any practical effect as far as the use of hormones is concerned. (Source: Biotechnology Bulletin, Vol. 7, No. 2, March 1988)

Two biotechnology directives

Brussels has published its proposals for two directives regulating biotechnology within the EEC. They are to be part of a legal framework to ensure that industry, while being able to exploit the new techniques of genetic engineering, can at the same time ensure protection of public health and the environment.

The first directive on the contained use of genetically modified micro-organisms seeks to regulate the use of biotechnology either in the laboratory or as part of a manufacturing process. The second on the deliberate release of gene-spliced organisms into the environment will regulate both experimental release and the marketing of products containing or consisting of genetically modified organisms in the EEC.

On contained use of gene-spliced organisms the proposed directive differentiates between small-scale processes such as laboratory and pilot-scale operations and large industrial manufacturing processes. It also defines two groups of micro-organisms. Group 1 micro-organisms are those which are generally safe whereas group 2 organisms have a certain degree of risk.

For all contained operations the national authorities must be notified of the intended use and the operator must provide a safety assessment of the project. For non-industrial use of group 1 organisms the principles of good microbiological practice will be applied.

For group 2 organisms more stringent conditions will be imposed. Special measures will have to be taken for containment such as air filtering, inactivation of waste and emergency provisions to deal with any accidental escape of micro-organisms.

Member States will have to collect information on any accidents involving group 2 organisms which pose a risk to public health or the environment. Furthermore this information will be passed to the European commission which plans to keep a register of accidents throughout the EEC. The Commission intends to analyse causes of any accidents which occur and will recommend ways of avoiding similar accidents in the future.

Some Governments within the EEC have already established their own notification procedures for experimental work in contained conditions but others have relied on application of existing laws regulating dangerous substances. Almost all member States are still undecided as to the ideal framework and the commission believes that its proposals will fit this bill.

On deliberate release of genetically engineered organisms into the environment member States have a clearer idea of their goals although the response is polarized. Denmark and the Federal Republic of Germany are not very keen on deliberate release while the Netherlands is currently drawing up its own proposals. France and the UK are currently authorizing deliberate releases on a case-by-case basis while Italy and Belgium are using existing legislation.

Under the new proposals, member States will be responsible for overseeing projects for deliberate release of modified organisms for R&D purposes into the environment within the context of EEC law. All R&D proposals will need to be registered with the competent authorities in the member States and must meet the requirements of the directive.

The Commission is to establish an information exchange system which will contain summaries of each notification for the benefit of other member States. Member States will also be able to ask for additional information.

Manufacturers will be required to supply details of new products in confidence to the competent authorities along with details of risk assessments, and plans for labelling and packaging. Once approved for marketing the member State will send the details to the Commission which will be responsible for informing other member States.

Once other products have been approved in one member State the manufacturer will be able to sell the product throughout the EEC. Disputes over approvals will be dealt with by a new committee being established by the Commission. The whole EEC process will have strict time-limits and will adhere to confidentiality rules. (Source: European Chemical News, 11 April 1988)

New European programme proposed

The European Commission has proposed a five-year, $100-million programme of precompetitive research - based for large part on biotechnology - designed to stimulate the agricultural industry. The European Collaborative Linkage of Agriculture and Industry through Research (ECLAIR) will focus on new or improved agricultural products of industrial value, on industrial products that will benefit agriculture, and on integrated projects, such as whole-crop harvesting. Approximately 10 contracts should be awarded in each of these three areas on a competitive basis, starting later this year. (Source: Bio/Technology, Vol. 6, April 1988)

France

New impetus for AIDS health education campaign

Faced with a projected 10,000-15,000 declared cases of AIDS (acquired immune deficiency syndrome) in 1989, France is to step up its health-education campaign and provide more facilities for the care of AIDS sufferers. FF930 million ($165 million) has been set aside in 1988 for prevention, education and health care.

At the end of last year, 3,073 cases of AIDS had been recorded in France, including its overseas territories, of whom 45 per cent had already died.

Among the public health measures undertaken so far was the mandatory, anonymous notification of all AIDS sufferers; the availability to all of anonymous screening; the systematic screening of donors of organs or sperm; the establishment of 11 information and care centres; the signing of a legal agreement between the US Department of Health and Human Services and the Institut Pasteur ending the patents dispute over the antibody test; the deregulation of public advertising of condoms; and the availability, without prescription, of hypodermic syringes. In addition, the antiviral agent AZT is to be released into the market.

In addition to the 11 existing AIDS clinics and advice centres, a further 11 are to be opened, two of them in overseas departments, French Guyana and the Antilles. (Extracted from Nature, Vol. 331, 28 January 1988)

India

Sex test banned

Maharashtra has become the first state in India to ban prenatal sex determination testing on pregnant women. Chief Minister S.B. Chavan said the decision was taken because of "deep concern" over the widespread abuse of the test for aborting female fetuses. Legislation is to be introduced in February.

The ban applies only to private hospitals and laboratories. Government-run hospitals and research institutions of the Indian Council of Medical Research can carry out the test provided the woman is over 35 years of age and already has a child with an inherited defect.

Selective abortion of females has long been the subject of controversy in India and Maharashtra's action follows complaints from women' groups. Although gynaecologists are divided over the wisdom of a blanket ban on private practitioners, it is likely that more states will follow Maharashtra's. (Source: Nature, Vol. 331, 14 January 1988)

Ireland

National biotechnology boost

Ireland's National Biotechnology Programme has been given a major boost with the establishment of a new contract research organization, BioResearch Ireland.

A joint research project between Smith-Kline Beckman and BioResearch Ireland will create a "European Biotechnology Reference Centre" and develop new instrumentation for this area of research.

The centre, the first of its kind in Europe, will be active in a wide range of biotechnology-based research projects involving immunology, genetic engineering, infectious diseases, and cell and tissue culture techniques.

The National Biotechnology Programme was launched last summer and so far £600,000 has been spent on three research centres at Irish universities.

No financial details have been discussed on the joint venture, but it is understood that BioResearch is planning to spend well in excess of £1 million in 1988. (Source: Manufacturing Chemist, March 1988)

Biotechnology products launched

Medlabs Limited, Dublin, has announced the market release of two new biotechnology products.

- Protein A, Ireland's first commercial product manufactured using recombinant DNA technology, and
- MUKIT, a novel "ELISA" (Enzyme Linked ImmunoSorbent Assay) test kit to measure a specific blood protein (GST-mu) that may be a marker for high-risk smokers.

Both are the result of successful collaboration between Bioprep Limited, the Research and Development subsidiary of Medlabs and teams of researchers in Trinity College, Dublin. Work on Protein A was carried out in co-operation with Professor Tim Foster and Dr. Arvind Patel, in the Department of Microbiology. This protein is used in a number of immunological laboratory procedures including the purification of antibodies, and the detection of antigen-antibody complexes. These techniques are at the heart of many developments in the growing area of biotechnology, particularly immunodiagnostic test kits. Medlabs is expanding its interest in immunologically-based products incorporating novel recombinant markers involving protein engineering.

Medlabs MUKIT was developed in co-operation with Dr. Tim Mantle in Trinity College Dublin's biochemistry department. This exclusive "world first kit" requires only 0.2 ml of blood for testing and can be carried out in most hospital laboratories. Currently the kit is being used in a clinical study in Ireland to confirm the recent USA finding that the absence of this protein is associated with an increased risk of lung cancer in smokers. The collaboration between Bioprep and the researchers at Trinity has been so successful that a campus company is to be set up to provide a strong research base for the manufacturing side of Bioprep. Initially the company - "BIOTRIN", will be based in the innovation centre of the O'Reilly Building, which is currently under construction but will probably be located ultimately in the proposed new Biotechnology Building. (Source: Technology Ireland, March 1988)

Israel

IL-2 inducer may reduce side effects

A compound that can induce the body to produce interleukin-2 could provide an effective cancer treatment without the normal side effects of IL-2, according to researchers at Bar-Ilan University (Ramat-Gan). The synthetic ammonium trichloro compound known as AS-101 induced production of therapeutic levels of IL-2 and splenocytes with high levels of IL-2 receptors. The drug also induced production of colony-stimulating factor. The drug limited the growth of fibrosarcomas in mice and prolonged survival of mice with metastatic lung carcinomas. No toxic effects were observed when the drug was administered to rats in doses of 2 mg/kg three times a week. The median lethal dose for rats was 500-1,000 times higher than the immunologically effective dose. AS-101 apparently raises calcium levels in lymphocytes, inducing the cells to produce more IL-2 and to generate more IL-2 receptors. (Extracted from Medical World, 25 January 1988)

Italy

Biotechnology consortium established

The Fiat Group has decided to take positive action in the biotechnology sector and has set up a consortium for the research and development of technologies in applied genetic engineering in the areas of veterinary medicine and chemistry, through two of the companies it controls: Sorin Biomedica (75 per cent of which is owned by Bioengineering International B.V., belonging to Fiat International Holding), and Caffaro (owned by Snia Bpd, also belonging to the Fiat Group). Public support for the programme should be assured by the participation of the CNR (National Research Council).

The laboratory of the Institute of Chemistry of Brescia University, one of the major centres of biotechnology research, is expected to be the headquarters of the "Consortium for Biotechnologies", directed by Prof. Alberto Albertini, who has also been appointed chairman of the board of directors of the newly-established consortium. Mr. Ennio Denti, from Sorin Biomedica, and Mr. Giuseppe Ferrarini, from Caffaro, are also on the board.

Sorin Biomedica, which recently gained a firmer foothold in the haemodialysis and pacemakers sector, achieved consolidated sales of 82.3 billion lire during the first half of 1987, with 13 per cent growth over the same period in 1986, and before-tax profits of 12.7 billion lire. During the first half of 1987, Caffaro - one of whose chemical plants is in fact located in Brescia - had sales of 269.6 billion lire (plus 3 per cent and before-tax profits of 28.7 billion lire. (Source: Il Sole 24 Ore, 28 November 1987)

Italy expects less cattle breeding, less cattle, more milk

The Italian livestock scene will change radically because of EEC regulations and the introduction of bovine growth hormone, or somatotropin, according to speakers at Agrobiotech, a conference held in Bologna. Prof. G. Piva, from the Institute of Science and Nutrition at the Cattolica University, Piacenza, noted that average gross farm revenue could rise by 5-30 per cent when somatotropin is widely used. He also expects a reduction of up to 16 per cent in the number of cattle reared and a decrease of up to 10 per cent in the area of farmland devoted to fodder production. Details from: Ente Autonomo per le Fiere di Bologna, Piazza Costituzione 6/40128 Bologna, Italy or on (051) 28.21.11. (Source: Technology Bulletin, Vol. 6, No. 12, January 1988)

Japan

Japan fights fears of gene manipulation

The Japanese Government is edging towards allowing field tests of genetically manipulated organisms. The Government named a panel of scientists to work out guidelines for field experiments, which are at present illegal in Japan.

The panel will spend three years collecting information from researchers. A recent opinion poll suggests that most people in Japan are worried about the release of genetically engineered organisms into the environment.

In the survey, 42 per cent of respondents thought that Japan's rules covering genetic engineering were too slack while 10 per cent said they were too strict. Just over a quarter agreed that controls were "about right".

The working party will also investigate ways of marking genetically manipulated micro-organisms to make them easier to identify in the environment. (Source: New Scientist, 28 April 1988)

Bioelectronic device R&D

Introduction

The purpose of this project is to implement the living organisms' excellent information processing functions into electronic devices. Rapid progress in silicon-integrating technology will confront its limitation in the future, and the clue to overcome this limitation will be the excellent functions which living organisms inherently have. Learning, memorizing and pattern recognition are the excellent information processing functions which living organisms possess. And plasticity, molecular recognition and self-organization are the excellent molecular-level functions by which living organisms perform the information processing. This project begins with the study of biological information processing and functional biomolecules, and the new information processing devices based on the aforementioned function is then developed.

With basic understanding of the above, research on a "Bioelectronic Device" was selected in fiscal 1986 as a new R&D theme in the Research Project for Developing Basic Next-Generation Industrial Technologies. The whole theme is divided into two: (1) the elucidation of information processing in living organisms and its application, and (2) development of molecular organization devices.

The first term (first five years) of the project is devoted to establishing the model which will explain the information processing functions in living organisms, and to establish the basic technology by which molecular organization devices are constructed. This will be followed by trial fabrication and evaluation of prototype devices. In the final term (last 5 years), the feasibility of each demonstration device will be examined.

Described briefly below are the targets of R&D activities presently being advanced by the Electrotechnical Laboratory (ETL), Chemical Technology Research Laboratory (CTRL) and eight private corporations consigned with related R&D projects.

Elucidation of information processing in living organisms and its application

1. Simultaneous multiple-site optical recording of neuronal activities (electrotechnical laboratory)

The aims of this consignment are to elucidate the molecular mechanisms which govern the various information processing functions in neurons. For this purpose, technology called the simultaneous multi-site optical recording of neuronal activities is being employed.

2. Towards a model of visual information processing (NEC Corporation)

NEC's goal in this project is to elucidate the mechanism of biological visual information processing and to develop a model of it. Specifically, an overall model which links the primary visual cortex, integration process towards global information and feedback system is being developed.

3. A cerebellar neural network model for generation and learning of motor programs (Fujitsu Limited)

Fujitsu is aiming at developing a motion learning model based on a neurophysiological understanding of the cerebellum. Specifically, the development of a plane motion learning model which utilizes the understanding of the cerebellar network such as plasticity, feedback, microzone etc., and application of the model to the multiple joints robot are being examined.

Development of molecular organization devices

1. Molecular ordering in Langmuir-Blodgett films (Electrotechnical Laboratory)

In order to overcome the limitation of the conventional Langmuir-Blodgett (LB) method, this project is aimed at developing an expanded LB method which utilizes the diffusion/adsorption method.

The development of a method to fabricate a heterostructure in which a superlattice structure with transition metal complexes is formed and the improvement of the characterization systems of molecular ordering are also being attempted.

2. Development of materials for molecular organizates (National Chemical Laboratory for Industry)

The goals of this project are, first, to synthesize molecules with liquid crystalline properties and those of a host-guest complex, and second, to construct LB films with the above molecules. Optical characteristics of these LB films are under investigation.

3. A photosensitive device model using high-specific protein assembling units of antibody (Hitachi, Ltd.)

The fabrication of an optical information processing device which utilizes the living organism's excellent information processing functions is the goal of this project.

Specifically, construction and evaluation of the molecular organization with hybridized antibody and rhodopsin on organic thin film are emphasized. The feasibility of the optical information processing device with a rhodopsin-hybrid antibody-thin organic film complex will also be demonstrated.

4. High functional electronic device based on electron transport proteins for information processing (Mitsubishi Electric Corporation)

Mitsubishi is attempting to construct a molecular organization with electron transport proteins, to clarify the mechanism of electron transfer in it, and to fabricate the organic devices in a molecular dimension.

Specifically, the goals are to construct and evaluate an electron transferable molecular organization with cytochrome C and a functional LB film. Devices with diodes or switching characteristics and information processing devices with the molecular organization are expected to be developed in this project.

5. Development of visual information processing devices using photosensitive proteins (Sanyo Electric Co., Ltd.)

Sanyo is seeking to fabricate a visual information processing device with a light-sensitive protein.

Specifically, construction of an orientation controlled molecular organization film with light-to-proton conversion characteristics is being aimed at by using the pigment rhodopsin's purple membrane. Evaluation technology of the film is also to be developed.

The realization of a light-electricity conversion device using this film, and the realization of an electrically plastic device (which varies its electrical conductance depending upon the number of times an electric field is applied) using an electrochemically polymerized membrane, are being examined.

By combining these devices, realization of a visual information processing device in which noise reduction would be achieved by plasticity, is expected.

6. Development of an artificial neural device composed of functional organic molecules (Matsushita Research Institute Tokyo, Inc.)

Realization of a neuron-like element by functional organic molecules is being aimed at.

Specifically, the goal of this consignment is to construct a molecular organization which shows one-dimensional electrical conductance and its change by an external field which may be an electric field using a functional organic film such as phthalocyanine film. Evaluation technology for it is also to be developed. The device thus developed is expected to have a threshold operation of switching operation which we can see in a neuron's operation.

7. Development of sensor information processing device using organic film (Sharp Corporation)

Realization of a sensory information processing device which features molecular recognition and pattern recognition is being sought in this project.

Specifically, a gas molecule recognizing film which changes its light absorption spectrum on absorption/desorption of gas molecules, and photochromic film which changes its light absorption spectrum on irradiation of two light beams, is to be developed. Upon combining these films, realization of a sensory information device, in which gas absorption is sensed and recognized optically, is expected.

8. Research and development of optical information processor by molecular assembly technique (Mitsubishi Chemical Industries, Ltd.)

This consignment is attempting to fabricate an excellent photo-electro converting device by artificial control of the self-organization which is inherent in living organisms.

Specifically, the study will examine the design and synthesis of organic molecules which have excellent photo-electro conversion efficiencies and good self-organizing properties. From this research, an LB film featuring these characteristics will be developed. (Source: JETRO, April 1988)

Kenya

Control campaign in Kenya kicks off with $3 million

Kenya is now launching its five-year programme to control the spread of AIDS. The country's National Committee on AIDS presented the final blueprint of its five-year campaign at a meeting of donor agencies held in Nairobi last October. So far, donors have pledged a total of $US 2.94 million toward the first year of the campaign. The national committee says it will need an additional $US 11.32 million to keep the programme operating over the following four years.

Doctors in Kenya diagnosed the first case of full-blown AIDS there in 1983. Since then, the number of reported cases has climbed to 625, though the number of people infected with the human immunodeficiency virus is, of course, unknown. Cases of AIDS are equally distributed between the sexes, and about a third are not Kenyan citizens.

The national committee now estimates that between 1 and 2 per cent of blood donated in Kenya is infected with the virus. Yet Kenya has at present no adequate facilities to screen blood for HIV. The country's health budget is already stretched to its limit in the struggle to eradicate malaria, cholera, diarrhoea and malnutrition.

Now that funds are available, the national committee plans to spend nearly half of its first year's budget on HIV testing kits and on training laboratory technicians in screening techniques. At present, only eight laboratories in Kenya perform serological testing for antibodies to the virus. By mid-1988, the committee, in preparation for a nation-wide survey that will involve nearly 16,000 people, hopes to have testing facilities in most provincial hospitals run by the Government.

Health authorities also plan to step up their health education programme on AIDS for medical personnel.

Preparations are also under way to produce brief radio programmes to inform listeners about the ways in which they can protect themselves from becoming infected with HIV. Volunteers from the Kenyan Red Cross also began last February to distribute over a million leaflets on the prevention of AIDS, in English and Swahili, in Nairobi and Mombasa.

One of the educational programme's more ambitious and potentially controversial activities will be the production of a 30-minute film to explain the silent spread of AIDS.

Epidemiological data collected by the National Committee on AIDS show that 65 per cent of the people with AIDS in Kenya are in the western part of the country, 30 per cent are in and around Nairobi, and 5 per cent live in the Rift Valley and the eastern and coastal provinces. Epidemiological studies on the transmission of AIDS in Kenya have so far focused on high-risk groups in Nairobi.

Kenya, like many Western countries, now faces several political and social dilemmas as the AIDS epidemic takes hold. Some Kenyan doctors say they are unsure about whether they should inform patients with AIDS that they are infected with the virus. Meanwhile, the Kenyan Government has made AIDS a reportable disease. According to a recent report by the national committee, the Government will soon require doctors to send the names and addresses of patients with AIDS to the Ministry of Health. (Extracted from New Scientist, 7 January 1988)

Republic of Korea

Detention for carriers of HIV

The Republic of Korea has decided to imprison certain categories of people infected with the human immunodeficiency virus in an attempt to prevent further transmission of HIV. New laws which become effective early this year mean that prostitutes, homosexuals and intravenous drug users who are infected with HIV could soon find themselves locked up.

The Government has, however, rejected a proposal to introduce compulsory screening for all foreign visitors to the Republic.

The country has only 12 reported cases of infection with HIV, including one person with AIDS. Yet the Government is building a new unit to house people with AIDS and those infected with the virus, at a cost of 910 million won ($US 1.1 million).

In a recent screening programme, 80,000 people had tests for infection with HIV. Only 12 people had positive results, of whom eight were prostitutes who "predominantly served foreign servicemen and other foreigners", according to reports from the health ministry. Prostitutes already face mandatory testing for infection with HIV in the Republic. (Extracted from New Scientist, 4 February 1988)

Sweden

Genentech, Inc. licenses peptide hormone process from KabiGen AB

Genentech, Inc. and KabiGen AB announced that Genentech will license KabiGen's proprietary process, the EcoSec™ System, for the manufacture of Insulin-like Growth Factor-I (IGF-I) and other peptides now in development. The licence provides exclusive marketing rights in the USA and Canada for IGF-I produced by the KabiGen process. IGF-I is a human hormone that may be useful in the treatment of wounds and burns and postmenopausal osteoporosis.

IGF-I is a peptide hormone of 70 amino acids, similar in three-dimensional conformation to insulin, and which stimulates growth and metabolism. The majority of IGF-I is produced in the liver; small amounts are also produced in many tissues, where it has an autocrine or paracrine effect. IGF-I has been shown to stimulate the growth and differentiation in vitro of muscle, bone, nerve and blood cells: this indicates it may be useful in the repair of damaged tissues such as burns, skin ulcers, surgical wounds or bone fractures.

IGF-I is produced in a process developed by KabiGen, the EcoSec™ System; this is an E. coli expression system in which the product is secreted directly into the surrounding culture medium.

KabiGen is also using the EcoSec System to produce several other peptide hormones.

A further development and application of the EcoSec System is the manufacture of vaccine components. KabiGen has produced a number of different vaccine components for animal health companies.

The technology which is the basis for the EcoSec System has been jointly developed together with scientists at the Royal Institute of Technology in Stockholm.

The EcoSec System is an Escherichia coli expression/secretion system for the production of peptides in large amounts; applications include the production of biologically active peptides for pharmaceutical purposes, antibodies to peptides, and sub-unit vaccines. The initial product is a fusion protein, which is secreted directly into the medium.

The purified fusion protein may be used as a peptide immunogen or as a sub-unit vaccine. Or, the fusion protein may be cleaved, to release the desired peptide.

The KabiGen is currently developing and selling peptides produced with the EcoSec System for research purposes. Laboratory trials with potential sub-unit vaccines are also being carried out with several companies.

Other projects at KabiGen include proteins involved in blood coagulation and fibrinolysis. Factor VIII is used in the treatment of haemophilia, and KabiGen is developing a mammalian cell line for the production of Factor VIII under contract to KabiVitrum. (Source: Company News Release, 19 April 1988)

United Kingdom

LINK programme includes eukaryotic genetic engineering component

The first five LINK programmes were announced in February by Lord Young, Secretary of State for Trade and Industry and Kenneth Baker, Secretary of State for Education and Science. The Science and Engineering Research Council (SERC) is supporting four of these programmes jointly with the Department of Trade and Industry (DTI): (1) molecular electronics; (2) advanced semiconductor materials; (3) industrial measurement systems; and (4) eukaryotic genetic engineering.

Proposed LINK collaborations

	£ million	Years
Molecular electronics	20.0	5
Advanced semiconductor materials	24.0	5
Industrial measurement systems	22.0	6
Eukaryotic genetic engineering	4.7	4
Nanotechnology	12.0	4

The programmes listed in the table will involve universities, polytechnics and SERC establishments in collaborative research projects with industrial partners. Up to £83 million will be spent over six years. SERC's expenditure on these programmes is expected to rise to over £3 million a year. The fifth programme, on nanotechnology, is being supported by the DTI at this stage. Details from: Stuart Ward, LINK Co-ordinator, Science and Engineering Research Council, Polaris House, North Star Avenue, Swindon, Wiltshire SN2 1ET or on 0793 26222 ext 2257/2256. (Source: Biotechnology Bulletin, Vol. 7, No. 1, February 1988)

SERC interdisciplinary research centres

Three interdisciplinary research centres will be established by the Science and Engineering Research Council (SERC). They will focus on engineering design (Glasgow University), surface science (Liverpool) and molecular sciences (Oxford). The announcement is the culmination of a process in which SERC considered some 80 bids in seven strategic areas of science and engineering.

The Oxford Centre's programme is based around the study of proteins and their interactions with other molecules to control biological functions. Problems to be addressed are protein folding and specificity; blood clotting and fibronolysis; immunology; signal transduction; viruses; and enzymes of secondary metabolism. In view of the Medical Research Council's interest in the Centre, discussions about a joint funding mechanism are under way. Details from: Science and Engineering Research Council, Polaris House, North Star Avenue, Swindon, Wiltshire SN2 1ET or on 0793 26222 ext 2257/2256. (Source: Biotechnology Bulletin, Vol. 7, No. 2, March 1988)

New AFRC research consultative committee on protected crops

The biological control of crop pests and diseases is one of the priority areas for the Agricultural and Food Research Council's new independent short-term consultative committee. Other areas the committee will focus on include product quality, efficiency of production, energy saving and alternative crops. It will be trying to identify priority areas for government funding and business support, and expects to report to the Priorities Board by 31 July. (Source: Biotechnology Bulletin, Vol. 6, No. 12, January 1988)

Deliberate release: PROSAMO

If transgenic animals, novel biopesticides and genetically manipulated crop plants are ever to realize their commercial potential, they will have to be released into the environment. This fact is causing considerable concern among environmentalists, and it is also attracting considerable attention from regulatory agencies. This whole area will be covered by the new Genetic Manipulation Regulations, currently under revision by the Health and Safety Executive, and by the Directives being drafted by the Commission of the European Communities.

Two new initiatives will focus on the deliberate release of genetically engineered organisms: the Department of Trade and Industry's research programme on the Planned Release of Selected and Manipulated Organisms (PROSAMO) and a conference, to be held in April, the First International Conference on the Release of Genetically Engineered Micro-organisms (REGEM).

PROSAMO, which is being established by the DTI, aims to provide industry with "the tools and understanding needed to study ecological interactions and which can be used to assess the likely effects of introducing genetically manipulated organisms into the environment". Topics such as pollen dispersal, seed and tuber survival, the role of vectors in spore and virus dispersal, the spread of natural resistance (to herbicides and fungicides) and the survival and dispersal of deliberately introduced macro- and micro-organisms will be covered in a number of state-of-the-art reports.

At this stage, there have been no firm commitments from companies to support the programme, although the DTI's Biotechnology Unit says that there has been considerable interest. Meanwhile, university departments and research institutes have been invited to submit proposals in line with the recommendations of a number of working parties. It is hoped that the research programme will start in the second half of 1988. Details from: Keith Cowley, Biotechnology Unit, Laboratory of the Government Chemist, Cornwall House, Waterloo Road, London SE1 8XY or on 01-211 8854. (Source: Biotechnology Bulletin, Vol. 7, No. 1, February 1988)

Review of biotechnology

As a major review of Britain's biotechnology research begins, another report on manpower in the biotechnology industry highlights shortages in some fields, notably fermentation, protein chemistry and plant molecular biology.

The review of biotechnology has been commissioned by the Science and Engineering Research Council. Chaired by Professor Tom Blundell of Birkbeck College, half a dozen academics and industrialists will examine the achievements of SERC's biotechnology directorate and advise on SERC's future role.

The biotechnology directorate was created in 1981, and can take credit for establishing a nationally co-ordinated research programme, which makes use of industrial collaboration in the form of research "clubs" and, more recently, under the auspices of LINK. A programme on biotransformations was up for approval as a LINK programme and the directorate hopes to get a plant metabolism programme nestled safely under LINK's wing in the future.

The review body is likely to consider privatization as one of the options, though at least some in the directorate believe the science is too far away from commercialization. The group will report back to SERC by the end of the year.

Meanwhile, the Association for the Advancement of British Biotechnology has reported on surveys of employers and employees, intended to help assess manpower and training needs in the UK industry. It found about a fifth of companies experienced shortages at the graduate and PhD levels. In addition, companies also reported shortages in immunology, enzymology and chemical engineering.

In its survey of 10 companies with 290 staff, AABB unsurprisingly found employees highly qualified (91 per cent had one or more tertiary qualifications) and young (mean age, 32.4 years). And, as in other sectors of British industry, men outnumber women, especially at the higher levels.

The report also notes that biotechnology companies and their employees expect a "considerable increase" in demand for scientific updating, conversion training, induction training of new personnel and awareness training of non-scientific staff. However, constraints such as time (for managers) and money (for graduates) were cited by at least a third of staff questioned. (Extracted from Chemistry and Industry, 21 March 1988)

UK biosensor needs

A survey of the UK biotechnology industry has exposed several areas where improved biosensors could greatly aid fermentation processes. Specifically, the study recommends support for R&D into fermentor sampling and membrane technology.

For both chemical and biochemical monitoring, demand is great for on-line probes to replace the off-line analysis of samples - not least because sampling always carries a risk of contamination, says the survey. Satisfactory on-line probes should be protected against fouling during operation and be able to withstand steam sterilization.

Room also exists for improvement in current on-line electrodes for the detection of pH, oxygen, carbon dioxide, and specific ions. Of possible ion-selective electrodes, demand is greatest for robust ammonium and nitrate probes.

Since on-line biosensors will take time to develop, there is considerable need as well for the production of biosensors that can be used for rapid and local off-line analysis.

Several enabling technologies are in urgent need of support, the survey concludes. There is an immediate demand for more sturdy, reliable sampling systems - preferably automated - that guarantee sterility. Membrane technology is singled out as a priority because it may provide the solution to problems of sterility, fouling and sample purification.

Collaborative initiatives involving a consortium of institutions and a national technology transfer centre are seen as the best way forward. (Source: Biotechnology, Vol. 6, January 1988)

British research on human genome

A British attack on the human genome is to be launched by Dr. Sydney Brenner with the help of the Medical Research Council (MRC), the Imperial Cancer Research Fund (ICRF) and SmithKline Beckman Corporation, the pharmaceutical company. The company is to give $2.25 million to the School of Clinical Medicine of the University of Cambridge to which Brenner will move his MRC unit later this year for refurbishing and equipping laboratories at the School of Clinical Medicine and on supporting research over the next five years.

For Brenner, the move represents the beginning of the end of a long struggle to find backing for a serious attempt to apply his technique for mapping the genome of the nematode worm Caenorhabditis to the much larger human genome.

Molecular research into cardiovascular disease, virus infections and autoimmunity will receive priority. The company retains the option to patent and commercialize the outcome of its investment; royalties will accrue to the university.

Exactly how ICRF will contribute to Brenner's mapping efforts has yet to be worked out but is likely to take the form of a group of ICRF-supported scientists working alongside Brenner. There will be close links between the Cambridge scientists and the group of Drs. Hans Lehrach and Anna-Marie Frischauf at the ICRF laboratory in London, which has already begun work on human genome mapping.

The result should be a powerful and concerted programme of research on the human genome in Europe. Discussions on including other European partners, particularly in France, are under way. (Extracted from Nature, Vol. 331, 28 January 1988)

Molecular biology infiltrates schools

It may be too soon to start teaching translation from the genetic code alongside translation from French, but the study of biotechnology has already penetrated many secondary schools. The question asked at a November conference on Biotechnology in Schools, organized by GB Biotechnology Ltd. (Swansea, U.K.), was how best to incorporate biotechnology into the school curriculum.

British schools seem particularly fixed on introducing classroom biotechnology by means of the fermentor. Equipment ranges from converted pop bottles to simple computer-linked continuous fermentation systems.

Plant tissue culture is another favourite form of classroom biotechnology. School suppliers produce kits for experiments that begin with seeds and illustrate how plants can be cloned via callus or leaflets. Most work well but they tend to be expensive, inflexible and slow to produce results.

More advanced kits demonstrate the induction by Agrobacterium of tumours on plant seedlings and the emergence of doubly-resistant Escherichia coli from co-cultures of two strains, each of which is resistant to a single antibiotic.

While the plant and bacterial experiments are most appropriate for the biology courses, fermentation could enhance the study of chemistry as well. And a soon-to-be-available gel immunoprecipitation kit will be best suited to domestic science or home economics courses.

One unusual vehicle for disseminating such materials is the University of Surrey's Biotechnology Bus, which tours schools in southeast Britain with laboratory facilities for up to 12 teachers. The bus follows in the tire tracks of Cold Spring Harbor Laboratory's (Cold Spring Harbor, New York) mobile laboratory - the Vector Van. (Extracted from Bio/Technology, Vol. 6, January 1988)

Designer genes available

British Bio-technology (Oxford, England) expects its "designer gene" sales to nearly quadruple to $5.5 million by 1991, as compared to over $1.4 million in the fiscal year ending May 1988. It sells custom-made genes to pharmaceutical firms that lack the expertise, time or manpower to generate their own. It now has 19 genes in its catalogue. The custom genes will be used in the development of new drugs or enzymes to combat specific diseases. They are packaged in vials containing 10 millionths of a gram of DNA. British Bio-technology produces two new catalogue genes per month.

The firm represents a new stage in the maturation of the biotechnology industry, and does not yet have any direct competition. It sees itself as producing state-of-the-art research tools. Custom genes are synthesized, with the client specifying the length of molecule (up to 2,000 base pairs of nucleotides) and the precise nucleotide sequence. Its blend of biology, chemistry and computer science for total gene synthesis offers an alternative to the more traditional method of genetic engineering - taking natural DNA, slicing it up with specialized enzymes and rearranging the DNA segments. In total gene synthesis, nucleotides of DNA can be linked together in any workable sequence desired. Construction of designer genes involves design, synthesis, assembly, cloning and sequencing. (Extracted from New York Times, 16 March 1988)

Screen tests for next cyclosporin-A

Founded in 1986 by Dr. Louis Nisbet, Xenova Ltd. is looking for novel biopharmaceuticals in some

rather unusual places. In the wake of the October storm, for example, some of Xenova's scientists went hunting under uprooted trees for soil microbes which had lived undisturbed for decades, even centuries.

Although there are known to be more than 100,000 different species of micro-organism and more are discovered every year, barely 5 per cent have been exploited as sources of microbial metabolites for drug production. The 8,000 microbial metabolites developed to date have widely different chemical structures, from simple organic acids to complex lipo-glycopeptides. Previous money-spinners found through microbial screening include the beta-lactams and cyclosporin-A.

Anti-microbial screening programmes to determine the medical potential of these metabolites have opened up a new market in antibiotics worth over $8 billion a year, based on cephalosporins, thienamycins, tetracyclines, aminoglycosides and macrolides. Screening for pharmacological activities has already produced new immunosuppressives, cholesterol-lowering drugs and anthelminthics with a combined sales potential in excess of $1 billion a year.

Xenova's current discovery programmes are focusing on the following targets:

Interleukin-1 (IL-1) antagonist: IL-1 has a number of actions on human cells and is involved in growth and differentiation, inflammation, thrombus formation and tissue catabolism. Xenova has developed a screen which detects antagonists of IL-1 and is now applying this screen to its microbial collection for metabolites with potential in the treatment of rheumatoid arthritis, certain types of cancer and cardiovascular diseases.

Metalloproteinase inhibitors: Metalloproteinases are a family of enzymes that are involved in the destruction of cartilage in the human body. They are strongly associated with certain degenerative conditions such as rheumatoid arthritis. Xenova is looking for small molecules that inhibit the formation of such harmful enzymes. The market for arthritis drugs is valued at nearly $4 billion.

HIV (AIDS) projects: Much existing HIV research is focusing on vaccines or other large molecules which may inhibit the infectivity of the virus. Xenova is looking for small molecules that will interfere with normal virus infection and replication processes.

Cancer: Here the focus is on the control of growth factors, a family of large proteinaceous molecules thought to stimulate or control cell growth. Xenova is looking for alternatives to today's extremely toxic chemotherapeutics.

Agrochemicals: Xenova is aiming to produce a new generation of naturally derived pesticides for agro-chemical applications. The market for agrochemical insecticides, herbicides and fungicides is worth nearly $20 billion a year. Xenova is looking for new compounds which are more potent, more specific and less environmentally harmful than currently available pesticides.

Xenova hopes eventually to selectively screen 5,000-10,000 microbes a year. The company has already patented a radio-ligand assay and an immunoassay which are used in screening. Details from: Clive Crooks, managing director, Xenova Ltd., 345 Ipswich Road, Slough, Berkshire SL1 4EQ or on 0753 692229. (Source: Biotechnology Bulletin, Vol. 7, No. 2, March 1988)

Canadian grant to Oxford company

The Ontario Ministry of Colleges and Universities, through its University Research Incentive Fund, has awarded a grant of C$650,000 for work carried out on behalf of Oxford Virology Ltd. by Professor Yong Kang of the Department of Microbiology and Immunology at the Universtiy of Ottawa. The grant is being matched with a similar sum from Oxford Virology.

The research covers diagnostics and vaccines for Hantaviruses which cause haemorrhagic fever prevalent in certain areas of the world such as Scandinavia, the Mediterranean countries and the Far East. Using a protein from Hepatitis B virus this vaccine will be packaged into a chimeric vaccine where it is expected one inoculation will protect against the two diseases. Oxford Virology will have the option to manufacture any medical products that are developed and it is planned that this will be carried out in Canada. Details from: Oxford Virology Ltd., 10 Storey's Gate, London SW1P 3AY or on 01-222 9272). (Source: Biotechnology Bulletin, Vol. 7, No. 2, March 1988)

Agreement on manufacture of rennin

Celltech Limited of the UK has concluded an agreement with Pfizer, Inc. to license two Celltech patent families relating to chymosin (rennin) developed by recombinant techniques. The enzyme is used to clot milk for cheesemaking.

Pfizer plans to take the product derived from a genetically engineered organism through to market for use in cheesemaking, and says the US Food and Drug Administration has accepted for filing its petition for the product.

This is the first food additive involving a fermentation process using a genetically engineered micro-organism to have been accepted by the FDA.

Celltech's patent families, which include both granted patents and patent applications, cover key steps in the production process related to product purification and gene expression.

In return for granting the licence, Celltech receives undisclosed lump-sum payments and a royalty on sales of chymosin by Pfizer. (Extracted from Chemical Marketing Reporter, 8 February 1988)

United States of America

Biosafety committees

In planning for the anticipated enlarged volume of proposals to deliberately release genetically engineered organisms into the environment, officials at the Environmental Protection Agency (EPA) recently suggested decentralizing the process. Specifically, they recommended creating institutional-level "environmental biosafety committees" (EBCs), modelled on the National Institutes of Health (NIH) system of voluntary institutional biosafety committees (IBCs). During a meeting in January, an EPA advisory panel greeted the proposal with considerable criticism but eventually gave its endorsement to "the concept" of EBCs.

During the meeting, EPA's Biotechnology Science Advisory Committee (BSAC) discussed some serious apprehensions about the agency's proposal for establishing EBCs.

BSAC members - who are drawn from academic institutions, other government agencies, and public interest groups - urged EPA officials to carefully consider several concerns about EBCs. These include questions about the authority to be vested in EBC members; their relation to EPA; appeal, certification, and enforcement procedures; scientific guidelines for committees to follow; and potential unevenness between committees at different institutions.

In particular, BSAC members repeatedly raised the concern that, if an individual EBC were established strictly as an institutional committee, it would seem to embody a serious conflict of interest. (Extracted from Bio/Technology, Vol. 6, March 1988)

Another wrinkle in patchwork of US environmental release

Yet another layer of complexity will be added to the current regulatory patchwork governing the environmental release of recombinant organisms if plans at the US Environmental Protection Agency (EPA) come to fruition. The EPA's biotechnology science advisory committee voted to go forward with a scheme to institute a network of review committees - to be named "environmental biosafety committees" - for the purpose of approving field tests of genetically altered organisms. EPA is now in the process of extending its Toxic Substances Control Act to cover research and development work, and the environmental biosafety committees would oversee the application of this statute in biotechnology research settings.

EPA plans to model its environmental biosafety committees on the institutional biosafety committees, administered by the US National Institutes of Health (NIH) Recombinant Advisory Committee, that review all recombinant DNA experiments. There is wide agreement that the institutional biosafety committees have been a good way to control recombinant DNA experimentation without being unduly restrictive. As outlined, the EPA plan calls for setting up committees of five people - three scientists with expertise in areas of microbial or plant ecology and two representatives from the local community - at each university or company that would field-test recombinant organisms. The EPA's committees would differ from the NIH biosafety committees in that they would be backed up by regulatory statutes and infringers could be prosecuted.

The case-by-case review of proposed experiments by the environmental biosafety committees would also include the solicitation of public comment on the field test, and the committee would be responsible for addressing questions from the local community. The survey of attitudes toward biotechnology sponsored by Congress last year showed that the public had confidence in university scientists' assessment of environmental risks.

The environmental biosafety committee concept is likely to stir opposition from industry and university researchers, who are already confused by the federal maze of regulations governing biotechnology.

EPA is devoting increased staff time to working out the details of how the environmental biosafety committees would function, and the rules for establishing the committees is expected in the spring. (Source: Nature, Vol. 331, 14 January 1988)

Field test of modified bacterium

The Agricultural Research Service's (ARS) research centre in Beltsville is joining with Crop Genetics International (CGI) of Hanover, Maryland, in a field trial of a recombinant strain of the bacterium Clavibacter xyli. The modified organism contains the toxin-producing gene of another bacterium, Bacillus thuringiensis. CGI is expecting the new organisms will prove superior to chemical pesticides in controlling European corn borers, which are present in much of the nation's corn-growing areas.

ARS's 7,000-acre Beltsville research centre will host one of three 1.5-acre field tests that the company hopes to initiate this spring. A second will be conducted at the company's 200-acre farm in Ingleside, Maryland, and a third in France.

Bacillus thuringiensis contains a protein that kills insects that feed on plants inhabited by the bacterium. It has been sprayed on crops to control pests for decades. CGI hopes to demonstrate that the altered bacterium, which expresses the toxic B. thuringiensis protein, will work the same way. The C. xyli bacterium resides in the xylem, a part of the vascular system containing vessels that transmit water along the length of the corn plant. In CGI's experiment, test plants will be individually inoculated with the modified bacterium. The company's goal, however, is to develop a process for inserting the recombinant bacterium into corn seeds.

The agreement signed with CGI on 12 December calls for Beltsville research teams to study whether the altered C. xyli bacterium has an adverse effect on soil micro-organisms and to confirm that it remains within the corn plant and does not migrate to other plants. CGI also will allow ARS scientists to use its bacterium in other research. (Extracted from Science, Vol. 239, by Mark Crawford, p. 719, 12 February 1988. Copyright 1988 by the AAAS)

Biotechnology standards

The American Society for Testing and Materials' (ASTM) committee on biotechnology is close to bringing two new standards to final balloting - one a guide for the determination of purity, impurities, and contaminants in biological drug products; the second on the practices for preservation by freezing and freeze-drying, and for low-temperature maintenance of bacteria, fungi, protista, viruses, genetic elements, and animal and plant tissues.

Moreover, draft documents on identification of herpes simplex virus, standard for bacteriophage lambda, standard for cauliflower mosaic virus, standard for molecular weight cut-off evaluation of ultrafiltration membranes, and a guide for modelling exposure to genetically engineered micro-organisms are all in development. One of the biotechnology committee's newest undertakings, by the subcommittee on environmental issues, is to devise a decision matrix as a method of evaluating the impact of genetically modified organisms. (Source: Bio/Technology, Vol. 6, January 1988)

Bill on biotechnology submitted

A new bill (S-1967) was submitted late last year. Divided into three parts, the "Biotechnology Competitiveness Act of 1987" addresses regulation and funding of the US biotechnology effort, the proposed project to sequence the human genome, and programmes managed through the National Library of Medicine (NLM).

Perhaps the most intriguing new proposals in S-1967 are its provisions to create a free-standing National Biotechnology Policy Board. The board would

"review and appraise" overall US research efforts in biotechnology - in the federal sector as well as industry. Besides examining regulatory policies, the board also would advise the President on funding and other matters - such as personnel training, technology transfer, and tax incentives - that affect the industry's ability to compete internationally. The proposed board would include representatives from virtually every federal department overseeing biological research, from the academic and industrial sectors, and from private foundations as well as an expert in biomedical ethics.

By establishing a National Advisory Panel on the Human Genome, the bill absorbs and modifies several of the legislative recommendations made earlier. The new bill specifies that the advisory panel would be chaired jointly by the NIH director and the head of the Department of Energy (DOE).

Finally, S-1967 would establish a National Centre for Biotechnology Information within NLM. The bill authorizes annual appropriations of $10 million through fiscal year 1993 for co-ordinating the masses of biotechnology information now accumulating worldwide. (Extracted from Bio/Technology, Vol. 6, February 1988)

EPA approves biological nematicide for market

Ingene Biotechnology (Columbia, Md.) has received approval from the Environmental Protection Agency (EPA) to market a new biological nematicide for unrestricted use. The nematicide, known as ClandoSan, which is made from the shells of crabs and other shellfish, is a complex of residual protein and chitin, or poly-D-glucosamine, with chitin as the active ingredient. ClandoSan acts indirectly, stimulating naturally occurring soil micro-organisms to produce enzymes, like chitinase and urinase, that destroy nematodes and their eggs. In 1982, the latest year for which figures are available, nematodes accounted for more than $5.1 billion in US agricultural losses in fruits, nuts, melons, vegetables and other field crops. The nematode problem has worsened significantly in recent years, following state and federal bans on many synthetic chemical nematicides, including halogenated hydrocarbons, carbamates and organophosphates. The company expects to use about 20-30 million pounds of shellfish wastes annually to make ClandoSan. (Source: Chemical Week, 30 March 1988)

First step toward national strategy to combat AIDS

The first step toward an integrated national strategy for dealing with acquired immune deficiency syndrome (AIDS) was taken by the Presidential Commission on the Human Immunodeficiency Virus (HIV) Epidemic in February.

At a press conference in Washington, D.C., the commission chairman, Adm. James D. Watkins, released a 60-page document bearing his comprehensive recommendations for action in three areas: basic research and vaccine and new drug development; health care; and intravenous (IV) drug abuse treatment and prevention. The panel's first policy proposals call for broad new programmes costing some $2 billion a year over the next 10 years - split between federal and state or local governments. The proposals indicate the Commission is now well on its way, after an initial period of controversy and resignations.

The Commission started work last September. Its final report is not due at the White House until 24 June. However, the Commission believes it knows enough to issue an interim report with recommendations in the three areas.

The panel finds major changes needed in the entire US health care delivery system, not just for AIDS patients. Indeed, Watkins says, a health care system for AIDS could be a model for other health crises.

The report makes several proposals to enhance basic research and drug development. It suggests access by a broader spectrum of the infected population to clinical tests; greater information gathering and sharing on drug development and clinical trials (for example, standardized computer software for all trials); freeing government-sponsored basic research from bureaucratic restrictions; and promoting greater collaboration between firms, and between industry and government.

Crucial to expediting drug development, Watkins says, is to expand resources and personnel devoted to AIDS-related products at the Food and Drug Administration. Accelerating research budgets at the National Institutes of Health and in industry have doubled investigational new drug (IND) applications for HIV-related drugs every two years for the past four years.

He urges immediate doubling of FDA reviewers for HIV-related products and linking the number of reviewers to future IND increases.

To reduce the high level of false positive tests for AIDS antibodies, the report urges quick FDA approval of more accurate antibody tests. Effective antigen testing devices also should get rapid approval. And FDA should adopt an international standard for data in preclinical studies, permitting acceptance of high-quality data from abroad.

To enhance basic biomedical research in this area, the report recommends expansion of investigator-initiated grants; appropriation of new "add-on" funds rather than transfers from other programmes; and use of prestigious, visible awards to attract young talent. (Abstracted with permission from Chemical and Engineering News, 29 February 1988. Copyright 1988 American Chemical Society)

Biotechnology research consortium formed

A co-operative research and development consortium of seven companies has been formed to conduct biotechnology R&D. Called Biotechnology Research & Development Corp., the organization will be located in Peoria, Ill., and includes as members American Cyanamid, Amoco Technology Corp., Dow Chemical, Ecogen Inc., Hewlett-Packard Co., International Minerals & Chemical, and Agricultural Research & Development Corp. (ARDC). The consortium was organized by ARDC, which is a joint venture between Cilcorp Ventures Inc. and the Economic Development Council for the Peoria Area. The BRDC will use public and private funding and will work very closely with USDA's Northern Regional Research Centre in Peoria and the University of Illinois' biotechnology centre in Urbana to perform basic research and technology development in fermentation and associated biotechnologies. (Reprinted with permission from Chemical and Engineering News, 28 March 1988. Copyright 1988 American Chemical Society)

US microbiology market

The US micro-organism testing market has traditionally focused on time consuming methods, but

newly emerging techniques, including direct monoclonal antibody identification of organisms and the use of DNA probes for direct testing, have begun to allow for fast and accurate identification of certain species. However, these techniques need much more research and development before they become the mainstay of the microbiology laboratory. The trend is away from relatively cheap tests involving a high time input towards more expensive but faster tests.

At the moment, US sales at the manufacturer's level are estimated to have been worth over $430 million in 1987, with an annual average growth rate (AAGR) of 5.7 per cent forecast, in constant dollars, to 1992 - resulting in forecast sales of over $567 million that year.

According to "New Directions in Micro-organism Testing", Business Communications Co. (BCC), the microbiology market consists of products sold to clinical, food and dairy, industrial and research, veterinary and environmental testing laboratories for the identification and, in some instances, the antibiotic susceptibility testing of micro-organisms. Product lines mainly include media for growing organisms and related media and chemicals for identifying species and measuring antibiotic susceptibility of these organisms. The report predicts that:

- Media sales will remain fairly flat through 1992, with a projected 1.6 per cent AAGR, yielding of $173 million in 1992.

- Significant growth in testing using antibody reagents, which will grow from $90 million in 1987 to $139 million annually in 1992, an AAGR of 11.7 per cent.

- Gene probes will show "remarkable" growth, 42 per cent AAGR, rising from only $2.6 million in 1987 to $15 million in 1992.

- Faster antibody - and gene probe-based tests will produce a contraction of some 3 per cent a year in the rapid differential test market, mainly made up of kits for Enterobacteriaceae species. The decline will take the market from an estimated $60 million in sales in 1987 down to $39.5 million in 1992.

- Growth from antibody reagent and gene probe testing in the clinical food segments will be accompanied by dramatic growth in testing volumes in the veterinary market segment, with the introduction of DNA probe testing for the presence of feline leukaemia virus.

Details of the report (No. C-084), published in January 1988 and priced at $1,950.00 from: Business Communications Co., 25 Van Zant Street, Norwalk, CT 06855, USA or on + 1 (203) 853 4266.
(Source: Biotechnology Bulletin, Vol. 7, No. 1, February 1988)

Patent application backlog

A backlog of patent applications threatens the development of the US's biotechnology industry. Financiers, industrialists and academics told a congressional subcommittee on small businesses how the backlog discourages investment, the commercialization of products and research.

The problem arises because applications of biotechnology are flooding into the patent office and there are not enough trained staff to assess the complicated science of, in particular, processes for recombining genetic material.

Over the next decade, analysts in the US expect the domestic market for biotechnology products to be worth $13 billion annually. They predict an international market worth three times that amount.

Ron Wyden, the chairman of the subcommittee, said that the number of biotechnology patents that are pending increased from 3,900 in January 1985 to 7,300 in August 1987. "In a recent visit, subcommittee staff found nearly 50 supermarket style shopping carts overflowing with patent applications in the agency's mailroom. The cheques for the filing fee were still attached; some were weeks old."

Groups seeking patents for biotechnology products face a far longer wait than applicants in other areas of technology. In its request for funds for 1989, the patent office cited an average wait of 19 months for a decision on a patent application. In biotechnology, it can take 27 months to receive initial information, or first action from the patent examiner, and a further 25 months to award or deny a patent.

The first action suggests to industry and universities whether they have an original idea that will eventually earn a patent. One problem faced by the US's biotechnology industry is that this first action comes after the date by which they must file for patents overseas.

For small biotechnology companies the cost of filing for foreign patents is also critical.

Yet another difficulty for biotechnologists is that they may go ahead in good faith with a line of research which may be covered by a pending patent. (Source: New Scientist, 7 April 1988)

Biotechnology regarded as hope for the future

In the next 10 years, biotechnology and genetic engineering will have a greater economic impact on society than any other scientific or technical development, according to Monsanto Company, which has staked much of its future hopes on the success of the technology.

Citing a survey of national opinion leaders, the company says the poll also indicates that the appreciation of biotechnology among opinion leaders exceeds their knowledge and understanding of it.

The poll, conducted for Monsanto Company by the Wirthlin Group, surveyed 100 people who make or influence policy, including members of Congress and their staffs, executive branch officials, the media, academics and other influentials. Monsanto commissioned the poll in order to assess attitudes and perceptions toward biotechnology and its future impact.

When asked, unaided, which technology would have the greatest economic impact in the next decade, 28 per cent of the respondents named biotechnology, followed by superconductivity at 24 per cent and computer technology at 11 per cent.

When asked specifically what they would like to know more about, 26 per cent mentioned its economic effects. Another 21 per cent wanted more information in general on developments and the progress of research. (Source: Chemical Marketing Reporter, 18 April 1988)

Keeping track of released microbes

Scientists in South Carolina have shown for the first time in the US that it is possible to monitor

genetically engineered micro-organisms after release into the environment. In parallel experiments, researchers in Britain, led by David Bishop from the Institute of Virology in Oxford, have already succeeded in monitoring genetically altered organisms released outside the laboratory.

Last November, Ellis Kline and colleagues at Clemson University in South Carolina began field trials with a genetically engineered bacterium developed by researchers at Monsanto, a chemicals company in St. Louis.

The trials demonstrated the feasibility of monitoring genetically altered organisms released into the environment. The bacterium, a strain of the soil bacterium Pseudomonas fluorescens called PS373ZRNL11, was developed by David Dranos and his collegaues at Monsanto. Dranos and his team introduced into the bacterium two genes from Escherichia coli, a bacterium that normally lives in the human gut. These genes enabled the host Pseudomonas to grow on a substrate of lactose, which other fluorescent pseudomonads cannot live on.

Before beginning the trials, the bacterium went through a rigorous screening procedure to show that the organism would not harm the soil or any plants or animals.

This showed that the altered bacterium does no harm, but neither does it bring any benefits. It is designed solely as a model for monitoring altered organisms at large. Once the strain of Pseudomonas received approval from the EPA, Monsanto handed it over to Kline for the next part of the testing.

At Clemson University's Edisto Research and Education Centre near Blackville, South Carolina, Kline planted rows of wheat in furrows 20 centimetres apart. He inoculated some rows with the bacterium and left others free of the marker.

Around the test plot is a barrier of alternating bands of bare soil and strips of plants to contain the bacteria should they travel too far. Two fences keep out animals that might carry the bacteria away from the site, a short dense one to keep out rabbits and other small mammals and a high, wire fence to keep out deer.

When the wheat germinated, the bacteria quickly colonized the roots of the inoculated plants. Since then Kline and his team have been testing the plants, soil and water at and around the site. The early results look promising.

After 10 weeks, the bacteria show little sign of movement. They stay close to the roots of the inoculated plants, even when the wheat roots spread out into the next furrow.

The bacterium has not, so far, crossed onto the roots of adjacent un-inoculated plants. None of the strain has been found in puddles of water at the edge of the plot after heavy rain or in a pond about 300 metres from the test plot. Every four weeks, the researchers are analysing samples of the bacteria to look for any changes to their genetic make-up. So far, they have found no change.

After harvesting the wheat in March, Kline and his team will plant a crop of soybeans, followed by another crop of wheat, to find out if the engineered bacteria persist in the soil in the absence of their original host.

Dranos calls the test "extremely positive". It paves the way for the release of genetically engineered organisms that will bring benefits, such as bacteria that kill plant pathogens.

David Bishop in Oxford has already successfully tagged a baculovirus, which infects caterpillars. His next stage is to tinker still further with the genetics of the microbe so that it cannot survive for long periods in ultraviolet light from the sun. (Source: New Scientist, 18 February 1988)

Joint research collaboration on cancer therapy

PolyCell, Inc., a subsidiary of Quest BioTechnology, Inc. of Detroit (Michigan) has announced the signing of an agreement with Cetus Corporation of Emeryville, California on a collaborative research project to produce an immunological agent having activity against specific cancer cells.

Under the agreement, PolyCell will fuse Cetus' proprietary hybridoma cell lines that produce monoclonal antibodies specific to breast cancer with a hybridoma producing antibodies specific to certain "effector cells". The fusion will utilize PolyCell's patented Recombinant Monoclonal Antibody (RMA) process to produce a QUADROMA™ hybrid hybridoma. The inventor of the process will perform the fusion.

The QUADROMA hybrid hybridoma in turn secretes biofunctional monoclonal antibodies in which the two binding sites are specific to the two parental cell lines. In this case, the bifunctional monoclonal antibody will have the ability to identify and bind to breast cancer cells and to bind to a cytotoxic effector cell. Cetus will carry out studies to determine whether the resultant QUADROMA hybrid hybridoma will produce antibodies having binding specificity of both parental hybridoma cell lines. Such a bifunctional antibody, according to Cetus Scientist Dr. L.L. Houston, "has the potential to utilize a subject's own effector cells to specifically kill particular tumor cells."

Quest BioTechnology, Inc. acquires, develops and commercializes biotechnological and human health-care products and processes and acquires and operates entities that own such products or processes. (Source: Company News Release, 13 January 1988)

Technologies donated to the Michigan Biotechnology Institute by CPC International Inc. will create opportunities for new industrial development in Michigan

Patents and technologies donated to the Michigan Biotechnology Institute (MBI) by CPC International Inc., for the production of chemicals from carbohydrates, will create opportunities for new industrial development in Michigan. Completion of development of these technologies, within the next five years by MBI, will result in products to be used in the formation of a new biotechnology business in Michigan.

Combining Michigan's strengths in agriculture and industrial manufacturing, this new business will use the technologies to manufacture industrial products from surplus crops such as corn, providing up to 2,000 jobs over the next decade.

The donation was made at the end of 1987 as a result of restructuring by CPC International of Englewood Cliffs, New Jersey, a major international corn and food processing company

The donated technologies, independently valued at $15.3 million, include 10 US and 33 foreign patents, and over 100 pending US and foreign patent applications. Essentially, these technologies offer alternative means of producing certain chemicals that are currently produced from petroleum.

Receipt of the donation places MBI approximately six years ahead of its schedule to help diversify the economy of Michigan through the creation of a new biotechnology industry in the state.

The completed technologies will be used by the for-profit sector as a key component in developing a new corn utilization industry in Michigan. This prospective industry would manufacture corn products for cereals and other food uses as well as non-food products, such as speciality and bulk chemicals. These chemicals can be used in the manufacture of products such as road deicers, solvents, composite plastics, polyesters, nylon and food ingredients. (Source: Company News Release, 1 February 1988)

Union of Soviet Socialist Republics

Interphasal cell destruction inhibitor

The USSR has developed an unspecified technique to inhibit interphasal cell destruction following exposure to nuclear radiation. Interphasal cell destruction is caused by chromatin disintegration, which in turn is caused by protein decomposition following exposure. Damage to DNA occurring immediately after radiation generally heals: when lesions appear two to six hours after exposure it does not. (Extracted from The Times, 18 January 1988)

Zaire

Transfusions and malaria

Researchers in Zaire have shown that many children testing positive for the human immunodeficiency virus in Kinshasa probably became infected after receiving contaminated blood transfusions to treat the anaemia that malaria often causes.

Scientists from Zaire, Belgium and the US examined the link between malaria and HIV infection after previous studies in Zaire and Venezuela had suggested an association between the two diseases. The researchers studied transfusion practices at Mama Yemo Hospital in Kinshasa in 1986. They found that children with malaria often suffered from anaemia and had blood transfusions. Malaria is the most common reason for blood transfusions to children in Mama Yemo Hospital.

Many African hospitals do not routinely screen blood destined for transfusions. At Mama Yemo, the rate of infection with the human immunodeficiency virus among those giving blood was 6.3 per cent.

They conclude that the development and distribution of rapid, accurate and inexpensive tests to screen donated blood for antibodies to HIV are "urgently needed to arrest this mechanism of HIV transmission". (Source: New Scientist, 6 February 1988)

Zambia

Mining companies face increasing burden

In many countries, the economic impact of AIDS will depend on which group of workers the human immunodeficiency virus has hit most severely. In Zambia, the health of those who work in the copper mines in the north of the country is of paramount importance.

B. Nkowane, of the University Teaching Hospital in Lusaka, said that the spread of HIV has significant implications for the mining industry and its associated employers. In Zambia, as in many central African countries, the virus is spreading among the general population.

Nkowane posed the question: how long can an industry afford to continue investing in people who are infected with HIV? Issues which still need further discussion in Zambia, he said, include the implementation of screening before employment and the rights of existing employees who refuse to be tested.

The economy of Zambia is highly dependent on copper: income from this industry accounts for 20 per cent of Zambia's gross national product. Out of the country's labour force of 56,000, 6 per cent work in the mines. (Extracted from New Scientist, 17 March 1988)

C. RESEARCH

Research on human genes

Genes switch on early in human embryos

A human pre-embryo first "expresses" its genes when it is between the four- and eight-cell stages of development, according to new research by Peter Braude, Virginia Bolton and Stephen Moore at the Embryo and Gamete Research Group at the University of Cambridge. The discovery could lead to an improved success rate for *in vitro* fertilization. The researchers say that it could enable biologists to develop ways of screening pre-embryos for some inherited diseases, before a pregnancy is established *in vitro*.

Braude and his colleagues found that pre-embryos began to produce a new pattern of proteins from the four-cell stage onwards, between 24 and 48 hours after fertilization. A pre-embryo starts out as a single cell after fertilization, and reaches this stage after two cycles of cell division.

Before a pre-embryo activates its genes, it produces proteins from genetic information laid down in the egg by the mother, in the form of messenger RNA, the intermediary between genes and proteins. Braude and his colleagues have found that if a pre-embryo does not successfully switch on its genes at the four-cell stage, its development is blocked. The researchers suspect that pre-embryos cultured *in vitro* are particularly sensitive at this time.

The researchers at Cambridge say that their findings have "important consequences for the development of certain techniques for preimplantation diagnosis of genetic disorders". If researchers try to diagnose a disease by looking for proteins produced from the defective gene, they must ensure that they are looking at proteins produced from the genes of the pre-embryo, rather than from the messenger RNA passed down in the egg. So this kind of test would have to be carried out on pre-embryos that had progressed at least to the eight-cell stage. (Source: New Scientist, 7 April 1988)

Gene makeup a surprise

A recent study shows that two blood proteins with very different functions have surprisingly similar

gene sequences and structures. New data indicate that apolipoprotein(a), a plasma protein that may be a culprit in atherosclerosis and heart disease, bears a remarkable similarity to plasminogen, a precursor of the enzyme that dissolves blood clots. The genetic and physical similarity between two proteins, previously thought to be unrelated, is completely unexpected. Richard Lawn, John McLean, James Tomlinson, Dan Eaton, and their colleagues of Genentech in South San Francisco, and Angelo Scanu and Gunther Fless of the University of Chicago report the complimentary DNA sequence of apolipoprotein(a) and its protein organization.

The new results show that the internal structure of apo(a) contains an unusual series of repeated protein units or domains. They are particularly striking because of their number - 37 in all for apo(a) in contrast to five such units for plasminogen. The gene structure that codes for this redundant arrangement in the apo(a) protein is also highly repetitive.

The repeated domains of both apo(a) and plasminogen proteins are called kringles because their twisted three-dimensional shapes look like a kind of Danish pastry. "Kringles contain binding sites for the molecule and orient it properly," says Lawn. For example, the kringles of plasminogen allow it to bind to fibrin, the protein that actually forms blood clots. This permits a separate region of the plasminogen protein to be activated by plasminogen activator to form the enzyme plasmin. Plasmin is the enzyme that dissolves the clot.

The kringles of apo(a) are different, not only because there are many more of them, but also because they contain a large number of sugar residues. Although no one knows the function of the apo(a) protein, researchers believe that it somehow invites trouble.

Researchers used to think that only certain people had lipoprotein(a) in their blood but now they recognize that everyone has at least some of it. However, no one is certain whether the amount of the lipoprotein(a) or the type of apo(a) that it contains presents the greater risk. People inherit a certain form of apo(a) and cannot eliminate their risk solely on the basis of diet. This characteristic distinguishes lipoprotein(a) from other low-density lipoproteins, such as the B-100-containing lipoproteins that are affected by diet. Like lipoprotein(a), they also carry cholesterol around in the blood but are not thought to be dangerous unless they occur at very high levels.

The new findings should make it possible to devise methods for measuring the amount and type of apolipoprotein(a) and lipoprotein(a) in the blood, and how apo(a) and lipoprotein(a) lead to atherosclerotic plaque formation. (Extracted from Science, Vol. 238, 11 December 1987, by D.M. Barnes, p. 1513. Copyright 1987 by the AAAS.)

X-ray holography helps to probe the human cell

Biologists have long wanted to obtain a three-dimensional view of what happens inside a living cell - how a disease attacks a cell, for example. With currently available technology such intense scrutiny is not possible, but X-ray holography may provide the answer.

Two recent experiments in California and New York indicate that X-ray holography - a technology that was first suggested in a theoretical paper by A.V. Baez in 1952 - may one day provide the dynamic view of cells that molecular biologists are after.

Unlike conventional holograms, X-ray holograms should reveal what is happening below an object's surface. Soft X-rays, when generated at a wavelength between 23 and 44 angstroms, interact with matter in a spectral region called the "water window". The region provides a high contrast between protein and water - an ideal characteristic for making a hologram.

Physicists at Lawrence Livermore National Laboratory near San Francisco used Nova, the world's most powerful laser, to make the first X-ray laser hologram. And at the National Synchrotron Light Source at Brookhaven, New York, scientists from UCSF, Lawrence Berkeley Laboratory (LBL), IBM, and the State University of New York at Stony Brook, have produced a hologram of unprecedented resolution. The hologram - with a resolution of 400 angstroms - was 25 times smaller than what had been achieved before by the same group.

At Brookhaven, the group led by Malcolm Howells from LBL made a hologram of zymogen granules from rat pancreatic cells. They used a beam of soft X-rays with a 25 angstrom wavelength to create a coherent beam with laser-like properties. When the beam hit the sample, it scattered, causing spherical waves to hit the detector, or "resist". The waves mixed with the beam's unscattered waves to form interference fringes on the resist which acts much like a photographic plate.

Howell's group stored the hologram as numerical data in a computer. To reconstruct the hologram on the computer, the resist was developed in a solvent to create a system of exposed and unexposed areas. The result looks like a relief map. An alloy of 60 per cent palladium and 40 per cent was sprayed on the resist to increase the contrast, so that it could be photographed using a transmission electron microscope. A microdensitometer converted the image into a form that could be read by the computer.

The hologram still only appears in two dimensions because the depth of focus is about the same as the thickness of the sample. They expect to obtain a three-dimensional image soon by reducing the resolution to 100 angstroms or lower.

Another problem is that the holegram has an exposure time of 80 minutes, but this will be reduced when brighter light sources are used, first at Brookhaven and later in a new Advanced Light Source planned for LBL. Cell division and secretion of hormones, enzymes and neurotransmitters could be readily studied over time periods of one minute or less.

The experiment conducted by James Trebes and his colleagues at Livermore was much faster: the exposure of the hologram on film took less than a nanosecond because the source was so bright. However, the soft X-rays that were used were at a wavelength of 200 angstroms, which was too long to penetrate the samples - in this case carbon wire and a gold bar. In the next few weeks an X-ray beam of 43 angstroms will be available and the group will be able to penetrate the water window.

The Nova laser was designed for research into fusion power. To create the hologram, the laser was fired into selenium foil to form an electrically-charged plasma that emitted coherent X-rays. A multi layered mirror separated the X-rays from other beams made in the lasing process. The X-ray beam was focused by the mirrors and

reflected on to the sample. Again, the scattered light mixed with the light that missed the object to form an interference pattern. But resolution was no better than a few microns. A visible light laser was used to reconstruct the hologram.

Some scientists have said that X-ray holography will be able to capture the invasion of a virus into a living cell, or the division of DNA in a cell, but watching DNA would require a resolution of about 10 angstroms, which is far less than will be achieved in the foreseeable future. (Source: New Scientist, 4 February 1988)

Peptide turn-on for the ACh receptor gene

Before an animal can move, its muscles must be stimulated appropriately. In order for this to occur, there must be a sufficient number of acetylcholine (ACh) receptors on muscle cells to receive chemical messages from motor nerves. Until recently, neuroscientists knew that electrical activity in muscle cells turns the ACh receptor gene off; and they also knew that high concentrations of cyclic adenosine monophosphate (cAMP) inside the cell turns it on. They questioned whether some positive signal increases acetylcholine receptor synthesis in muscle cells; and whether electrical activity or something else triggers the production of cAMP.

Jean-Pierre Changeux of the Pasteur Institute in Paris and Thomas Hökfelt of the Karolinkska Institute in Stockholm investigated whether calcitonin gene-related peptide (CGRP), which Hökfelt had observed in the cell bodies of motor neurons, might somehow control gene expression for the acetylcholine receptor. Their new data indicate that it does. CGRP turns on the gene for the α subunit of the acetylcholine receptor and also increases intracellular cAMP concentrations.

CGRP is a 37-amino acid peptide that occurs in several parts of the nervous system, unlike its genomic neighbour - the calcium-balancing hormone calcitonin. Changeux, Hökfelt and their colleagues recently identified CGRP as a positive signal for acetylcholine receptor synthesis.

Acetylcholine is the primary neurotransmitter released from the endings of motor neurons. It causes electrical activity in skeletal muscle cells and stimulates them to contract. In order to have this effect, however, acetylcholine must first bind to the two α subunits of its receptor. In 1985, Changeux and his co-workers reported that electrical activity itself turns off the gene for the synthesis of the α subunit. But muscle cells contract spontaneously, at least as they are developing in tissue culture. It was clear, therefore, that something else overrides the electrical block to acetylcholine receptor synthesis.

In his presentation at the neuroscience meeting, Changeux reported that others have shown that CGRP is released from nerve terminals along with acetylcholine. "There are at least two signals for acetylcholine receptor gene expression coming from the motor neuron. CGRP increases acetylcholine receptor synthesis, and acetylcholine causes electrical activity and decreases synthesis".

Simply identifying the signals that turn genes on and off is only the first step, however. In the case of the gene for the acetylcholine receptor, CGRP and electrical activity must somehow be translated into messages inside the cell, which then have a specific effect on gene expression. Changeux points out that chemical second messengers fulfil this role, and that they might be different for the on and off regulation of the acetylcholine receptor gene.

"The positive signal, CGRP, simulates the production of cyclic AMP in muscle cells," he says. "It may be one of several regulating factors that have this effect. But the negative signal, electrical activity, acts through a different second messenger pathway. It seems to stimulate the production of diacylglycerol and inositol trisphosphate and raises the intracellular calcium concentration. But we still do not know whether it is through this pathway that the acetylcholine receptor gene is turned off."

Changeux does not yet know when during development CGRP exerts its effect on the muscle cell gene genome. To date, he has focused primarily on signals that regulate the gene for the α subunit of the acetylcholine receptor. Now, he and his collaborators are beginning to study what controls the activity of the genes that code for the other subunits - β, γ, and δ. (Source: Science, Vol. 238, 18 December 1987, by D.S. Barnes, p. 1652. Copyright 1987 by the AAAS)

Human lymphotoxin gene cloned

Scientists at Kyowa Hakko Kogyo Co. (Tokyo) have cloned the structural gene for human lymphotoxin and mass-produced the protein in E. coli at levels of up to 5 per cent of the total bacterial protein. Purification steps yielded highly stable human lymphotoxin that was 57-90 per cent pure. Lymphotoxin, a 157-amino-acid protein naturally produced by lymphocytes, kills some cancer cells without damaging normal cells. The structural gene for human lymphotoxin was first cloned by scientists at Genentech (South San Francisco, CA); Kyowa Hakko researchers used the published DNA and protein sequences to re-isolate the gene in-house. Although all the versions of the human lymphotoxin gene cloned by Kyowa contain short deletions at the beginning of the structural gene, the researchers found these recombinant proteins to have higher cancer cell-killing activities than native lymphotoxin. (Source: Bio/Technology, Vol. 6, February 1988)

Lipocortin gene sequenced

Shionogi & Co. (Osaka) scientists have determined the DNA sequence of the structural gene for lipocortin, a protein that could prove useful for controlling tissue inflammation and may play a role in tumour metastasis. Lipocortin inhibits the enzyme phospholipase A-2, which catalyzes the first step in the synthesis of prostaglandins and other compounds that promote inflammation. Biogen (Cambridge, MA) had first cloned the cDNA encoding human lipocortin, but Shionogi opted to isolate the rat gene in order to facilitate animal experiments. (Source: Bio/Technology, Vol. 6, April 1988)

Second protein involved in Alzheimer's

Scientists have taken a step closer to understanding what goes wrong in the brains of people with Alzheimer's disease. Two groups in the US and one in Japan have discovered a protein that may be at least partly responsible for the abnormal deposits that are the characteristic features of the disease.

Deposits of amyloid form the core of areas of decaying nerve terminals called senile plaques. Last year, scientists discovered that the main protein component of the amyloid, A4, was probably part of a larger protein whose gene they had identified.

It seemed likely that this gene or its product might have some role to play in causing the disease, so scientists around the world set out to discover what the larger protein (for the time being named the amyloid protein precursor, or APP) normally does.

Groups led by P. Ponte in California, Rudolph Tanzi in Boston and Nobuya Kitaguchi in Japan have discovered a second form of the precursor which could have a clear biological role.

The new form of APP is identical to the previous one, except that it contains an extra sequence. When the researchers compared this extra sequence to those of other known proteins, they found it was very similar to a family of enzyme inhibitors. These molecules prevent enzymes such as trypsin from breaking down other proteins.

The two forms of APP turned out to have different distributions in the body. The version including the enzyme inhibitor turns up in most of the tissues, while the shorter version seems to be more common in the brain than elsewhere. Tanzi's group linked the shorter version specifically to the association areas of the brain; these are also the areas that show the largest numbers of plaques in Alzheimer's disease. The group also found that in the brain of one Alzheimer's patient, there was less of the protein lacking the enzyme inhibitor than normal.

The significance of these findings is not yet certain. The protein has to be isolated and studied in more detail, but there is a clear possibility that the plaques that form in Alzheimer's disease may be caused by an alteration in the balance of the two forms of APP. They both appear to be derived from the same gene, the different forms being produced by alternative splicing. The aim will be to discover the factors which determine which of the two forms the protein will take. (Source: New Scientist, 10 March 1988)

Alzheimer's protein is also in infant brains

A protein previously thought to exist only in the brains of Alzheimer's disease patients or people with Down syndrome, also occurs in normal infants. Peter Davies, Benjamin Wolozin, and Angela Scicutella of the Albert Einstein School of Medicine in New York reported new data showing that protein A68 is present in the brains of foetuses at 34 weeks of gestation or older and in infants until two years of age. The finding itself is surprising, and it adds a dimension to controversies about A68.

Two years ago, Davies and his colleagues reported that an antibody known as Alz 50 stains protein A68 in post-mortem brain tissue from Alzheimer's and Down syndrome patients but does not stain the brains of normal aged people. Last year, the New York group showed that A68 is also present in the spinal fluid of Alzheimer's patients, which Davies hopes will lead to a diagnostic test for early Alzheimer's.

"The new idea is that the A68 protein is expressed early in development and then later in a neurodegenerative disease," says Davies. There are differences between the two cases, however. First "a five-month-old baby has A68 staining, but only a small fraction of cells in the baby's brain are positive. Probably a thousand times more cells stain positive for A68 in the brain of an Alzheimer's patient".

A second contrast is that A68 staining occurs in different brain regions of infants as compared to Alzheimer's patients. "In Alzheimer's, layers three and five of the cortex have A68," says Wolozin. "In the infant cortex, the protein occurs deeper - in layers five and six - and also in the white matter. So it is not a match."

Questions about A68 and the Alz 50 monoclonal antibody that labels it persist. For example, Dennis Selkoe of Harvard Medical School thinks that Alz 50 recognizes an altered form of the tau proteins, which are associated with the so-called paired helical filaments contained in Alzheimer's tangles. "It would be wrong to say that Alz 50 is just another monoclonal antibody against tau," says Selkoe. "It is a very special antibody to tau that recognizes a form of the protein that is especially prevalent in brain tissue from Alzheimer's patients." He also acknowledges that Alz 50 may recognize a protein that is not tau but that has a conformation similar to that of the tau protein.

Davies and his colleagues have yet to determine the exact nature of the A68 protein recognized by Alz 50, but they do not believe that A68 is a tau protein. Last year the New York group thought that A68 might be kinase, an enzyme that adds phosphate groups to other proteins. The finding was inconsistent, however, because they could not detect kinase activity in every preparation of A68.

In his presentation at the recent neuroscience meeting, Davies said that his group now has new antibodies against the A68 protein that are more specific than Alz 50. But, like Alz 50, they also stain numerous amyloid plaques and neurofibrillary tangles in brain tissue from Alzheimer's patients. Large numbers of these structural abnormalities characterize Alzheimer's, and the fact that both stain for A68 raises several questions.

For instance, do the same nerve cells produce both plaques and tangles? Is A68 a marker for cells that are preprogrammed to develop the abnormal structures and die - in a developing brain or in a degenerating one? And how does A68 fit into the growing repertoire of information about abnormal genes for β amyloid proteins in Alzheimer's?

"These are all questions that we would like to know the answer to," says Davies. "We are hoping to get some of the answers when we sequence A68." (Source: Science, Vol. 238, 18 December 1987, p. 1652, by D.S. Barnes. Copyright 1987 by the AAAS)

Proteins contribute to radiation cell damage

Researchers at Leicester University have found that proteins surrounding DNA inside a cell's nucleus help to break it down when the cell is irradiated. This conclusion could upset a cherished belief, held by most biologists, that damage to proteins by gamma radiation is less important than damage to DNA.

When molecules are irradiated by gamma rays they invariably break down to form highly reactive fragments of organic molecules. These fragments are known as free radicals. Martin Symons and his colleagues have found out, for the first time, where these free radicals are most likely to be formed in proteins and in DNA.

When gamma rays strike a protein or DNA, they excite an electron out of a chemical bond. The chemical bond becomes unstable and the molecule ultimately breaks down.

The unstable chemical bond contains only one unpaired electron, and so has an overall magnetic moment. An electron spin resonance (ESR) spectrometer detects unpaired electrons and the spectrometer will detect them long before the unstable chemical bond has a chance to break down. Symons used an ESR spectrometer to study the breakdown of protein and DNA when they are irradiated with gamma rays. He found that gamma rays excite electrons mainly from the amide backbone that links the protein together.

Symons and others also studied the effects of gamma rays on DNA outside a cell. They found that electrons tended to be lost from guanine, and gained by thymine to give $G^{+\cdot}$ and $T^{-\cdot}$ free radicals in roughly equal amounts. Chemists believe that DNA starts to break in places where these free radicals form.

In the nucleus of a cell, DNA is not isolated. It is surrounded by proteins called histone complexes. Symons again used an ESR spectrometer to look at the effect of radiation on DNA in a cell.

He saw that $G^{+\cdot}$ and $T^{-\cdot}$ centres were once again formed, but this time there were many more $T^{-\cdot}$ radicals. This could have happened, he reasoned, only if excited electrons were hopping from the histone proteins onto the DNA's thymine bases. (Source: New Scientist, 4 February 1988)

Protein reveals damage from radiation

Scientists in California have invented a revolutionary technique for measuring the effects of radiation on the human body. The researchers hope that the technique will help them to assess the radiation dose that a person has received. It might also identify those people who are genetically prone to cancer.

Survivors of Hiroshima and Nagasaki have a higher incidence of cancer, such as leukaemia, than the general population. Their cells also exhibit more chromosome aberrations than average. The increases appear to be due to the doses of radiation received at the time of the nuclear explosions in 1945. A direct assessment of the biological effects of radiation, though, was difficult, until now.

Scientists from the Lawrence Livermore National Laboratory in California are refining a method to determine how much biological damage a person has suffered as a result of exposure to radiation. The technique is so sensitive that the degree of biological damage caused by radiation could provide a measure of the radiation dose received.

The technique exploits the fact that human red blood cells (erythrocytes) have two versions of a protein, called glycophorin A, sitting in the membrane of the cells. One version of glycophorin - GPA(M) - differs very slightly in its structure from the second version, known as GPA(N).

Different genes code for the two proteins. Genetic damage to one gene in a parent cell, or "stem" cell, which divides to produce many genetically identical "daughter" cells, means that the daughter cells possess only one kind of protein in their membrane.

Radiation damages the gene responsible for GPA(M), so stem cells that receive a dose of radiation will divide to produce daughter cells that lack the GPA(M) protein in their cell membranes, and so only have GPA(N).

The researchers from Lawrence Livermore have devised a technique for labelling and counting cells that possess GPA(M) and GPA(N) protein. They use monoclonal antibodies, which recognize and bind to specific types of protein. One monoclonal antibody binds only to GPA(M), the other binds only to GPA(N).

The researchers from Lawrence Livermore have tried the technique on three groups of people. The first group was healthy and had no known exposure to radiation. The second group consisted of people suffering from cancer, who were about to undergo radiation treatment or chemotherapy with drugs that cause mutations. The third group were cancer patients who had undergone radiation treatment or chemotherapy.

The technique distinguished the group exposed to radiation and chemical mutagens from the two other groups. The results showed that there were slight differences between the cancer patients who had yet to undergo therapy and healthy people, indicating that the technique might identify people who are prone to cancer. The researchers are now investigating whether the technique can be applied to predict cancer in different people.

The scientists from Lawrence Livermore have tried the technique on blood taken from survivors of Hiroshima and Chernobyl. In both instances, the researchers say, the technique can accurately gauge how much radiation these individuals received.

A remarkable finding, according to the researchers, is that the radiation damage to red blood cells has lasted, in the case of Hiroshima survivors, for over 40 years. With the analysis of chromosome aberrations, the body seems to be able to repair the changes over time, and so it is more difficult to measure radiation damage after such long periods. (Source: New Scientist, 14 January 1988)

Possible 21st amino acid used in proteins

The amino acid selenocysteine may be incorporated into proteins by living cells, according to researchers at the University of Munich. Conventional wisdom holds that only 20 amino acids are used in proteins, but this selenium analogue of cysteine may be the 21st. The transfer RNA that transports the selenocysteine is significantly different than that used for the other 20 amino acids. (Abstracted with permission from Chemical and Engineering News. Copyright (1988) American Chemical Society.)

Bone marrow transplants used in Krabbe's disease

Bone marrow transplants may be effective in treating the galactosylceramidase enzyme deficiency known as Krabbe's disease, according to researchers in the US, the Netherlands and Japan. A strain of mouse that lacks the enzyme can be used as a model to study bone marrow transplants. The donor cells can even cross the blood-brain barrier to supply tissue most affected by the lack of enzyme. Without the enzyme, toxic fat accumulates in nerve tissue, causing deterioration and death by the age of two years in humans. Mice that lack the enzyme die in about five weeks. But if transplants are performed at the ninth to twelfth day, the enzyme levels are restored and myelin around the nerves are at least partly restored. Twitcher mice given transplants live four to five times longer than untreated mice. (Extracted from Science News, 5 March 1988)

Structure determined for oncogene protein

The structure of the protein that is produced by the oncogene ras has been determined by a team of US and Japanese researchers. The first oncogene protein to have its structure determined, it is also by far the most common one found in human cancer cells. Sung-Hou Kim of the University of California, Berkeley; Susumu Nishimura of the National Cancer Research Institute in Tokyo; Eiko Ohtsuka of Hokkaido University in Sapporo; and their colleagues find the protein - called p21 - has a structure very much as had been anticipated based on knowledge of its biological activity. The protein is a guanosine-nucleotide-binding protein (G-protein), and other researchers have suggested that its role in

transforming normal cells into cancerous ones involves loss of the normal protein's ability to split off the third phosphate of guanosine triphosphate (GTP). The crystal structure reveals that all the single mutations that can change a normal ras gene into an activated oncogene result in amino acid changes in one of three loops of the protein. Two of these loops are in contact with guanosine diphosphate when it is bound to the protein; the third loop is adjacent to one of these first two loops. Thus, it is plausible that changes in amino acids in these portions of the protein would interfere with GTP hydrolysis. (Reprinted with permission from Chemical and Engineering News, 29 February 1988. Copyright (1988) American Chemical Society.)

Chemical messengers

Research on leukotrienes, a family of messenger molecules, still goes on and some of it looks promising. In a year or so, drugs based on leukotrienes might offer a new treatment for asthma.

Leukotrienes are molecules released by leukocytes (a type of white blood cell) when they are fighting damage or disease in the body. They are distress signals of various kinds.

Some researchers believe that such a distress signal sounded in the lung is responsible for asthma attacks. Leukotrienes fighting damage in the lungs tell the muscle cells encircling the lung's airways to contract. This partly seals off the lungs, cutting down the flow of noxious air. In an asthmatic attack the same sort of thing happens unnecessarily because the lung's defence system is too sensitive: it objects to things like pollen and household dust.

A drug could be designed to have a blocking effect. It would work by mimicking the part of the leukotrienes which identifies them as bona fide messengers, but not carrying any message. So a cell would accept the drug but not do anything about it. Leukotriene-receptors on the cell's surface would fill up with meaningless messages; when a real leukotriene arrived it would have nowhere to go.

When Dr. Bengt Samuelsson at the Karolinska Institute in Stockholm discovered the structure of a leukotriene in 1979 many people thought the wonder-drugs for asthma (and for other leukotriene-based diseases, like the skin disease psoriasis) were just around the corner.

The optimists had not bargained with the leukotriene family's complexity. Though the leukotrienes all share a common ancestor - the fatty molecules that make up a cell's outer layer - they are a diverse bunch. There are five of them, A4, B4, C4, D4 and E4. Not all have the same effects on the body.

Although such a large family offers drug-makers plenty of targets to aim at, which is good, it may be that more than one has to be hit to have any effect, which is bad. Worse still, the body defends itself with a constellation of chemical messengers: other substances - histamines, for example - may be potent enough to trigger an asthmatic attack on their own. If so, leukotriene-based drugs might be useless.

New drugs have been developed by a number of drug companies, including ICI, SmithKline Beckman and Merck. They all block the effects of leukotriene D4 - a junior, yet potent, member of the family. The drugs work in animals given asthma artificially, and the various companies are engaged in clinical studies.

If asthma can be prevented by drugs which block leukotriene D4, then several inflammatory diseases, such as kidney infections, gout and rheumatoid arthritis, might be prevented by drugs that block leukotriene B4, the black sheep of the family. If the drugs based on D4 work, then drug companies will put their weight behind B4 research. (Source: The Economist, 2 April 1988)

The complex role of the skin

Scientists are finding that human skin, far from being just a waterproof wrapper, is a surprisingly complex organ that produces or remodels hormones, enzymes and other substances that may have vital effects throughout the body.

Some functions of skin cells appear to supplement the liver, the body's main chemical processing plant. The skin, the body's largest organ, also appears to act closely with the immune defences.

The picture of the skin's functions has been changing rapidly in recent years with the help of better techniques for growing cells in the laboratory and better tests for detecting and analysing a cell's chemical products.

The latest findings, some reported by scientists at a meeting in New York City last week, may help explain why it is so difficult to save some people who have suffered serious burns. It may also explain why some drugs act differently in the rodents in tests than in humans, and perhaps even why Homo sapiens got along so well in the early years of the species without the fur that covers all other mammals.

In a severe burn, for example, some of the skin's biochemical functions may be lost, creating problems that go beyond the loss of the skin as a barrier to the outside world. Moreover, human skin differs biochemically from that of mice and rats.

As to the evolutionary question, human skin has potent chemical and immunological as well as physical defences; these may have given early humans a powerful defence against infections and other invasions through the skin even in the absence of fur.

Research with important implications was reported by several scientific teams at the New York City conference.

Dr. Yann Barrandon's group at the Harvard Medical School reported that they had successfully transplanted a gene for human growth hormone into laboratory cultures of skin cells and found that the genetically engineered tissue produced and secreted the hormone. The findings suggested that the use of skin cells might be a worthwhile strategy for attempts at gene therapy, but left questions as to how well the hormone would be delivered to other parts of the body.

Dr. Lorne B. Taichman of the State University of New York reported that skin cells growing in the laboratory produce apolipoprotein E, a substance made primarily by the liver that has an important role in the body's use and breakdown of cholesterol. The skin makes only about one fiftieth as much of the substance as the liver does, and the role of the skin's production is unknown. (Extracted from International Herald Tribune, 25 February 1988)

Breast milk may stimulate immunity

Scientists have long recognized that breast milk contains maternal antibodies that help newborn mammals, including human babies, to fight infection. Now researchers are finding evidence that one or more proteins in breast milk may also stimulate babies' own immune systems. The as-yet-unidentified protein or

proteins speed the maturation of cultured B lymphocytes and prime them for production of antibodies, says Michael F. Julius of McGill University in Montreal.

Maternally acquired antibodies are very useful to the newborn, whose immune system is not fully developed, Julius said in an interview.

Julius first noticed that sheep colostrum - the milk produced immediately after the birth of a lamb - enhances the growth and differentiation of cultured white blood cells. Since then, he says, he has seen similar activity in human milk. (Extracted from Science News, Vol. 133, 26 March 1988)

Sex-determining gene of human embryo identified

An international team of scientists has discovered a single gene that determines the sex of a human embryo. The presence of the gene in the chromosomes of the fertilized egg will stimulate the foetus to develop testes and grow to be a male, the scientists believe. The gene may act as a biological switch, turning other genes on or off in a complex series of events.

Through the use of new gene-probe techniques, the scientists discovered that women carry a gene almost identical to the male-forming one. The study details how researchers found that abnormal men with two X chromosomes have a small piece of the Y chromosome. Moreover, the same piece is missing in an abnormal woman who has 99.8 per cent of a Y chromosome, suggesting that this piece is what determines maleness. Scientists also found an almost identical male-determining gene on the X chromosome, contrary to popular belief that males come exclusively from the Y chromosome.

Discovery of testes determining factor (TDF) by D.C. Page of Whitehead Institute of Biomedical Research at MIT, principal author of the report, and colleagues at the University of British Columbia and the University of Helsinki could lead to the identification of other genes involved in the sexual differentiation process. TDF appears to be situated on a small specific part of the Y chromosome. A large portion of TDF has been cloned for further study of its properties. (Extracted from New York Times and Wall Street Journal, 23 December 1987)

Simple sugars are key to complex fertilization

It is common knowledge the fertilization in higher animals results from a fusing of egg and sperm. But only recently have scientists begun to describe the molecular mechanisms that govern the binding and interaction between these two unique cell types.

The study, led by Paul M. Wassarman of the Roche Institute of Molecular Biology in Nutley, N.J., focused on the insoluble outer coat, or zona pellucida, of the mammalian egg. Previous research had shown that the zona contains three varieties of glycoproteins (protein chains with carbohydrate branches), called ZP1, ZP2 and ZP3, and that ZP3 contains the specific receptor to which a sperm must bind to induce fertilization. But little was known about which part of the ZP3 molecule is critical to this binding, and even less was known about the "hardening" of the zona that follows within moments of fertilization.

Working with mouse eggs, which are very similar to human eggs, Wassarman focused on the so-called O-linked oligosaccharides, complex sugar chains that grow like branches off ZP3's protein "trunk". He induced minor changes in the branches to see which part of the oligosaccharide molecule actually binds to sperm. He reports that the six-carbon sugar alpha galactose appears to be the critical link to sperm recognition. Moreover, he found, if the No. 6 carbon on alpha galactose is oxidized to its aldehyde form, C-h=O, it fails to recognize sperm. In its reduced form, CH_2-OH, the molecular complex binds to sperm, triggering a cascade of reactions that leads to the dissolving of cell membranes and the fusing of genetic material from the sperm and egg. Further research may lead to development, better contraception and fertilization techniques. (Extracted from Science News, Vol. 133, No. 9, 27 February 1988)

Mass-produced chimeric monoclonal antibodies

Scientists at the Biological Engineering Laboratory of Teijin Ltd. (Osaka, Japan) have mass-produced chimeric antibodies that contain murine light- and heavy-chain antigen binding domains linked to human light- and heavy-chain constant regions. Since these chimerics consist largely of human sequences, they should interact with the immune system in a fairly normal way and not elicit the harmful immune response caused by some mouse monoclonals used in therapy. Completely human monoclonal antibodies would be ideal to prevent immune responses in patients but are difficult to produce directly. Teijin makes its chimerics via hybridomas grown on a large scale in a novel, two-cylinder culture system that allows continuous production and simplified purification. (Source: Bio/Technology, Vol. 6, March 1988)

BSF-2 increases vaccine effects

Ajinomoto (Tokyo), one of the world's leaders in lymphokine research, has demonstrated in mouse experiments that B-cell stimulating factor-2 (BSF-2) significantly increases the effectiveness of vaccines. Injecting this lymphokine along with vaccines doubled the amount of antibody initially produced and increased by 11-fold the amount of antibody produced following a second exposure to the antigen. The Ajinomoto scientists, working in collaboration with Tadamitsu Kishimoto's research group at the Protein Engineering Centre of Osaka University, found that BSF-2 strengthens the immune response primarily by enhancing the proliferation of B lymphocytes. (Source: Bio/Technology, Vol. 6, March 1988)

Key protein absent in muscular dystrophy

Molecular biologists have found the biochemical defect responsible for Duchenne muscular dystrophy. The discovery of a protein that is missing from the muscles of victims may lead to better diagnosis, characterization, and eventually treatment of the disease. Currently there is no treatment.

The key protein was isolated from normal human muscle tissue by a research team led by Louis M. Kunkel, at Howard Hughes Medical Institute's Children's Hospital in Boston. The protein, which the researchers named dystrophin, is completely absent from humans with Duchenne muscular dystrophy.

Kunkel and his co-workers from Harvard Medical School and the University of Iowa also located the site in normal muscle cells where dystrophin is found. The same group previously reported that the gene that codes for dystrophin is located on the X-chromosome.

Dystrophin is a very large molecule (400,000 molecular weight) but it makes up only about 0.002 per cent of total muscle protein. In normal individuals,

dystrophin is found at triadic junctions, structures in muscle tissue where two membranes come together and information is passed from a nerve impulse to contractile muscle cells, according to Kunkel.

Mice that have a genetic defect like Duchenne muscular dystrophy also are missing dystrophin from their muscle tissue. Kunkel points out, however, that such mice have much less muscle wasting and live normal lifespans. Discovering why the disease is so different in mice than in humans is one important research goal, Kunkel says. (Abstracted with permission from Chemical and Engineering News, 4 January 1988. Copyright (1988) American Chemical Society.)

Peptide to lower blood pressure synthesized

Scientists at Asahi Breweries (Tokyo) have synthesized a peptide that, at very low concentrations, lowers high blood pressure caused by defects in the renin-angiotensin-aldosterone (RAA) system. RAA disorders represent the most frequent cause of high blood pressure. The peptide works by inhibiting angiotensin-converting enzyme (ACE), a liver protease that cleaves the decapeptide angiotensin-1 to form angiotensin-2. It is the accumulation of angiotensin-2 in the serum that causes blood vessels to contract, resulting in an increase in blood pressure. Although Squibb Corp. (Princeton, NJ) and Merck (Rahway, NJ) already market synthetic inhibitors of ACE, Asahi's peptide may prove more potent. If so, it could be administered at lower doses, thereby decreasing the risk of unwanted side-effects. Asahi is upgrading its testing of the peptide and will increase production from the several hundred milligrams-scale to the tens of grams-scale. (Source: Bio/Technology, Vol. 6, February 1988)

Phosphate probe marks cancer-causing chemicals

Scientists in California claim to have detected for the first time genetic damage caused by the action of a single, artificial pollutant in the air. They used a new technique to sample blood, devised by a chemist at Baylor University in Texas. The work may help to pinpoint the link between exposure to a chemical and the subsequent onset of cancer.

Stephen Rappaport, from the School of Public Health at the University of California at Berkeley, said that the technique may replace the expensive and complicated epidemiological studies that are now needed to suggest that a given chemical has caused cancer. To date, it has been difficult to pinpoint the cause of the genetic damage observed in a patient.

Rappaport said that for the first time, his team had measured the precise chemical interaction between molecules of DNA in the blood and compounds in the blood resulting from exposure to a foreign chemical. The chemical involved is styrene, a component of glass fibre. It reacts in the body to form styrene oxide.

Styrene is a "possible" carcinogen, according to a classification last year by the World Health Organization. Styrene oxide binds with DNA. This is a necessary condition for causing cancer.

Scientists at Berkeley and at UC San Francisco collected blood samples from 50 people in California who worked in industrial plants making boats and bathroom fixtures. They also took air samples from the immediate working environment. Styrene is used in the manufacture of glass fibre products. It is also used widely in the automobile industry and in the manufacture of computer consoles.

The research team used a new analytical method called ^{32}P-post labelling, devised by Kurt Randerath, a chemist at Baylor, to study the effects of styrene on DNA.

With a radioactive phosphate, the researchers can trace extremely small molecular interactions involving genetic material. If a chemical - in this case styrene oxide - binds with the DNA, it will form a product called an "adduct". The technique has been used before to detect damage from cigarette smoking, but because so many carcinogens are involved, researchers have been unable to identify the carcinogen that actually damages the tissue.

Su Fen Liu, a visiting scientist from the Institute of Environmental Chemistry in Beijing, China, managed to isolate the adducts produced by the interaction of the styrene oxide with the DNA. So far, a third of the samples have damaged DNA.

If styrene does not cause cancer, the research may determine why. The researchers will also study exposure of workers to other substances. (Source: New Scientist, 31 March 1988)

Rats and humans join forces to fight cancer

The treatment of cancer and other conditions, such as the rejection of tissue transplants, is about to undergo a revolution. Medical researchers in the UK have developed a technique for manipulating the genes of humans and rodents to create a super-antibody that can attack and destroy unwanted cells, such as cancer cells.

The researchers, from the Medical Research Council's Laboratory of Molecular Biology and the University of Cambridge's Department of Pathology, attach pieces of antibody protein derived from a rat to a human antibody. The result is a hybrid antibody that combines the power of a rodent antibody to destroy unwanted cells, with the ability of a human antibody to avoid rejection by the body.

The technique, which allows the researchers to perform the tricky task of combining antibodies from two species, is so important that the Medical Research Council has taken the unprecedented step of making sure that no single company has sole rights to the process. The Council has therefore retained the patent itself instead of giving it to an industrial partner - the first time in recent history that the Council has kept one of its own patents.

The industrial liaison officer of the Laboratory of Molecular Biology, Gordon Koch, said that the process is potentially too important to human health for any one company to have a monopoly. The Council has already signed licencing agreements with five companies to develop applications for the technique. These are: Celltech, Wellcome, Scotgen, Unilever and Behring of the Federal Republic of Germany.

The technique is the result of work by Greg Winter and Lutz Riechmann from the Council's laboratory, and Michael Clark and Herman Waldmann of the University of Cambridge.

The researchers isolated antibodies from rats that had been injected with human white blood cells. Some of the rat antibodies were active against a particular human protein, or antigen, called CAMPATH-1 (short for Cambridge Pathology-1). CAMPATH-1 is an antigen that appears on some mature white blood cells, but not on younger cells from which they were derived, called stem cells.

Certain parts of the rat antibody, called hypervariable regions, are active in binding to the antigen. The researchers therefore isolated these hypervariable regions and synthesized the sequence of DNA that would produce or "code" for them.

They then joined this to another synthetic strand of DNA that this time coded for a human antibody known as IgG. The result is DNA that codes for the "tail" of the human antibody and the tips of the "arms" of the rat antibody.

When this DNA is inserted into a cell and coded into protein, the end result is a hybrid antibody with hypervariable regions derived from rat, but with the main part of the antibody derived from human protein. Cells that make such antibodies can be fused with cancer cells to create hybridomas which manufacture one type of antibody - called a monoclonal antibody.

The importance of creating hybrid antibodies against CAMPATH-1 is that such antibodies will identify and destroy all mature white blood cells bearing this particular antigen.

The new type of antibody, therefore, can be used to destroy cancer cells in patients suffering from leukaemia. The researchers plan clinical trials with leukaemia patients later this year.

The technique marks a breakthrough in medical treatment with monoclonal antibodies because until now, such antibodies derived solely from rodents can only be injected once into humans because the body mounts an immune response against the foreign protein. (Source: New Scientist, 31 March 1988)

Peptides may regulate tumour growth

A section of natural opioid peptides may regulate neuroendocrine tumour growth, according to researchers at the Universities of Chicago and Stanford. A 4-peptide sequence (Tyr-Gly-Gly-Phe) can be recognized by monoclonal antibody 3-E7. Normal cells in endocrine glands probably also make the opioids. The new monoclonal might be used to determine the origin of cancer cells spread throughout the body. The opioid peptides may suppress the production of antibodies and interfere with natural killer cells. (Extracted from New Scientist, 4 February 1988)

A porphyrin used against tumours

A chemical similar to porphyrin can destroy tumours under the skin, according to D. Dolphin of the University of British Columbia in Canada. People who suffer from porphyrias suffer from exposure to sunlight and may suffer from hirsutism, conditions that may have led to legends of werewolves. Injections of the porphyrin heme can treat porphyrias. Porphyrins exposed to light produce singlet oxygen, which destroys cells around it. Haemotoporphyrin derivative that locally accumulates in cancerous tissue can thus be used to destroy that tissue when exposed to light. The new compound is a porphyrin that absorbs infrared, which can penetrate the skin far deeper than normal light, and so could be used to treat tumours deeper under the skin than is possible with existing haematoporphyrin derivative. (Extracted from New Scientist, 2 April 1988)

An anticancer agent in fruit and nuts

A basket of fruits and nuts may be both a gracious hospitality gift and a tasty cancer preventive, say scientists from the Medical College of Ohio in Toledo. A substance called ellagic acid - found in fruits like strawberries and in Brazil nuts - scavenges carcinogenic chemicals and prevents normal cells from becoming cancerous, says Gary D. Stoner. He and his co-workers are studying its effects on carcinogenesis caused by different chemicals.

Among the cancer-causing agents included in the study were polycyclic aromatic hydrocarbons (PAHs) found in tobacco smoke and auto exhaust, nitrosamines found in tobacco smoke and foods, and aflatoxins found in certain foods such as stored nuts. Assays using cultures of mouse and human lung tissue showed that ellagic acid reduced DNA damaged caused by PAHs, for example, by 45 to 70 per cent. Ellagic acid, which is a member of the phenol chemical group, also inhibits the formation of PAH-induced lung cancer in mice. The researchers observed similar inhibition against aflatoxins and nitrosamines tested in the same system.

Stoner says the group is considering large epidemiologic studies in China, where people living in certain valleys have high rates of cancer that some researchers think are related to the nitrosamine-containing chemicals used to pickle food.

Although the researchers have yet to define the exact mechanism of cancer inhibition, they suspect that the ellagic acid competes for DNA receptors that are also used by the carcinogens. Because purified ellagic acid has difficulty crossing intestinal walls, the group is tinkering with its structure to improve its absorption into the body. The substance, which apparently is bound to glucose in nature, may be more easily absorbed in its natural state. (Source: Science News, Vol. 133, 2 April 1988)

Pharmacists discover mechanism of depression

Research at the University of London's School of Pharmacy suggests that the lithium treatment commonly used on manic depressives works by interfering with the metabolism of inositol phosphate (IP) by brain cells.

Alan Drummond of the School of Pharmacy has put forward an explanation which involves the metabolism of inositol phosphate (IP). There are several IPs, of which the most important is 1,4,5-IP_3. This is now recognized as an important secondary messenger molecule, used to transmit signals within cells. It is generated from an inositol phospholipid in the cell's membrane.

Scientists have known for many years that lithium disturbs the metabolism of inositol phosphate but not why it should affect only brain cells. Drummond explains that lithium in the brain can cut back the supply of 1,4,5-IP_3 by stopping the supply of inositol. If the level of 1,4,5-IP_3 is reduced calm is restored. This effect is limited to brain cells because brain cells can recycle their internal inositol, unlike other cells which get their supply from the blood.

Using pituitary tumour cells labelled with tritium and high performance liquid chromatography, Drummond and Philip Hughes have shown that as many as 10 different IPs may be present in cells.

They identified some IPs, especially those with fewer phosphate groups that are produced as the 1,4,5-IP_3 is recycled back to inositol. Depending on how much phosphate is lost, the first step could lead to 1,4-IP_2, 1,5-IP_2 or 4,5-IP_2. Loss of the number 5 phosphate occurs most readily; this is demonstrated by the abundance of 1,4-IP_2. Surprisingly, its concentration is raised during lithium treatment, which suggests that lithium blocks further dephosphorylation.

The 1,5-IP_2 isomer has not been identified; 4,5-IP_2 has been, though only about 2 per cent of 1,4,5,-IP_3 exits by this route. Drummond believes that the step which lithium blocks is the loss of the last phosphate from I-IP_1. Lithium treatment cannot prevent the inositol from being activated. What it can do is to prevent more being made.

Further research has shown that lithium ions may inhibit production of guanine-nucleotide-binding proteins in the brain, accounting for lithium's effectiveness against mania and depression, according to researchers at Ben Gurion University of the Negev (Beer Sheva). The G-proteins are critical in mediating cellular response to outside stimulants. Lithium ions inhibit one G-protein that stimulates many types of cell response, while inhibiting two other proteins that inhibit the responses stimulated by the first G-protein. This may explain how lithium can treat both mania and depression. (Source: New Scientist, 11 February 1988 and Chemical and Engineering News, 8 February 1988)

Cartilage transplants bring hope to arthritics

Patients suffering from severe arthritis have until now been offered one long-term solution - replacing joints with artificial ones. But the high cost of the prostheses, problems with gradual decay of the glues that hold them to healthy bone, and the loosening of mechanical bonds, have together spurred research into the possibility of transplanting cartilage to repair the damaged surfaces of the joint.

Unlike skin, flesh and bones, cartilage does not regenerate if damaged, which is why arthritis is essentially irreversible. Research has been aimed at transplanting cartilage cells from donors into the damaged areas, but no successful techniques have yet been brought to the stage where they can be tried out on humans.

Recent research at Tel Aviv University looks as though it may be applicable to human patients within five years. The research team, headed by Zvi Nevo, has taken embryonic cartilage cells from 10-day unhatched chicks and, after culturing them and suspending them in a suitable medium, packed them into wounds in the ankle joints of chickens. Two months after surgery, there was almost no difference between the repaired joints and undamaged ones.

Similar research is being carried out in the Federal Republic of Germany and the United States, but Nevo's group has gone further by culturing the cartilage cells successfully and then making them not only stay in place, but also bond completely with the surrounding bone and its cartilage cover.

The key to the work, the results of which have been published in Clinical Orthopaedics, has been taking the cartilage from young embryos. At this stage a greater proportion of bone tissue is still cartilage, and the cells are still able to reproduce. The number of cells typically grew 20 to 30 times. Reducing the oxygen in the atmosphere from 18 per cent to 8 per cent, or adding antioxidants such as vitamins C and E, boosted the growth rate.

The second success was that after the material was packed into the holes in the joints, the cartilage cells carried on growing until they completely bonded with the surrounding tissue, while the fibrinogen-based medium was absorbed by the body. The implants did not produce any scar tissue (fibroblasts) that could immobilise the joint with adhesions, but developed the same smooth surface as the original cartilage.

The implanted cartilage cells are relatively insensitive to normal immunity rejection mechanisms, thanks partly to a mucopolysaccharide envelope. It is not yet clear how well they would stand up to the extreme autoimmunity that causes the breakdown of bone and joint tissue in arthritis sufferers. In principle, says Nevo, the new cartilage will not only be more resistant to attack but will also secrete more of the antioxidants that can inhibit attack on the surrounding tissues.

Tests on older (two-year-old) hens should come closer to imitating the reactions of older arthritis sufferers. The trials are now progressing from chickens and rabbits to monkeys and pigs, which are physiologically closer to humans. Cartilage cells from aborted human embryos (10 to 18 weeks) have also been successfully cultured, but clinical trials are not expected for perhaps five years. (Source: New Scientist, 28 January 1988)

Some research into aging

Most scientists now believe the maximum lifespan is about 120 years - no matter what we do. "The aging process is built in, we have obsolescence," says Robin Holliday, head of genetics at Britain's National Institute for Medical Research.

But just finding ways to stave off the infirmities of age is a tall order. The long downhill slide of life begins to accelerate at about the age of 30. It involves hundreds of thousands of minute changes in the body's cells. Many of them may be either triggered by genes or caused by errors in the genetic coding that controls functioning of the cells and membranes that form the brain, skin, bones, and other organs. Lifestyle, too, plays a role.

Many of those changes are visible - wrinkling skin, graying hair, and sagging muscles. But much is not - like the millions of brain cells that die and the immune system's weakened ability to stave off disease. Nor do the changes occur at the same rate in each person.

So far, the search for clues has generated no fewer than 11 theories of aging, replete with dead ends, inconclusive evidence - and controversy. For now, the hottest clues point to the genes, the internal machinery of cells, the body's system of chemical messengers, and the immune system.

Some of the most compelling leads are coming from a colony of aged laboratory rats being studied by Edward J. Masoro, a physiologist at the University of Texas at San Antonio. These rodent Methuselahs are alert, active, and healthy, with the shiny white coats of adolescent rats. By cutting the caloric - but not the nutritional - intake of the rats to 60 per cent of what they would normally eat, Masoro has extended their average lifespan by 50 per cent, compared with rats on a normal diet.

He and others working on so-called diet restriction, first explored in the 1930s, believe the changes in diet somehow retard many of the physiological changes that occur with age. Masoro hopes to find out just what makes the rats live longer - and, consequently, what makes normal rats get old - by carefully measuring changes in key hormones, disease, and metabolism.

Already, researchers have a pretty good idea of some of the processes likely to be involved. Not the least is the body's disease-fighting immune system. Scientists have already observed that the thymus, the master gland that controls the production of white

blood cells, is one of the first organs in the body to reach old age. It shrinks away until it is almost invisible by age 50. So the body's ability to recognize foreign invaders deteriorates, and it becomes more likely to develop diseases caused by the malfunctions in the immune system itself, such as rheumatoid arthritis.

Help may be on the way from the camp of cancer research, however. Biotechnology made it possible to isolate substances produced in the body that control the immune system and to produce them in large quantities. Most testing of immune boosters, such as interleukin-2, so far has been on cancer patients and people whose immune systems are being destroyed by AIDS. But some researchers, including Dr. Jordan U. Gutterman, a leading oncologist at the University of Texas, think small doses of these substances may be just what the doctor ordered for the aged.

One biotechnology company, Alpha 1 Biomedicals Inc. in Washington, is already testing the idea. It is giving a combination of immune system boosters and flu vaccine to elderly patients. Because their immune systems are weak, only 25 per cent of the elderly who are given vaccine alone build an immunity. But when it is combined with thymosin, a thymus hormone, the number jumps to 65 per cent.

Studies of other glands are also turning up intriguing leads. A fall-off of the production of pituitary growth hormone contributes to the loss of muscle tissue and skin wrinkling. DHEA, a steroid pumped out by the adrenal gland, also declines with age. But in rodents, DHEA injections can inhibit various cancers and delay the onset of diabetes. This approach could lead to preventive treatments for the elderly.

What about memory? Scientists have discovered that glucocorticoids, stress hormones produced by the adrenal gland, can touch off what Caleb E. Finch, professor of the neurobiology of aging at USC, describes as "a vicious cycle of stress-induced aging" that can hasten memory impairment.

Recently, Robert M. Sapolsky, a neuroscientist at Stanford University, found out why. He exposed rats to high levels of chemicals that mimic these stress hormones and found that the neurons in their brains shriveled or died faster than normal. Under stress - and during aging - the hormones build up and block the neurons' ability to absorb nutrients.

Avoiding stress can help, but drugs may also intervene in the process. Beta blockers, for example, which are used to treat hypertension, work by blocking the cellular receptors that respond to adrenal hormones. Scientists recently identified a group of chemicals, dubbed nerve-growth factors, that revitalize damaged neurons and trigger new nerve connections that compensate for damaged cells. Give the factors to rats and they can recall maze patterns they had forgotten.

Hormones are not the only natural substances that can wreak havoc in the body. Look at free radicals. These molecules are created as the cells perform their daily work, and they contain a highly reactive form of oxygen. Studies show that free radicals can damage blood vessels and the heart. They are also implicated in cancer, arthritis, and glaucoma.

The body has its own defences against these renegade oxygen atoms. Some 15 anti-oxidants such as vitamin E, beta-carotene, sodium oxide dismutase (SOD), and glutathione course through the cells. Popping anti-oxidants is a popular anti-aging remedy, even though evidence that they work is sparse. But studies in rodents do show that beta-carotene can help prevent lung cancer, and the National Cancer Institute is conducting a study to see if it can prevent cancer in humans. Meanwhile, DDI Pharmaceuticals Inc. and others are testing SOD as a way to prevent tissue damage after heart attacks and strokes.

What scientists would really like to know, however, is why those organs and other cells in the body deteriorate at an apparently programmed rate. Even skin cells, when removed from the body, will divide about 50 times and then simply stop and die. The University of Pennsylvania's Christofalo and James R. Smith, professor of cellular genetics at Baylor College of Medicine, have found evidence of proteins that turn cell division on and off.

All the indications point to genetics. Each species lives out its existence to a different limit suggesting that genes are the master agents of lifespan. Now, with the tools to identify and clone genes and even insert them in mice to see how they behave, it will be possible to identify the genes for longevity in mammals, including humans, says Thomas E. Johnson, professor of molecular genetics at the University of California at Irvine.

That may take a decade or more. Scientists do not expect to find just one gene that "turns on" aging. Instead, they believe there are a number of "gerontogenes" that directly or indirectly affect the changes of aging. Martin at the University of Washington estimates that as many as 7,000 of the 100,000 genes in humans could play a role.

There is little question, though, that such gerontogenes exist. Early evidence comes from a lowly worm called C. elegans that has only 10,000 genes. Last year, Johnson hit the jackpot when he identified a gene he has christened AGE-1. When he removes this gene, the worms live some 70 per cent longer - about five weeks. The rest of the development is normal, except that those worms without the gene produce 25 per cent fewer offspring than their cousins, indicating that the very genes that encourage reproduction may lower the rate of survival later on in life.

Researchers have also identified one complex of genes that seems to influence life expectancy. Called the MHC locus, it controls the machinery that causes organ transplants to be rejected and seems to play a role in the body's ability to repair damaged genes. Scientists have found that some long-living mice have a certain combination of these genes. Last year, a similar genetic pattern was identified in a group of centenarians at Okinawa.

Taking a very different approach to the problems of aging, one company believes it can grow new organs to replace those that wear out. Headed by Eugene Bell, a 69-year-old retired biology professor from the Massachusetts Institute of Technology, Organogenesis Inc. has fabricated skin and blood vessels. Experiments indicate that bones, the pancreas, and thyroid glands could be fashioned as well.

The secret is taking advantage of the way specialized cells are programmed to behave in the body. Graduate biology students at MIT studying cell growth were amazed when skin cells in a solution spontaneously formed themselves into living skin. They had simply created the right environment for the cells.

The company's "living skin equivalent" will soon be tested on burn patients at Western Pennsylvania Hospital in Pittsburgh. The "living blood vessel equivalent" is being tested in animals. Supplied with nutrients, both blood vessels and skin can sit on a shelf for up to a year. For these two products alone, Bell predicts multi-billion-dollar markets.

And then there are the Methuselah rats. "Who knows? It may turn out that we are eating ourselves to death," says Ronald W. Hart, director of the National Centre for Toxicological Research. At least one researcher is convinced that is the case, and he is not waiting for any studies.

Roy L. Walford of Venice Beach (California) promotes his "120-year diet" of 1,500 calories - half the average American's intake - with such staples as tofu and whole-wheat spaghetti. Walford, a respected gerontologist at the University of California at Los Angeles has formulated a theory for the role of the immune system in aging. Walford is not interested simply in living longer but in retaining vitality in old age. "I'm talking about people being chronologically older and functionally younger," he says.

Even if dietary restriction does not live up to its promise, both Walford and Johnson may be onto something else: Use it or lose it. "A lot of what we commonly call aging comes from disuse and atrophy," says Everett L. Smith, director of the biogerontology laboratory at the University of Wisconsin.

Indeed, a properly tailored programme of aerobic exercise, such as brisk walking, can postpone such physical changes as muscle deterioration, bone loss, and shrinkage of lung capacity "by as much as 20 years", says Roy J. Shephard, director of the School of Physical & Health Education at the University of Toronto. The same holds true for the brain. Psychologists have repeatedly shown that healthy, mentally active elderly people do not suffer the debilitating slowdowns of the less active. (Source: Business Week, 8 February 1988)

Research on animal genes

Perfect livestock cloning

Grenada (Houston, TX) has cloned seven genetically identical, pure-bred Brangus bull calves. It is among three companies competing to market cloned animals, and the technique used could increase the number of superior animals produced in the $30 billion beef and $18 billion dairy industries. The state-of-the-art technology blends cell fusion with several widely used animal reproductive technologies, the most important of which is the ability to transfer animal embryos from the genetic mother to a surrogate.

Artificial insemination of a prize Brangus cow that had been treated with hormones yielded 10 embryos. One of these was identified as a male through analysis of its chromosomes. Using microsurgical tools, scientists removed the nuclei from 16 of the embryonic cells, then removed the nuclei and part of the cellular material from an equal number of unfertilized bovine eggs collected from ordinary cows. Researchers transferred the embryonic nuclei into the unfertilized eggs, and the engineered embryos were implanted in surrogate mothers. Eight of the 16 embryos produced calves, and seven survived. Under natural conditions, a cow bred to a bull produces a calf 70 per cent of the time. Calves are rarely produced from 50 per cent of cloned embryos implanted (the rate of success is closer to 10-30 per cent), and each attempt now costs thousands of dollars. (Extracted from International Herald Tribune, 19 February 1988)

Rat pancreatic peptide gene cloned

The DNA sequence of the structural gene for rat pancreatic peptide has been determined by scientists at Kissei Pharmaceutical Industries (Matsumoto City, Japan, working in collaboration with Hiroshi Okamoto's research group at the Medical Sciences Department of Tohoku University. Pancreatic peptide is thought to play a role in reducing appetite and various aspects of digestion (intestinal peristalsis, lipid absorption, and secretion of gastric acid and pancreatic enzymes) by acting on the hypothalamus. Injection of pancreatic peptide into a strain of obese rats reduced feeding and the absorption of fat. The next step will be to use the cloned gene to search for compounds that induce the synthesis of pancreatic peptide in vivo. (Source: Bio/Technology, Vol. 6, April 1988)

First test-tube chickens born

Test-tube chickens have been born, paving the way for genetic manipulation of chickens, according to M. Perry at the Institute of Animal Physiology & Genetics Research. Chickens could be genetically engineered with the new culturing technique, which allows foreign genetic material to be introduced to a single-cell fertilized embryo. The fertilized ovum is first taken from the oviduct of a hen and put in a glass jar containing albumen and a salt solution. The embryo is then placed in a different albumen-salt solution and then transferred to a prepared eggshell sealed inside a sealed vessel until hatching. The in vitro technology could soon produce transgenic chickens. (Extracted from New Scientist, 4 February 1988)

Glowing frog eggs throw light on colour blindness

Scientists at the Institute of Ophthalmology in London have made frog eggs respond to light by injecting them with the messenger RNA (mRNA) from the visual pigments of cows. Their work may help scientists better understand how light is converted into electricity in the eye and what is going wrong in visual disorders like colour blindness.

The group are trying to work out the detailed biochemistry of the conversion of light into an electrical signal: the first step in vision.

Phototransduction happens in photoreceptors in the eye or more commonly known as the rods and cones. Rods and cones convert light into electrical signals using compounds known as visual pigments. Each visual pigment is a combination of a vitamin A derivative, called retinal, and a protein called opsin. Light excites the pigment and splits the retinal from the opsin. This dissociation causes an electric current to flow.

Exactly what happens between the pigment dissociating and the current flowing is not clear. Researchers believe that retinal changes shape several times before the channels open to let ions into the cell.

According to Claire Mitchell, one of the scientists that developed the light-detecting frog-eggs, this is the first time anyone has had control over the way in which mRNA, for visual pigments, tells a cell which proteins to form. (Source: New Scientist, 4 February 1988)

Mice accept gene for haemoglobin

Genetic engineers have successfully introduced a human haemoglobin gene into the bone marrow cells of mice. This could help researchers to devise a treatment for thalassaemia by replacing defective genes in humans.

The condition could be remedied by "infecting" the suffer's bone marrow cells - which normally produce the red blood cells carrying haemoglobin - with a normal haemoglobin gene. The bone marrow could then produce enough haemoglobin using this foreign gene.

A team led by Richard Mulligan of the Whitehead Institute for Biomedical Research in Cambridge, Massachusetts, along with Thalia Papayannopolou of the University Hospital, Seattle, have attempted to carry out this so-called "gene therapy" on mice. They have made a retrovirus that carries a copy of the human beta-globin gene.

The researchers removed bone marrow cells from mice and infected them with the virus. They then injected the infected cells back into mice to see whether they accepted the donor marrow. The team reports that a large proportion of the mice ended up with a "foreign" bone marrow that produced human (as well as mouse) beta-globin.

If a safe human virus can be found, and normal levels of a correct haemoglobin gene achieved in an "infected" bone marrow, then physicians and biochemists will be able to try the gene therapy on a patient with thalassaemia. (Source: New Scientist, 3 March 1988)

Viruses stop mouse diabetes

A California researcher reported that injecting a specific virus into mice predisposed to diabetes seems to prevent the disease. Using non-obese diabetic mice and the lymphocytic choriomeningitis virus (LCMV), Michael B.A. Oldstone of the Research Institute of Scripps Clinic in La Jolla found that the virus interacts with certain immune cells to stop the destruction of insulin-producing cells in the mice.

Because of the autoimmune reactions against their own pancreatic cells, non-obese diabetic mice develop life-threatening diabetes. Prompted by his earlier findings that viruses may alter the autoimmune response, Oldstone injected mice with LCMV, which can infect a range of animals that includes humans. Of the mice injected when newborn, none developed diabetes within nine months. Of those injected at age six weeks, only 6 per cent became diabetic within the same period of time, compared with 95 per cent of the untreated mice. About 20 mice were in each of the three treatment groups.

Emphasizing that he does not advocate injecting whole viruses as potential therapy, Oldstone says he is searching for a component of the virus that can give the same protection, with possible applications as a treatment for human diabetics. (Extracted from Science News, Vol. 133, 6 February 1988)

DNA studies may help endangered cranes, falcons

Studies of genetic material promise benefits for whooping cranes and peregrine falcons, according to Jonathan Longmire of Los Alamos National Laboratory. Both are endangered species. Longmire and his colleagues identify genetic fingerprints or markers for the birds by examining the DNA in their blood.

The Los Alamos work with peregrine falcons is designed to help explore their migratory routes. The birds are found on every continent but Antarctia. Those native to Alaska, Canada and Greenland, for example, nest in the north in summer and fly as far south as Argentina in winter.

Genetic markers, it appears, can be used to differentiate groups of peregrines from different locales. Longmire says he can now distinguish between peregrines native to Greenland and to Argentina.

The Los Alamos biologist is seeking genetic markers for additional groups of peregrine falcons. To date, volunteers have sent him blood samples from more than 2,000 of the birds in the Arctic Circle, Alaska, Canada, Scotland, Greenland, Spain, Northern Africa, Peru, Argentina, and Fiji. One day it probably will be possible to use genetic markers instead of the traditional leg bands to learn, for example, whether peregrines follow the same migratory routes and whether they return consistently, like salmon, to their birthplaces. (Abstracted with permission from Chemical and Engineering News, 11 April 1988. Copyright (1988) American Chemical Society.)

Sugar pills for tsetse flies

Researchers probing the biochemistry of the tsetse fly believe that a group of glycoproteins might form the basis of an immune system in insects. If they are right, these proteins could provide a more effective weapon against one of the worst plagues of Africa than any available to date.

The tsetse fly carries the parasite that causes trypanosomiasis, a disease that debilitates and often kills the more productive breeds of cattle, and in one form, causes human sleeping sickness. The tsetse transmits the parasite to game animals too, but they are mostly resistant to the disease.

Yet, even in areas where virtually all the game animals are infected, less than 10 per cent of the flies seem to be carriers. Ian Maudlin of the Tsetse Research Laboratory of Bristol University has shown that the susceptibility of flies to trypanosomes seems to be passed on through the female line. Electron micrographs showed bacteria in the cytoplasm of susceptible flies. The bacteria resemble Rickettsia and are known as Rickettsia-like organisms or RLOs. Maudlin believes that the bacteria increase the fly's chances of becoming infected.

Maudlin has gone on to demonstrate further links in the chain of infection and resistance to trypanosomes.

Tsetse flies that are resistant to infection, so-called refractory strains, seem to fight the trypanosomes with lectins. These proteins and glycoproteins are common in insects and plants: they are known to bind to carbohydrates, to cause cells to stick together and to stimulate cell division. Lectins are highly selective in their choice of binding site, attaching to specific carbohydrates in the same way that antibodies in mammals bind to specific proteins. The lectins seem to form a sort of insect immune system.

David Molyneux at Salford University studied the tsetse lectin in vitro and found which carbohydrate it binds to. Maudlin has now carried out tests on laboratory flies to see how the lectin functions in vivo. He fed one group of flies on glucosamine to inhibit the lectin. A control group received galactose, the insect equivalent of a sugar pill placebo. Maudlin then gave both groups a meal of blood infected with trypanosomes. After 28 days, he dissected the flies. Almost all those fed on glucosamine - and so lacking available lectin - were infected. Of the control group, about half were infected.

The RLO bacteria, which are inherited through the maternal line fit neatly into the picture. Susan Welburn, also at the Tsetse Research Laboratory, has grown RLOs in cultured mosquito cells and shown that they produce an enzyme called chitinase. The enzyme breaks down chitin, the structural protein in insects, to release glucosamine, the same sugar that blocks the lectin.

Trypanosomes also seem to use the same lectin as a signal for migration to the fly's salivary gland and mouthparts ready to infect a new host. Flies with established infections of the gut that were fed glucosamine throughout their lives never produced infective trypanosomes. All those fed the galactose placebo eventually became infectious.

The practical implications of these results are unclear. Perhaps releasing refractory flies into areas where control programmes have eliminated strains of flies that carry disease would prevent them from returning. Lectins might turn out to have a widespread importance as insect antibodies. Scientists have already found that they play a part in making mosquitoes resistant to malarial parasites. (Source: New Scientist, 7 January 1988)

New technology for the extraction of laminen and vitronectin

Iwaki Glass Co., Ltd. has succeeded in developing a new technology for extracting laminen and vitronectin, which are extracellular matrixes that promote the hyperplasia and differentiation of cells.

Extracellular matrixes, such as laminen and vitronectin, are indispensable for tissue culturing. Also included among these proteins are collagen, gelatine and others which display different effects with respect to various kinds of cells.

Laminen was obtained by injecting a mouse with EHS sarcoma, extracting the swollen sarcoma, and then separating and purifying it by liquid chromatography techniques. Meanwhile, vitronectin was produced by using a monoclonal antibody together with human serum, and then purification and separation was accomplished by using a column.

Both these substances are already being commercialized by an American medical drug manufacturer, but Iwaki Glass is able to produce them at lower costs by utilizing its newly devised extraction technology. (Source: JETRO, January 1988)

Red sea bream growth hormone

Researchers at Ace Pharmaceuticals, working in collaboration with scientists at the Japanese Ministry of Agriculture, Forestry and Fisheries, have used recombinant DNA techniques to isolate the structural gene for a growth hormone in red sea bream (Chrysophrys major). The team is now focusing on mass-producing this hormone in Escherichia coli for use in commercial fish production. The amino acid sequence of the 186 residues that follow the signal peptide is 68 per cent homologous to white salmon growth hormone and 45 per cent homologous to eel growth hormone. (Source: Bio/Technology, Vol. 6, February 1988)

Research on plant genes

Genetically engineered hybrid rice plants

Mitsui Toatsu Chemicals (Japan) has developed rice plants from genetically engineered hybrid cells. The hybrids are produced from protoplasts from a male-sterility rice plant and cultivated varieties. The nucleus of the male sterility rice protoplast was destroyed with X-rays. The hybrid cell has the nucleus of the Norin VIII rice variety, and the cytoplasm is a mix of the two cytoplasms. Male sterility is a trait carried by the mitochondrial DNA. The technique will aid the development of new rice varieties. (Source: Japanese Chemistry, 1 March 1988)

Agrigenetics improves corn with RFLP

A group of scientists at Agrigenetics Advanced Science Co. (AASCo) is using the restriction fragment length polymorphism mapping (RFLP, pronounced "riflip") technique to transfer resistance to maize dwarf mosaic virus (MDMV) into an elite line of corn. RFLPs are natural variations in DNA structure. They provide genetic signposts to find useful genes. These signposts make it easier to use standard breeding methods to take good genes from many different corn plants and to put them together in new combinations.

Corn breeders have found it hard to move MDMV resistance into hybrid corn. AASCo has found that this is because at least five different genes are needed to get good resistance and each gene is on a different chromosome. Previously, breeders had no way of knowing which plants had all five genes. Using RFLP, the AASCo group was able to detect the genes and to find the rare plants that had all five. (Source: Biotechnology Bulletin, Vol. 6, No. 12, Janaury 1988)

Haemoglobin found in plants

Researchers in Australia have reported the discovery of haemoglobin in the roots of a plant in the elm family. The finding represents the first time haemoglobin has been found in a plant lacking specially adapted "root nodules", and leads the researchers to suggest that haemoglobin genes might be present in all plants.

Scientists have for years been puzzled by the presence of haemoglobin, the oxygen-carrying component in blood, in some plants. It exists in single-unit monomers in plants, while in humans it combines into four-unit tetramers. Mysteriously, it has been found solely in the root nodules of a specialized class of plants that associate with nitrogen-fixing bacteria. It is not obvious, however, why haemoglobin would appear only in such plants.

W. James Peacock and his colleagues at the Commonwealth Scientific and Industrial Research Organization in Canberra used DNA probes to identify the haemoglobin gene in the non-nodulating plant, and confirmed by the presence of messenger RNA and protein that the haemoglobin gene was indeed active, although it is not clear what role haemoglobin might play in plants. (Extracted from Science News, Vol. 133, 19 January 1988)

Research on bacterial genes

Biting down on the culprit causing gum disease

New work is pointing to a specific bacterium, Bacteroides gingivalis, as at least one cause of periodontal disease. Dental researchers hope that by pinning down specific bacteria, they eventually may be able to interfere with the progression of periodontal disease, perhaps by preventing the key types from colonizing or by cutting off their food supply, which consists primarily of the by-products of other bacteria.

In recent years, scientists have repeatedly isolated B. gingivalis from diseased gums in adults and have linked it to the progression of periodontal disease in humans and monkeys, but they have not been able to say that it is a cause of periodontal disease. For example, when researchers tried to implant it in the mouths of rodents, they did not observe any resulting disease.

However, a group of researchers report that B. gingivalis does cause burst of periodontal

disease in monkeys, whose mouths have a microbiology and immunology similar to humans. Currently, the group is trying to determine whether other types of bacteria have a similar effect. (Extracted from Science News, Vol. 133, 9 January 1988)

Hot bacteria make safer sweets

The idea of using thermophilic bacteria that live naturally in hot springs in industry is not new, but it has not been exploited. Now scientists at the University of Kent have found ways to use them.

David Hardman at the university's Biotechnology Centre has developed a system for inserting extra copies of genes for enzymes into a thermophile, and anchoring them in place. Bacillus stearothermophilus has a lipase that can help break down fats into smaller molecules for use in confectionery. Its working temperature, 65 °C, kills other micro-organisms, sterilizing the product. The fats liquefy, making solvents unnecessary. This saves money and prevents hazards from solvent residues. (Source: New Scientist, 10 March 1988)

An engineered microbe is monitored in soil

The ability to track and monitor genetically engineered micro-organisms that are released into the environment has been successfully demonstrated by researchers at Clemson University (Clemson, S.C.). In November, microbiologist Ellis Kline began field-testing the soil bacterium Pseudomonas fluorescens that Monsanto (St. Louis) engineered to determine its distribution and survival in soil. In the test, rows of wheat inoculated with P. fluorescens were planted adjacent to rows of non-inoculated wheat. Extensive monitoring during the first 10 weeks of the test indicates that the bacteria successfully colonized the roots of the inoculated wheat plants and remained restricted to the area of planting, says Kline, adding that bacteria did not cross over to roots of non-inoculated plants. Monsanto engineered P. fluorescens to metabolize the sugar lactose, which the bacterium normally cannot utilize. The organism also contains markers for fluorescence, colour and resistance to the antibiotic rifampin. That provides a way to identify the organism among the multitude of native bacteria found in the soil, says Monsanto. The company adds that researchers can detect as little as one engineered P. fluorescens out of 1 billion organisms. (Source: Chemical Week, 24 February 1988)

Research on yeast and fungus genes

Milking leeches for drug research

Scientists at the Hebrew University of Jerusalem have found a way of milking leeches to extract hirudin.

Leeches produce hirudin to ensure that the blood of their victims keeps flowing. It neutralises thrombin, an enzyme that helps blood to clot. Doctors have exploited this property for some time, mainly to help to maintain blood flow and prevent necrosis after plastic surgery, but it has been difficult and expensive to extract. Bacteria can be persuaded by genetic engineering to make hirudin, but this too needs complicated purification.

Meir Rigbi and Miriam Orevid found that leeches do not need real blood to stimulate their appetites: they drool at the smell of a chemical called arginine.

The researchers mixed a little arginine into saline solution and put it into a beaker with a calf-gut (sausage-skin) membrane on the bottom. The leches bit, sucking until they had trebled their body weight or more. Then the researchers squeezed out the leaches, empyting them of the saliva-laden saline solution. The leeches remained hungry, so it was possible to milk them six or seven times before they died.

The milking technique yielded not only larger quantities of saliva; it also made it easier to separate the active compounds. The researchers were able to take what they wanted from a melange of proteins.

Apart from the hirudin, leech scientists have found a range of other valuable materials in the saliva. There are at least four separate chemicals that inhibit blood platelet aggregation, which is one of the main factors causing atherosclerosis and myocardial infarcts. The enzyme apyrase, which had already been found in potatoes, was isolated in leech saliva for the first time. They also isolated leech collagenase (which breaks down collagen, the basic connective tissue of the body), and two others of lower molecular weight, which are still being investigated.

What is important about these substances, according to Amiram Eldor of Hadassah Hospital's haematology department and head of the clinical side of Israeli leech research, is that they may not only reduce the risk of clot-related diseases, such as strokes and heart attacks, but they could also be used instead of complicated surgery to break down existing clots.

Despite the recent advances, drugs that come out of this research will probably not be genuine leech extract. The economics of leech farming do not allow it. The milking technique will prove useful for research; Rigbi expects genetic engineering to produce commercial quantities of these substances. (Source: New Scientist, 4 February 1988)

Fungal superglue

A strong new natural glue, spore tip mucilage (STM), has been discovered that, like other bioadhesives, may have applications in such diverse fields as medicine and materials science. In nature STM glues fungal spores of Magnaporthe grisea to leaves and other parts of rice plants that then succumb to rice blast disease, a devastating and costly blight. John E. Hamer and colleages at Du Pont, Wilmington, USA analysed glue release and spore attachment by observing these processes on Teflon films which, like the waxy rice plant leaves, are nonstick wet-resistant surfaces. The glue is apparently stored in dehydrated form in a specialized compartment at the spore's apex. When the spore is hydrated, STM is also hydrated and released it then effects attachment of the spore to the host plant. STM release occurs before spore germination; later, a germ tube is produced and still later the infection structure of the fungus, the appressorium, develops. The release of STM thus appears to be an important early event in fungal pathogenesis and, if the release process is an inhibitable one, effective control of rice blast disease might be possible. (Source: Science, Vol. 239, 15 January 1988, p. 239. Copyright by the AAAS.)

Fungus selectively kills jimsonweed

Jimsonweed is an invasive weed that competes with soybeans and cotton, and contains alkaloids that can harm livestock and humans. Moreover, once jimsonweed matures, it stubbornly resists control by many currently used herbicides. The fungus Alternaria crassa has been found to kill jimsonweed but not

crops, including soybeans and cotton, reports Clyde D. Boyette of the US Department of Agriculture's Delta States Research Centre (Stoneville, Miss.). The fungus - in the form of dormant spores - can be spread over vegetation several ways: in granules, gel pellets and water-based and oil-based liquid sprays. (Source: Chemical Week, 24 February 1988)

Intron exception

Molecular biologists have become used to the idea that genes often come in bits. Small stretches, called exons, that code for proteins, are separated by long, apparently meaningless, introns. In the chain from DNA to protein the whole gene, introns and all, is first translated into RNA. Special enzymes then snip out the introns and splice the exons together to make the messenger RNA (mRNA). This messenger carries the final code that will be translated into the protein. Now, thanks to a report from a team in Salt Lake City, we know that there are exceptions to this rule.

The gene in question codes for an enzyme that rearranges the structure of DNA. It belongs to a bacteriophage called T4, a virus that normally invades the bacterium Escherichia coli. The gene contains a full stop early in its code, which ought to mean that the protein it codes for is just 46 amino acids long. The actual protein is much longer - 160 amino acids. There is another coding area further down the DNA which is long enough to produce the observed protein.

Ordinarily, one would assume that the intervening sequence between the two coding regions is spliced out, but, try as they might, the researchers could find no evidence of any splicing. Instead, they suggest, the mRNA simply folds into a hairpin bend that tucks the offending intron out of the way. The translating machinery then reads the message on the RNA and ignores the intron. (Source: New Scientist, 17 March 1988)

Novel processes for enzymatic fat splitting

Industry now converts the triglycerides in low-value animal fats and vegetable oils into valuable fatty acids and glycerine. Yet current steam hydrolysis requires high temperature and pressure, which calls for huge stainless steel vessels and costly heating equipment. The enzyme lipase - a potential low-pressure and low-temperature way of splitting fats - has been known for years. The trouble has been that, so far, lipase has not been efficient enough. For one thing, reports show that it can hydrolyze only 95 per cent of beef tallow, generating a product that, without further purification, is suitable only for soaps.

The US Department of Agriculture's (USDA) Eastern Regional Research Centre (Philadelphia) has now developed two laboratory processes that, it believes, can push lipase hydrolysis of fats and oils to 100 per cent. One process uses a mixer containing an array of baffles that, without surfactants, creates a turbulent mixture of fat and water called a "pseudoemulsion". The second process reacts fat and water at a lipase-loaded membrane, using pressure to push fat through the membrane.

Neither process has as yet aroused much industrial interest. Nor has either undergone cost analysis. The mixer process uses an impeller blade mixer, a type often employed to ferment micro-organisms. The mixer is modified to operate at 400-1,000 rpm, with four baffles connected to the inner reactor wall. That accomplishes a lot of things, says the mixer's inventor, Samuel Serota, a retired research chemist. The baffles prevent mass swirling of the mixture, increasing turbulence and, thereby, providing a large oil-water interface, or pseudoemulsion, throughout the mixture. Such a pseudoemulsion maximizes the rate and degree of hydrolysis while allowing use of "minuscule" amounts of lipase. Heat generated by mixing is removed by a water-containing cooling coil positioned along the reactor's inner wall.

Reaction times vary with the fat or oil being hydrolyzed. Tallow, for example, may require about 72 hours, while many vegetable oils are hydrolyzed in about 24 hours, says Serota. Operating temperatures range from 3°C to 45°C, depending on the type of lipase used.

After hydrolysis, the fatty acids and glycerine are easily separated. Because of the absence of emulsifiers, they settle into two layers on standing, with spent lipase forming a thin film between the layers. In the hydrolysis of tallow with Candida rugosa lipase, the product separates into layers within 20 minutes at the reaction temperature of 40°C.

The process that reacts fats and water at a lipase-loaded membrane uses conventional microporous or ultrafiltration membranes. The membrane is loaded with lipase at a pH of 5.5, which makes lipase absorption "irreversible", says the process's inventor, Frank Taylor, a chemical engineer. The membrane divides a chamber with melted tallow at 45-50°C on one side of the membrane and an aqueous solution buffered at a pH of 5.5 on the other.

A pressure drop of 1-50 psi is maintained across the membrane from the oil side to the aqueous side by such conventional means as a peristaltic pump. That drop forces oil through the membrane, where it is split into fatty acids and glycerine. The products mix with the aqueous phase in what Taylor describes as a "crude mixture", not an emulsion, which is easily separated into two phases in a separation chamber.

When oil is pumped through the membrane, the membrane preferably is hydrophilic. That allows water to fill the membrane pores, enabling hydrolysis to occur readily. But when water is pumped through the membrane, the membrane preferably is hydrophobic, allowing oil to fill the membrane pores and hydrolysis to take place.

The system's reaction rate is high because oil, under pressure, does not have to diffuse into the membrane to reach the catalyst, says Taylor. Furthermore, the fatty acids formed do not have to diffuse back through the membrane to the oil side, because, under pressure, they will mix with the aqueous solution. (Source: Chemical Week, 23 March 1988)

Research on viral genes

Research on AIDS moving quietly forward

Research on AIDS (acquired immune deficiency syndrome), on related diseases of species other than humans, on the AIDS virus itself - (HIV) - and on related retroviruses is advancing scientists' understanding of the etiology of these devastating diseases. With increased understanding comes increased hope for treatment and prevention of AIDS.

However, not all research advances are comforting - to people with AIDS, people infected with HIV, or scientists trying to sort out the details of the remarkably complex disease. Recently, scientists have reported that:

- At least half of those infected with HIV will develop AIDS within nine years and another one fourth will develop AIDS-related complex (ARC).

- HIV infects cells of the intestine and is likely a direct cause of the chronic and debilitating diarrhoea often found in AIDS patients.

- Studies with feline leukaemia virus (FeLV), which causes an AIDS-like condition in cats, suggest that the most pathogenic variants of HIV may be missed when current isolation techniques are used to screen for the virus.

On a more positive note, scientists at a number of institutions working independently have shown that a soluble version of the CD4 antigen, which appears to be the primary target of HIV in its infection of susceptible cells, can block the infectivity of the virus in vitro. The protein might be able to slow the course of an HIV infection.

In another positive development of sorts, epidemiologists at the Centres for Disease Control, Atlanta, and the New York City Department of Health report that HIV infection continues to be confined primarily within the traditional high-risk groups and that the modes of HIV transmission have remained stable.

Scientists may be a long way from finding a cure for AIDS, but they are getting to know the AIDS virus in extraordinary detail.

Researchers have confirmed hypotheses about how the virus does its deadly work. The AIDS virus, one of the most difficult viruses to study, is better known than virtually any other human virus, said Dr. Dani Bolognesi of Duke University.

However, experts say the more they learn about what is more formally known as the human immunodeficiency virus, the more discouraged they are about the prospects for rapidly finding a cure or vaccine.

Until recently, scientists thought that the AIDS virus, like many others, was transmitted as a virus particle in blood, semen or vaginal fluid. This explanation seemed adequate for transmission through blood, in which many virus particles are present.

Recently, however, researchers have found that the main source of AIDS virus in semen and vaginal fluid is not free virus particles, but rather macrophages carrying viruses. Macrophages, as the immune system's scavenger cells, are well-suited for carrying the virus to other cells of the body.

Dr. Levy and his colleagues at the San Franciso General Hospital recently isolated the AIDS virus from rectal cells of AIDS patients, and Dr. Martin Hirsch and colleagues at Harvard Medical School recently found the virus in cervical cells.

These findings mean the virus can infect partners in anal or vaginal intercourse without any breaks or tears in the skin.

Many experts suspect that another possible path for the sexual spread of the virus is through Langerhans cells, other immune system cells. They closely resemble macrophages but are at the surface of mucous membranes.

The macrophage clue is particularly tantalizing. Other cells of the immune system, T-cells, normally activate the body's defences upon being signaled by macrophages that have engulfed invading viruses or bacteria. The macrophages could pass the AIDS virus to the T-cells, setting the stage for the destruction of the immune system.

Investigators, including Dr. Robert Gallo of the National Cancer Institute in Bethesda, Maryland, also have preliminary evidence that macrophages transmit the AIDS virus to the brain, where it infects microglial cells. These brain cells are thought to be a form of macrophage, Dr. Gallo said.

Finally, macrophages appear to be a continuing source of the AIDS virus as the infection continues.

The AIDS virus resides in special sacs inside the macrophage and is invisible to the immune system, he said. The virus can go from these sacs to other cells, or it can be released if the macrophage itself is killed.

Dr. Gallo cautioned that if infected macrophages looked perfectly normal to the immune system, a vaccine would not protect against them. And if killing infected macrophages releases the AIDS virus, then even the selective destruction of these cells would not defeat the disease.

Until recently, scientists were at a loss to explain how a small proportion of infected cells causes the demise of so many others. Now they have several answers, all of which seem correct they say.

One is particularly unpleasant. Many studies suggest that the dormant AIDS virus becomes active and multiplies when the body is responding to a new disease threat. These studies indicate that the biochemical signal to a T-cell to start replicating and activating the rest of the immune system instead causes the AIDS virus to replicate and destroy the T-cell.

The relation between T-cell activation and AIDS-virus release may cast a pall over attempts to treat AIDS patients by boosting their immune systems with drugs such as interferon. The immune system boosters activate T-cells, said Dr. Jeffrey Laurence of Cornell University School of Medicine in New York, which means that they could cause the virus to be spread from infected cells.

Still, experts believe that more is going on than simply the spread of virus among T-cells. They reason that too few T-cells are infected to account for the destruction of the immune system.

Until recently, the leading hypothesis was cell fusion. The idea was that infected T-cells had viral proteins on their surfaces that made other T-cells stick like iron filings to a magnet. The resulting mass of cells were unable to function and so were eliminated by the body's immune system.

The fusion hypothesis is being supplanted by another proposal that experts say is compelling: that viral proteins released by HIV-infected T-cells stick to healthy T-cells and lead to their destruction.

Dr. Bolognesi noted that an infected T-cell throws off fragments of viral protein.

The proteins bind to the surfaces of healthy T-cells, coating them. Antibodies the body has made in an attempt to fight the infection then bind to the viral proteins, signaling the immune system to destroy the healthy cells. (Extracted from International Herald Tribune, 24 March 1988 and Chemical and Engineering News, 28 March 1988)

Nets cast to catch the second virus

The second human immunodeficiency virus - HIV-2 - has made its appearance in Britain. Scientists at the Middlesex Hospital in London found the virus, which is

sufficiently distinct from HIV-1 to warrant a different name, in a blood sample taken anonymously from a homosexual man attending a clinic for sexually transmitted diseases.

The discovery of the virus coincides with a new study which began to monitor the spread of HIV-2 in people attending clinics at seven hospitals in London. These are the Middlesex, University College Hospital, St. Thomas's, St. Bartholomew's, St. Mary's, the West London and King's College Hospital.

Richard Tedder, a virologist at the Middlesex, says that the seven centres have access to 10,000 test kits that can identify the presence of antibodies to HIV-2 in the blood of patients. Everyone attending the centres who is tested for infection with HIV-1 will also be tested for infection with HIV-2.

The discovery in Britain of the second virus is the result of monitoring over the past year of groups who are considered at high risk of being infected with HIV-2. The risk groups for HIV-2 are essentially the same as the groups most at risk for HIV-1 infection, plus people who have had contact with West Africa.

The only case of HIV-2 infection that has so far appeared in the US is in a West African patient living in the US. This person was suffering from loss of weight and neurological disorders. Doctors made the diagnosis of HIV-2 infection in December 1987. According to the Centres for Disease Control in the US, "The case undoubtedly represents infection acquired in West Africa since illness began before the patient's arrival in the United States".

In Britain, the Public Health Laboratory Service has tested about 10,000 samples of blood for infection with HIV-2. The fact that just one positive sample has turned up shows that the virus is still extremely rare.

A spokeswoman for the Department of Health said that if the virus becomes more prevalent then the Department would have to consider screening blood donors for infection with HIV-2, in addition to the existing screening programme for infection with HIV-1.

In the US, blood tests for HIV-2 infection, carried out on nearly 23,000 people, including 8,500 blood donors chosen at random, failed to reveal any signs of infection with HIV-2.

Tests for antibodies to HIV-1 do not always detect the presence of antibodies to HIV-2. The tests used in the US, for instance, are estimated to detect between 40 per cent and 90 per cent of infections with HIV-2. The viral proteins of HIV-2 are similar to those for HIV-1 and so the test for antibodies to HIV-1 can sometimes identify antibodies to HIV-2.

The problem, however, is that there is no guarantee of this. A separate test, made from the viral proteins of HIV-2, has to be used to make sure that all antibodies to HIV-2 are detected. Some companies are developing tests that will identify infection with either or both of the two viruses. But until there is evidence that HIV-2 is more widespread outside of West Africa, countries in Europe and the US are unlikely to give the go-ahead for more widespread screening of donated blood for infection with HIV-2. (Source: New Scientist, 31 March 1988)

Early HIV effects on nervous system found

In 1985, when scientists isolated the AIDS-causing human immunodeficiency virus (HIV) in brain tissue and spinal fluid, they realized that the virus directly affected the nervous system as well as the immune system.

But a new study is providing some of the first clues about when HIV begins to affect the nervous system, causing dementia and other impairments. The answer may mean earlier detection and treatment of HIV-infected individuals.

The study, which is the first to detect neurological impairment at various stages of HIV infection, was made after giving neurological and psychological tests to a group of 55 homosexual men. Igor Grant and his colleagues at the University of California and Veterans Administration Hospital in San Diego evaluated the subjects' mental abilities and found that HIV appears to have an early impact on the nervous system. In the group with fully developed AIDS, the impairment rate was 87 per cent; AIDS- related complex (ARC), 54 per cent; HIV positive, 44 per cent; and HIV negative (controls), 9 per cent.

At the Multicentre AIDS Cohort Study (MACS), which involves 5,000 homosexual men in Baltimore, Pittsburgh, Chicago and Los Angeles who were tested for HIV two years ago but who had not developed ARC or AIDS at that time, investigators are monitoring the neurological and psychological characteristics of those who have tested positive for HIV since entering the programme. This will help determine when HIV first affects the nervous system and also the effect's prevalence at each stage of infection.

Grant says that although it is premature to make any conclusions from this study, one implication is that physicians should know that HIV may cause neurological problems in otherwise healthy patients.

In addition, knowing the stage of HIV's impact on the nervous system is important because scientists need to know when to begin therapy with commercially available drugs. But they first must know whether early intervention would be beneficial. The NIAID and Burroughs Wellcome have set up a study of 1,600 asymptomatic, HIV-positive people to determine the drug's effect. (Extracted from Science News, Vol. 133, 2 January 1988)

Changes in viral virulence

Virus isolated from people infected with HIV may be more virulent in the later stages of the disease. This change in the biological properties of the virus may explain why infected individuals progress to AIDS.

Researchers in California took blood from four people over a period of several years. They isolated HIV from the blood cells of these people and studied the ability of the virus obtained to kill cells grown in the laboratory. They found that, as the disease progressed, the isolates of virus were more able to kill cells, and replicated to higher concentrations. In addition, it was easier to isolate the virus from each person's blood cells as the disease progressed.

One of the four subjects remained asymptomatic throughout the study. This person yielded viruses that were less virulent than those isolated from the other three.

Tests carried out by researchers suggested that sequential isolates from the same individual were closely related variants of one another.

The explanation that the researchers favour is that the virus originally transmitted must have mutated during the course of infection. They conclude that development of symptoms in people infected with HIV correlates with the emergence of more virulent strains of the virus. (Source: New Scientist, 28 April 1988)

Mutant virus loses ability to infect

Researchers in California have found that the envelope protein of HIV, which is produced in one large chunk, must be clipped in two if the virus is to infect cells. When the researchers created a mutant strain of the virus, from which they had removed the site at which the envelope protein normally splits, they found that the virus failed to infect human cells grown in the laboratory.

The finding has no clinical application at present, the scientists stress.

When HIV infects a cell, the cell is deceived into making viral proteins. One of the proteins, called gp160, is split in two, to form the envelope proteins gp41 and gp120, which sit in the viral membrane.

The researchers from Stanford and from Gene Laboratories, of Redwood City, removed the normal cleavage site on gp160, on which one class of enzyme works, and replaced this region with a site susceptible to a different kind of enzyme. The mutant virus was able to infect cells only after being exposed to the second kind of enzyme.

The enzyme responsible for cleaving gp160 in the infected cell appears to be a protease. Perhaps, one day, it might be possible to find a substance which could inhibit the enzyme. Instead of blocking the cleavage, it might also be possible to develop substances that bind to the portion of the envelope protein exposed by the split. (Source: New Scientist, 28 April 1988)

Drug firms race to develop AIDS blocker

Drugs and biotechnology firms are racing to develop a protein that may block the AIDS virus from attacking the immune system. Researchers at Smith-Kline & French Laboratories, Biogen, Genentech and the Hoffmann-La Roche-backed Basle Institute of Immunology have independently demonstrated that genetically engineered CD4 protein can prevent the AIDS virus from attacking the key immune system T4 cells.

The CD4 protein normally sits as a receptor on T4 cells. Researchers at the companies have synthesized soluble forms of the protein that can act as decoys, mopping up the AIDS virus and preventing it from attacking the T4 cells. All the research groups are still cautious about predicting the potential of the soluble gene-spliced CD4 protein but clinical trials are being planned.

Biogen is hoping to start the first phase of clinical trials with human patients by the end of this year and is committing very large amounts of resources to the project. The company expects to retain the technology for its own use but has not discounted the possibility of linking up with other firms to develop the product.

SmithKline & French, which has synthesized a CD4 protein that has the highest inhibitory effect, expects to enter clinical trials within one to two years.

All the firms have cautioned that while the protein shows promise in laboratory tests it may turn out to have unacceptable side effects or could block the interaction of immune cells triggering a different form of AIDS.

With the World Health Organization predicting that there may be more than 100 million sufferers of AIDS in the world by the end of the century, many firms are searching for potential treatments. So far only Wellcome's zidovudine has been approved as an AIDS therapy and is likely to remain unchallenged for the next few years.

Zidovudine is an analogue of the essential DNA component cytidine. Hoffmann-La Roche and Bristol-Myers are working on similar compounds. Roche is investigating dideoxycytidine (DDC) but laboratory tests indicate that the compound may be too toxic to prove reasonable in application usefulness.

One of the most promising compounds is Institut Merieux's immune system stimulator Imuthiol. The drug has orphan drug status in the US and is in phase II trials. It has been demonstrated that the drug may be useful in the early stages of the disease by slowing down progression of infection from ARC to AIDS.

Other immune system modulators in phase II clinical trials include HEM research's Ampligen, to which Du Pont has US exclusive rights, Imreg 1/2 and granulocyte macrophage stimulating factor which is being developed by Sandoz, Glaxo and Immunex. Vaccines to the AIDS virus are not expected for at least another five years.

Some antiviral drugs that are currently available for other indications are also attracting some interest as potential AIDS therapies. The Federal Republic of Germany's Degussa is investigating D-penicillamine which has shown inhibition of AIDS virus reproduction in patients with AIDS-related complex symptoms.

Fisons and Lyphomed are both developing pentamidine which may be a contender for treating some of the infections that thrive on the compromised immune system of AIDS victims. This drug could be in the marketplace by the end of next year. (Source: European Chemical News, 18 January 1988)

New approach to AIDS research

Two major Canadian organizations have initiated research into a new approach to AIDS therapy. Supplemented by an initial grant of $240,000 over three years from the Medical Research Council, the programme concentrates on finding new ways to make the white blood cells of an AIDS sufferer resistant to the AIDS virus. It is hoped it will be the basis for an effective treatment for the disease.

The research is being conducted by Drs. Sadhna Joshi and Wayne Davis of Allelix Biochemicals, a division of Allelix Inc., and Dr. Alan Bernstein, Head of the Division of Molecular and Developmental Biology at Mount Sinai Hospital Research Institute of Toronto.

Unlike most AIDS research, which is directed at developing drugs such as AZT that inhibit essential components of the virus itself, the new approach focuses on white blood cells which are attacked by the virus. When attacked, the white blood cells essentially become AIDS-virus factories. The objective is to make the white blood cells (specifically the T-4 cells) resistant to such attack. The approach has been dubbed VITA (Virally Induced Therapy for AIDS).

Steps in the process involve removing bone marrow cells from an AIDS patient, modifying the cells so the T-4 cells they produce are resistant to the virus, and replacing the modified cells. On return to the patient, the "converted" bone marrow cells hopefully will rebuild the patient's immune system because the T-4 cells they produce can neither be destroyed by the AIDS virus nor used by it to make more virus.

According to Dr. Wayne Davies, Scientific Vice-President at Allelix Biochemicals, the approach uses technologies that are for the most part well developed. "Cells have been made resistant to viruses in several systems, and modification of bone marrow cells is well established for animals. We now face the new challenge", he added, "of making human cells resistant to this particular virus".

Allelix Biochemicals is one of three divisions of Allelix Inc., Canada's largest biotechnology company. The division, with over 65 technical staff, concentrates on developing biopharmaceuticals, in particular therapeutic peptides and proteins, and on receptor-based drug design.

The Mount Sinai Hospital Research Institute, founded in 1985 and with over 200 technical staff, conducts extensive basic science and clinical research into more than 50 medical problems which make up several major programme areas. These include molecular and developmental biology, brain function, cancer, degenerative bone disorders, problems associated with the newborn and developing foetus, diseases of the nervous system, hearing disorders, diseases of the liver and digestive organs, and thyroid diseases. (Source: Company News Release, 21 January 1988)

AIDS virus growth inhibitor

Synthetic sulfonated polymers have proved effective in inhibiting the growth of AIDS virus and cancer cells, as shown by collaborative work done by the research groups of Toshiyuki Uryu at the Production Techniques Research Laboratory of Tokyo University, Naoki Yamamoto at Yamaguchi Medical School, and scientists at Ajinomoto's Central Research Institute. Although many polysaccharide derivatives are known to inhibit the growth of cancer cells and viruses, most have very low potency and cause unwanted side effects. In contrast, the sulfonated polymers - synthesized by a "dry sugar" sulfonation process carried out under high vacuum - inhibit transcription with high potency and seem to be relatively free of side effects.

The three classes of polymers with the highest anti-viral and anti-cancer cell potency are branched polymers of xylose (xylofuranan: average molecular weight 7,000), ribose (ribofuranan: average molecular weight 10,000), and glucose (dextran: average molecular weight 34,000). The researchers showed that sulfonated polymers of xylose and ribose effectively inhibit reverse transcriptase and RNA polymerase. Sulfonated polymers also inhibit the growth of the AIDS virus by 70-90 per cent when present at a concentration of 10 milligrams per milliliter, and 90-98 per cent at a concentration of 100 mg/ml. (Source: Bio/Technology, Vol. 6, March 1988)

Multiplicity and HIV's clinical course

A study of four people infected with the AIDS-causing HIV virus has found that, over a four-year period, the viruses isolated from the patients became more virulent - something scientists have suspected for some time. Researchers at the University of California at San Francisco have reported that the later isolates killed more white cells and multiplied faster than those taken from patients early in infection. Emergence of these more virulent viruses corresponded with clinical appearance of AIDS symptoms, say the scientists, who conclude the increased virulence occurred inside the body rather than during laboratory procedures. Jay A. Levy and others suggest that tracking HIV isolates as they change in vivo will help explain the symptomatic course of the disease. The study reiterates the problems caused by HIV's many isolates and its ability to mutate rapidly. (Source: Science News, Vol. 133, 9 April 1988)

Laboratory mix-up solves AIDS mystery

Two leading AIDS researchers have admitted that they made a mistake in announcing two new viruses that seemed to cause immuno-deficiencies in humans and in monkeys. Max Essex and Phyllis Kanki, from the Harvard School of Public Health in Boston, accept that a human AIDS virus they named HTLV-4 and a monkey AIDS virus, which they named STLV-3, are one and the same as another monkey virus, called SIV, which they had received from other researchers.

Just before Essex's paper on HTLV-4 appeared, Luc Montagnier of the Pasteur Institute in Paris gave a lecture in Portugal and announced his discovery of a new AIDS virus, which he had discovered in 1985. This virus subsequently became known as HIV-2. The big question was whether HIV-2 was the same as Essex's HTLV-4.

We now know that they are not the same virus. Essex and Kanki made a mistake in the laboratory. Somehow a sample of a monkey virus that they had received from researchers from the New England Regional Primate Research Centre in Massachusetts had contaminated their cultures.

A paper by Harry Kestler and colleagues from the primate centre points out that Essex's HTLV-4 and STLV-3 are both 99 per cent identical to SIV, which was discovered by researchers from the centre in 1985. Kestler and colleagues say that Essex's viruses "are not authentic, but were derived from cell cultures infected with [SIV]".

This resolves a mystery that has haunted virologists ever since Essex and Kanki announced STLV-3 and HTLV-4. Other researchers could not isolate an AIDS virus from African green monkeys using the same techniques as Essex and Kanki. Eventually, researchers in Japan did isolate a virus from this species of monkey but it turned out to be quite distinct from the virus Essex said he had isolated from green monkeys. The true virus is called SIV_{AGM}.

Another mystery was the relationship between HTLV-4 and the second type of true AIDS virus infecting humans, HIV-2. Kestler and colleagues now explain that these are not the same virus.

Essex's problem was that he was able to detect antibodies to a new virus in Senegalese prostitutes, but he had failed to go a stage further and isolate the correct virus from the blood. Inexplicably, SIV contaminated these blood samples, and Essex mistook this virus for the virus that was causing the production of antibodies in these prostitutes. A similar contamination must have occurred in his earlier isolation of STLV-3 from African green monkeys. (Extracted from New Scientist, 25 February 1988)

Increased sensitivity of polymerase chain reaction technology

One immediate application of Cetus Corp.'s polymerase chain reaction (PCR) technology is in detecting the latent AIDS virus (HIV). The virus can be present in the body but remain inactive or dormant for long periods of time. For that reason, it is important to detect the viral DNA which is present even when the virus is latent.

Finding the DNA is very much like looking for the proverbial needle in a haystack. Using PCR technology, scientists can copy target DNA sequences, leaving other DNA sequences untouched, in a replication chain which generates a massive increase in the copies of target DNA.

Cetus has now reported significant improvements in the specificity, efficiency and sensitivity of its PCR gene amplification technology using a heat-stable enzyme that synthesizes DNA. PCR involves as many as 30 repetitive heating and cooling cycles. Each cycle reaches high temperatures that inactivated the DNA polymerase enzyme previously used in the reaction. This inactivation made it necessary to add the enzyme at the beginning of each subsequent cycle, a cumbersome and time-consuming procedure.

Cetus scientists have got around this problem by isolating a DNA polymerase from the bacterium Thermus aquaticus, which thrives in hot springs. This heat-stable enzyme, known as Taq polymerase, does not inactivate at high temperature, eliminating the need to replenish the enzyme after every PCR cycle. As a result, the simplified PCR procedure is likely to find a broader range of applications in molecular biology, diagnostics, genetic disease research and forensics.

This increased sensitivity is extremely important in AIDS, since the AIDS virus is a retrovirus. Retroviruses incorporate their genetic information into the host's DNA, where they may be latent for long periods of time. Thus the virus itself cannot be detected; the only trace of the virus is in the DNA in the nucleus of the host's cells. Since PCR permits the amplification of viral DNA from one infected white blood cell among hundreds of thousands of normal cells, it is now possible to detect the virus even when latent. Cetus and Eastman Kodak are seeking approval for the PCR-based diagnostic test from the US Food and Drug Administration.

The PCR procedure also has many potential applications in forensic science. Other applications include work on 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. (Source: Biotechnology Bulletin, Vol. 7, No. 1, February 1988)

Lasers could kill pathogens in stored blood

Lasers might be used to kill pathogens in stored blood, according to the US Department of Defence, which is promoting the technology as a spin-off from SDI. The technique is said to have a 100 per cent viral kill rate without any detectable damage to normal blood components. The treatment uses a dye to sensitize the viruses to a xenon arc laser. The dye binds to viral particles, and exposure to the light initiates a chemical reaction that destroys the viruses. The treatment, developed by researchers at Baylor Research Foundation, Southern Methodist University and Southwest Foundation for Medical Research, is effective against the viruses that cause measles, herpes and AIDS. The system might be commercially available in two to five years. (Extracted from Science News, 13 February 1988)

Virus prevents diabetes in mice

A virus can prevent diabetes in mice that are genetically prone to type I diabetes, according to M.B.A. Oldstone of the Research Institute of Scripps Clinic (La Jolla, CA). The mice develop fatal type I diabetes within the first six months of life. An autoimmune process attacks the pancreatic cells that produce insulin, but infecting the mice with lymphocytic choriomeningitis virus that attacks helper T-cells prevented the development of diabetes. Apparently the virus prevents the T-cells from attacking the pancreatic cells. (Extracted from New York Times, 9 February 1988)

Granted partial immunity from hepatitis?

Scientists at the Medical College of Wisconsin in Milwaukee and the University of Wisconsin in Madison report that periodic boosters of hepatitis B vaccine may be needed to maintain sufficient immunity against the virus. Mary M. Horwitz and her co-authors, after finding certain factors may influence the duration of immunity in previously vaccinated individuals, tested the efficacy of a low-dose booster vaccine in a group of hospital employees.

Of the 245 individuals studied three years after their primary vaccination, 38 per cent had antibody levels so low they may no longer be protected, say the scientists. Factors directly associated with these low levels were older age, smoking and greater body weight. After receiving a single booster dose of vaccine, 78 per cent of the employees with low antibody levels developed high levels within one month.

Although scientists have known that various groups respond differently to hepatitis B vaccination, the current study showed a surprisingly high percentage who either had not responded well after the first vaccination, or had lost antibodies over time. (Source: Science News, Vol. 133, 6 February 1988)

Retroviruses linked to breast cancer

Researchers at the University of Liverpool have found new evidence for a link between retroviruses and breast cancer. Eddie Al-Sumidaie, Sam Leinster, Tony Hart, Chris Green and Kevin McCarthy have seen particles resembling retroviruses in cells taken from women with breast cancer. They have also found biochemical evidence of viral activity in the fluid in which the women's cells were grown. The evidence is the strongest yet of a possible role for retroviruses in causing human breast cancer.

Should future research confirm this, doctors may find new ways to treat the disease, which affects about 9 per cent of women in the Western world. The idea that retroviruses may be involved in breast cancer is not new. It arose in the 1930s when researchers showed that mice bred for susceptibility to breast cancer develop the disease if they are breast fed by female mice with mammary tumours. The substance in the breast milk was filtered out and shown to be a retrovirus. This was later called murine mammary tumour virus (MMTV).

Al-Sumidaie and Leinster were studying monocytes, specialized migratory scavenger cells of the immune system. Breast tumours spread, or metastasise, in the body when tumour cells become dislodged, enter the bloodstream and are deposited at a site suitable for growth.

The two surgeons wanted to find out whether monocytes could help to prevent metastasis. They noticed that monocytes from women with breast cancer did not migrate as well as monocytes from healthy individuals. Another attribute of monocytes is their ability to ingest foreign matter. This ingestion, called phagocytosis, was also less efficient in monocytes taken from breast cancer patients. The first hint that those monocyte abnormalities might be due to infection by retroviruses occurred when the researchers accidentally left the cells incubating for six days instead of the usual three.

They found that many of the cells had fused to form giant cells. One reason why monocytes should form giant cells is infection by retroviruses. The researchers investigated monocytes from 32 women with breast cancer and those from 27 healthy women. Electron micrographs of the monocytes from breast cancer patients revealed particles of the same shape and size as that of Human Immunodeficiency Virus (HIV), the retrovirus that causes AIDS.

The monocytes from breast cancer patients also contained enveloped particles with a fringed surface similar in size to known retroviruses. The genetic material of retroviruses is RNA. In order for them to reproduce inside host cells they must incorporate themselves into the DNA of host cells. Thus a hallmark of retroviruses is their possession of an enzyme called reverse transcriptase which converts retroviral RNA into DNA.

Biochemists test for the presence of retroviruses with an assay that detects the activity of reverse transcriptase. If the monocytes contained retroviruses the fluid in which they were grown should show activity. The team found reverse transcriptase activity in the culture medium of monocytes in 97 per cent of the patients with breast cancer compared with just 11 per cent of controls. Despite growing evidence linking human cancers and viruses (human papillomavirus with cervical cancer and Epstein-Barr virus with nasopharyngeal cancer, for example) there is little that links retroviruses to human cancers. The association between the retrovirus HTLV-I and adult T-cell leukaemia is possibly the only exception. Certain of the retrovirus class, however, are known to cause malignancy in animals; MMTV and feline leukaemia virus are examples. The researchers stress that their findings are only preliminary. The particles seen in the electron micrographs could be membranous vesicles as retroviruses. (Source: New Scientist, 14 January 1988)

Interaction with other infections is becoming clearer

AIDS may be causing a resurgence of tuberculosis in many parts of the world, officials of the World Health Organization believe. Other diseases, such as malaria and leprosy, may also be more common or more severe in people infected with the human immunodeficiency virus. These diseases could also hasten the onset of AIDS in people infected with HIV.

Doctors and scientists gathered at the end of 1987 in Nairobi, Kenya, to discuss links between AIDS and tropical diseases at a meeting organized by the WHO's Global Programme on AIDS and the Tropical Disease Research Programme, which is run by the WHO. The WHO chose Africa as the venue for the meeting for several reasons.

First, Africa is the continent most affected by the main tropical diseases. It also has nearly 9,000 registered cases of AIDS. This figure represents 12 per cent of all 75,500 cases of AIDS reported from around the world by January 1988; the estimated number of people with AIDS is at least twice that.

Furthermore, of the 5 to 10 million people in the world believed to be infected with HIV, an estimated two million are in Africa. In Central and East Africa, between 5 and 20 per cent of the adult population in towns are believed to be carrying the virus.

Some of these countries also suffer a high incidence of tuberculosis infection. WHO estimates that there are 10 million new cases of this disease a year in over 135 of its 166 member States. In Africa, there are around 140,000 cases of tuberculosis reported each year - probably only a tenth of the true total.

Jonathan Mann, director of the Global Programme on AIDS, explained how HIV can influence the course of tuberculosis. "There is strong evidence," he said, "that HIV infection can allow a hitherto silent tuberculosis infection to develop into full-blown tuberculosis disease." He cited several observations that suggest a link between the two diseases:

. Wherever tuberculosis infection is widespread, the disease is becoming more common among people aged between 20 and 40, the age group most at risk for infection with HIV.

. In the US, the number of new cases of tuberculosis took an unprecedented jump in 1986 to a record number of 22,768 cases. Until that year, the rate had been steadily declining.

. Similarly, in New York City, new cases of tuberculosis increased by 36 per cent (from 1,630 to 2,223 cases) between 1984 and 1986.

. In Kinshasa in Zaire, studies have shown that up to one third of patients with tuberculosis are infected with HIV. This rate is five times that of the general population living in cities.

Between 30 and 50 per cent of the adult population in many African countries probably have "silent" infections with the bacterium that causes tuberculosis. The immune system normally keeps this micro-organism in check. HIV might also be transmitted to a patient with tuberculosis who is receiving injections of antibiotics.

Tuberculosis may be more difficult for doctors to diagnose in people infected with HIV. Usually, the immune system confines the disease to the patient's lungs. In someone whose immune system is depressed, the disease may spread more freely to other organs, such as the brain and spinal cord, the bones and joints, and the kidneys.

The fact that African doctors said they were seeing a lot of tuberculosis just before AIDS exploded to epidemic proportions illustrates just how confusing the two diseases can be.

Infection with HIV may also influence the outcome of other tropical diseases, such as malaria and leprosy. Some doctors have reported that when people infected with HIV get malaria, the disease is more severe than usual. However, Mann believes that the evidence for a direct link between malaria and AIDS is scanty. The connection may lie with contaminated blood transfusions aimed at treating the anaemia that is often associated with malaria.

Tore Godal, the director of the Tropical Disease Research Programme, is a leading immunologist and expert on leprosy. He says that infection with HIV could influence any infection that normally provokes a strong immune reaction.

One reason why such interaction could take place is that the micro-organisms responsible for many diseases prevalent in the tropics live and multiply in macrophages. (Source: New Scientist, 4 February 1988)

Feline immunodeficiency virus

Cats can develop and die of immunodeficiency disease within three to four weeks of receiving an injection of a cloned hybrid virus. "Variant form" viruses that appear in the bone marrow of cats right

before the onset of disease were isolated by Julie Overbaugh and colleagues of the Harvard School of Public Health and Colorado State University from fresh tissues; these viruses were unable to replicate on their own in vitro but could be "rescued" for replication by "common form" viruses (that typically cause viremia but not immunodeficiency disease). The most pathogenic-defective variant viruses had subtle sequence changes in the extracellular glycoprotein gene and the long terminal repeat associated with the envelope gene when compared with minimally pathogenic helper type viruses. Overbaugh et al suggest that some highly pathogenic human immunodeficiency viruses might also, by analogy, be replication-deficient and that the AIDS viruses commonly studied may represent only a selected subpopulation, those capable of in vitro replication and not toxic for host cells. If AIDS virus isolates could be obtained and evaluated directly from fresh human tissues rather than after in vitro propagation, it might be possible to better understand their structures and activities. (Source: Science, Vol. 239, 19 February 1988, p. 906. Copyright 1988 by the AAAS.)

Cat AIDS crosses the Atlantic

A virus related to the AIDS virus but which affects cats, is reported to have surfaced in Britain. Feline immunodeficiency virus (FIV), was discovered last year in California. Tim Gruffydd-Jones and colleagues at Bristol University report the first case in Britain.

The team is keen to emphasize that the disease is not transmittable to humans, even though the feline disease shows similar effects and is almost certainly related.

The cat was a neutered female domestic shorthair aged eight years. It was sent to the veterinary school after an 18-month illness. The symptoms included fever, lethargy, lack of appetite and proneness to secondary infections. These were relieved by antibiotics, but after five months there was no improvement and the cat was destroyed.

Virus particles which resemble FIV were found in the blood. Tests to confirm this are being carried out at Glasgow Veterinary School, and a survey is under way to see how common the infection might be among cats. The disease has probably been around for some time. It may have accounted for some infections attributed to feline leukaemia or other disease. Feline leukaemia has been called "cat AIDS", although the agent that causes it is not related to the human virus. (Source: New Scientist, 4 February 1988)

Research instrumentation

Optical tweezers pluck living organisms

Researchers at AT&T Bell Laboratories in New Jersey have developed an optical technique to trap and manipulate living organisms. The technique will enable microbiologists to carry out experiments on living micro-organisms that are not possible at present.

Arthur Ashkin and his colleagues have trapped micro-organisms in a laser beam for the first time without damaging them. This technique is known as laser trapping. The technique is said to be "so elegant and so simple" that any university could develop such a tool for its microbiologists.

In a laser trap, particles are pushed to the centre of a laser beam by radiation pressure. The centre of the beam is, in effect, the eye of a radiation storm from which particles cannot escape. As the laser beam is moved the particles trapped in the centre are dragged along with it.

It is only recently, however, that the researchers have trapped living organisms without damaging them. Previously, laser beams were too hot and cooked the organisms they trapped.

Ashkin overcame this problem last year using an infrared laser. Micro-organisms are relatively transparent to infrared radiation and are unaffected by an infrared laser beam at low powers.

Ashkin discovered this fact when he was studying some non-living particles that were trapped by an infrared laser. He noticed that there were bacteria in the sample.

Ashkin then carried out further experiments on micro-organisms. In these he observed the reproduction of the bacterium Escherichia coli and yeast cells.

Ashkin points out that the technique is suitable for more than just observing micro-organisms. In a series of experiments last year, he demonstrated that the technique was a tremendously powerful tool for manipulating micro-organisms.

In a recent series of experiments, Ashkin dragged a bacterium into a glass fibre so that it could be introduced into another sample. Ashkin found that by using two laser beams he was able to hold both ends of a rod-like bacterium and rotate it.

He suggests that particles found within the cell could be trapped and used as probes to map out fine details of the internal structure of the cell. (Source: New Scientist, 21 January 1988)

Protein separation scale-up

With advanced matrix design and unique column construction techniques, Dominick Hunter are introducing a new technology for chromatography - Shallow Bed Liquid Chromatography (SBLC). This provides fast, high performance, low-pressure liquid chromatography of proteins. MEMSEP 2000 makes this technology available to users who need to scale up their laboratory processes. Details from: Paul Rogers, Dominick Hunter Molecular Separations, Dominick Hunter Filters Ltd., Durham Road, Birtley, Co. Durham DH3 2SF or on 091 410 5121. (Source: Biotechnology Bulletin, Vol. 7, No. 2, March 1988)

Laser beam used to cut chromosomes

Hamamatsu Photonics and the Japanese National Institute of Agro-Environment Science have successfully used a laser beam to cut chromosomes at any desired site. The method could significantly ease mapping of the human genome. The argon laser is controlled by a computer. Pieces cut off must be at least 0.3 microns long. The cut-off portions can then be separated by centrifugation. (Extracted from Japanese Chemistry, 28 January 1988)

An automated system purifies monoclonals

A high-speed automated system, MabLab, for purifying monoclonal antibodies, has been introduced by Oros Systems (Cambridge, Mass.). The system uses developments in artificial intelligence, chemical engineering and biochemistry to purify an uncharacterized monoclonal to 95 per cent purity, a level sufficient for all except therapeutic uses. Purification is completed within a matter of hours, says Oros, giving yields of up to 2 grams/day with minimal losses, an important consideration, since crude antibody can cost well over $3,000/g. MabLab employs affinity chromatography that uses Protein A - a component of the cell wall of Staphylococcus aureus - as an affinity ligand. Current manual purification of monoclonals requires a week or more to

purify each new monoclonal. The most widely used manual method involves precipitation of proteins from a crude antibody mixture, followed by ion exchange chromatography and, generally, gell filtration. The MabLab will be priced at about $100,000. (Source: Chemical Week, 2 March 1988)

Novel automatic gene amplification system

Cetus and Perkin-Elmer have jointly introduced an automated gene amplification system based on the polymerase chain reaction (PCR) technique. The system includes the GeneAmp research reagent kit, which provides a heat-stable DNA polymerase and other reagents, and the DNA "thermal cycler", a microprocessor-controlled temperature cycling instrument that performs the rapid temperature changes and incubations needed for PCR gene amplification. By using the heat stable enzyme (derived from the organism Thermus aquaticus), researchers can avoid the expensive, cumbersome task of adding new enzymes after every PCR cycle. According to Cetus, the new system can amplify a target DNA sequence in hours against the days or weeks typically required by conventional methods. Potential applications for the new system include DNA cloning, the expression of new proteins, research into genetic disorders, forensic analysis of tissue samples, tissue typing and the development of diagnostic tests for infectious diseases such as leukaemia and AIDS. (Extracted from Chemical Marketing Reporter, 30 November 1987)

Computer screening reprieves test animals

Researchers at the University of Surrey are offering to pharmaceuticals companies a rapid test to screen out compounds that are likely to exhibit particular toxic effects. The scientists claim that their method would have been able to predict such toxic effects of the anti-arthritic drug benoxaprofen (Opren).

The new method of predicting whether potential drugs will be toxic to humans may one day allow pharmaceuticals companies to reduce the number of tests they do on animals to meet current regulations.

David Lewis, Dennis Parke, and Costas Ioannides, of the university's department of biochemistry, identify potentially toxic compounds by examining computer graphics. They are now combining information on the electronic structure of a molecule with details of its three-dimensional conformation to improve the accuracy of their predictions.

The aim of the test is to find out which of the two families of enzymes, universal in human cells, is capable of breaking down the compound. The enzymes in these groups break down 95 per cent of organic compounds - such as cigarette smoke or petrol fumes - that enter the body. Much of this type of metabolism takes place in the liver, which is why this organ is often the first to suffer from a toxic drug.

The two families of enzymes are called the cytochromes P450 and the cytochromes P448. Cytochromes P450 metabolise organic compounds into an innocuous form which the body can easily eliminate. Cytochromes P448, on the other hand, activate the substances into forms which can interact with DNA, so causing cancer.

Initial research showed that molecules which are flat and thin, such as benoxaprofen, fit into the active site of the cytochromes P448. But globular molecules are more suitable substrates for the cytochromes P450.

As a result, modelling the shape of the molecules with the help of computer graphics can help researchers to predict which group of enzymes will break down a certain compound in the body. However, the team is now also incorporating additional information on the electronic structure of the compound.

Using one of the factors is insufficient on its own but with both, the team says that it can differentiate between substrates of cytochromes P450 and P448 with 95 per cent accuracy. (Source: New Scientist, 3 March 1988)

Superconducting biomagnetic measurement system

Shimadzu Corporation and Tokyo Denki University have jointly come out with a multi-channel superconducting quantum interference biomagnetic system capable of simultaneously measuring up to seven channels of feeble magnetism generated by living bodies.

The brain, heart, eyes, lungs and limbs of human beings and animals are known to generate feeble magnetic fields. The magnetism is generated by action from the activation currents of cardiac muscle and nervous cells and the magnetization of accumulated magnetic substances. The activation currents are generated by the movements of ions (charged particles) inside and outside the cells when these cells are activated, which generate feeble currents. The electrocardiogram is obtained by measuring the potential difference on the body surface generated by the activation currents of the heart. Brain waves are obtained by measuring the potential difference on the skull's surface that is generated by the activation currents of the brain.

The feeble magnetic fields generated by the activation currents exert their influences even outside living bodies. Therefore, by measuring these feeble magnetic fields externally, various information relating to the internal activities of bodies can be very accurately known by the non-invasive method.

The newly developed superconducting biomagnetic measurement system enables the information from seven specific signal sources to be measured simultaneously in real time. It is therefore highly effective for mapping the body's magnetic field distribution and for pinpointing the locations from where these signals are being generated inside the body.

The system uses a secondary differential form pickup coil that has a pronounced effect in eliminating the influences of external magnetic fields. Thus, measurements can be performed almost anywhere without having to use a special chamber such as a magnetically shielded chamber.

A superconducting quantum interference device (SQUID) that is presently attracting attention as a sophisticated superconducting electronic element is used as this system's magnetic sensor. This sensor uses a quasi planar Josephson junction, the RF-SQUID, developed by the company jointly with the Institute of Physical and Chemical Research. It is made entirely of niobium, which features an excellent heat cycle stability between cryogenic temperatures and room temperature.

By merit of these outstanding characteristics, the system is expected to lend itself to diverse applications, including the diagnosis of cerebral maladies such as epilepsy and senile dementia, the discovery of various kinds of physical abnormality in

connection with the heart and eyes, and the diagnosis of infant heart and cerebral irregularities. (Source: JETRO, December 1987)

High-resolution hydroxyapatite column for high-performance liquid chromatography

Toa Nenryo Kogyo K.K. has developed a new hydroxyapatite column and put it on the market as a separation medium for high-performance liquid chromatography. The new column product features an excellent capacity for separating proteins, nucleic acids or carbohydrates.

The hydroxyapatite granule developed by the company is completely spherical and porous, and has the average of 2 or 5 micron particle size. The new column packed with the granule is mechanically strong enough to show the pressure limit of 150 kg/cm^2, and has excellent chemical stability. It is, therefore, an extraordinarily efficient column for rapid separation of biopolymers such as proteins (especially monoclonal antibodies), peptides, nucleic acids, amino acids and enzymes. The column is also stable in many denatured reagents, such as SDS or urea. Therefore it is applicable to separate membrane proteins or nucleic acids in the presence of the denatured reagents.

As compared with existing analytical columns available on the market, the new hydroxyapatite column has about 10 times longer life expectancy than the other hydroxyapatite columns. (Source: JETRO, December 1987)

Biosensor with long service life

NEC Corporation has come out with a biosensor featuring a long service life expectancy which can be used repeatedly. It enables measurement of blood sugar values speedily from an extremely small sample of blood. In the future, it is expected to be used as a sensor in artificial internal organs through an integration of its control circuit.

Biosensors integrate a pair of field effect transistors on one side of a sapphire wafer, and on the other side a thin film containing a glucose oxidase enzyme. When the sensor comes into contact with glucose in the blood, an electric potential of different magnitude is generated allowing the blood sugar value to be read out from the potential difference.

A major disadvantage of this type of sensor is that accurate measurements become impossible when proteins in the blood adhere to the sensor's surface. Thus, it does not lend itself to repeated use.

To overcome this obstacle, NEC Corporation covered the biosensor's sensing section with a thin film of albumin, a type of protein which prevents the biosensor's properties from deteriorating. (Source: JETRO, January 1988)

Moderately priced multifunctional biosensor

Associate Professor T. Katsube and his research group of the Engineering Faculty's Electronic Engineering Department, Saitama University, Japan, have developed a multifunctional biosensor capable of simultaneously sensing the quantities of sugar and urea existing in the blood.

This is a new type of sensor that fixes several enzymes independently on a small chip by the manufacturing method known as the "electrolytic polymerization method". More specifically, the sensor's sapphire wafer is arranged with several gate electrodes, each provided at its tip with an enzyme-immobilizing film that enables various kinds of substances to be sensed simultaneously.

The enzyme-immobilizing film is produced by immersing a sapphire wafer fitted with gate electrodes and platinum electrodes into an aqueous solution containing pyrrol and enzyme. A voltage of about 1.1 V is then impressed on the solution. The pyrrol is polymerized, and a thin polypyrrol film containing enzymes is grown on the wafer. By impressing the voltage on only specific gate electrodes on the sapphire wafer, it is possible to produce the film only on those electrodes, thereby enabling separate enzyme films to be created accurately on the individual electrodes.

The research group succeeded in immobilizing glucose oxidase, a glucose decomposition enzyme, by the same method, and is presently engaged in further research to immobilize urease, a urea decomposition enzyme.

The associate professor claims that the biosensor can be produced for less than 100 apiece, and that a disposable biosensor will, in all probability, be commercialized. (Source: JETRO, January 1988)

Plant tissue culturing system

Toyobo's (Japan) new Plantex plant tissue culturing system includes a polyester fibre mat and a polystyrene vessel. The mat supports a culture in liquid media. Cell growth is excellent because nutrients and oxygen are transferred quickly. If culture conditions have to be modified the medium can be changed without transplanting the cells. The fibre mat measures 58 x 58 x 4 mm and the vessel 60 x 60 x 20 mm. The system costs 100. (Extracted from Japan Economic Journal, 20 February 1988)

Electrical cell-fusion apparatus

Nihon Bunko Kogyo (Tokyo) has begun marketing a continuous-flow electroporation and electrical cell-fusion apparatus to speed the introduction of foreign DNA into cells and enable the rapid creation of hybrid cells. The device, marketed under the name CET200, is reported to be the first of its type and will permit the large-scale processing of cells. The heart of the device is a flow chamber sandwiched between two panel electrodes. The use of panel electrodes allows the establishment of a stable, homogeneous electrical field within the chamber, which dramatically improves the efficiency of electroporation and cell fusion. According to the company, hybrids between protoplast-derived tobacco leaves and carrot roots can be obtained with a yield of 10 per cent at a processing rate of 100,000 cells per minute; foreign DNA can be introduced into cells with 95 per cent efficiency at a processing rate of 100,000 cells per minute. Nihon Bunko Kogyo anticipates selling about 100 of the $20,000 units during the first year. (Source: Bio/Technology, Vol. 6, January 1988)

Magnetic imaging homes in on early cancers

Cancer alters a person's blood chemistry in a way that shows up on images produced by nuclear magnetic resonance (NMR), according to a researcher at Beth Israel Hospital in Boston. Experiments with plasma now suggest that these imaging machines may be able to diagnose cancer at an early stage.

Eric Fossel, associate professor of radiology at Harvard Medical School, reported recently that his technique can now detect cancer 97 per cent of the time. At a meeting on cancer research at the National

Institutes of Health in Bethesda, Maryland, Fossel reported the results of tests on 2,127 people. Fossel compared the blood plasma of people with benign and malignant tumours against that of normal controls.

The spectra of methyl and methylene compounds in plasma show a consistent linewidth of about 30.5 hertz in patients with malignant tumours. Plasma from patients with benign tumours, however, show a spectral linewidth of 36.8 hertz. Linewidths for normal controls were easily distinguished at 40.1 hertz. Fossel puts the threshold for cancer at 33 hertz.

Fossel has no firm explanation for the change in these lipoprotein lipids, but he speculates that the change in blood chemistry is not created by the tumour itself but by the body's response to cancer. Chemo- and radio-therapy also appear to alter the readings on the NMR; as a tumour recedes, the linewidths increase. When patients relapse, the linewidths decrease again.

Fossel's technique cannot distinguish between different types of cancer. Furthermore, pregnant women and patients with benign prostatic hyperplasia showed the same linewidths as patients with malignant tumours. Fossel notes that people with high levels of triglycerides or those suffering from gram-negative shock produce false positive readings.

Currently Fossel has detected cancer only in patients who already have tumours. He has induced cancer in guinea pigs, however, and says he has detected the disease when the cancer has proliferated to about 1 million to 10 million cells.

Fossel hopes to hone his technique to detect cancer before a solid tumour shows up and to screen people at risk of cancer. (Source: New Scientist, 4 February 1988)

Du Pont's DNA sequencer employs fluorescent nucleotide analogues

Du Pont's new automated instrument for sequencing DNA chains represents the sort of technological advances that the US National Academy of Sciences says is needed throughout the human genome project. The sequencing system, which the company began shipping last month, centers on some clever chemistry that allows computerization of a process that had been painfully slow. The Du Pont sequencer has been deemed "elegant" by Leroy E. Hood, professor of biology at California Institute of Technology and one of the developers of a competing automated system marketed by Applied Biosystems Inc. (ABI) of Foster City, Calif.

The automated systems are modifications of the widely used enzymic sequencing technique that was developed in 1977 by Frederick Sanger and co-workers at the Medical Research Council in Cambridge, England. The enzyme in question is DNA polymerase, which uses a single strand of DNA as a template to make the complementary strand of the double helix from the four nucleotides deoxyadenosine 5'-triphosphate (dATP), deoxyguanosine 5'-triphosphate (dGTP), deoxythymidine 5'-triphosphate (dTTP), and deoxycytidine 5'-triphosphate (dCTP).

In the Sanger enzymic sequencing method, a single strand of the DNA chain whose sequence is to be determined is used as the template. But instead of complete complementary strands being synthesized, the process is interrupted by chain-terminating nucleotides that block further growth.

Four different reactions are carried out. Each employs a primer DNA sequence and radiolabeled dATP, dGTP, dTTP, and dCTP, but uses a different chain-terminating analogue that corresponds to one of the four nucleotides. The chain terminators are 2,3-dideoxynucleotides that lack the 3'-hydroxyl group needed to form a phosphodiester bond. Therefore, whenever the enzyme encounters a chain terminator instead of a normal nucleotide, the growth of the DNA chain is arrested.

The resulting products from each reaction are a mixture of DNA fragments of varying lengths. For example, the reaction to which the dideoxy analogue of dATP is added produces a family of oligonucleotides that all end with dATP.

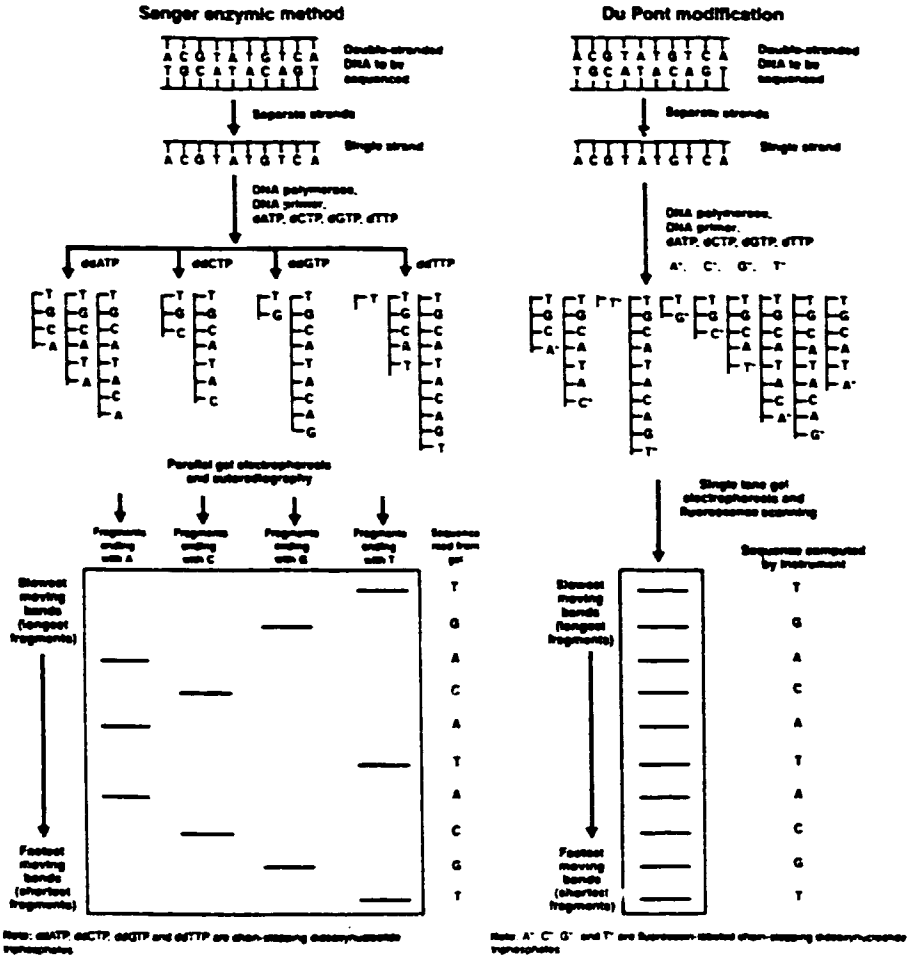
The mixtures are separated by polyacrylamide gel electrophoresis, a technique that can resolve DNA fragments differing in length by a single nucleotide. The bands on the gel are visualized by autoradiography, a slow process that takes days. Each band is a DNA fragment ending with a known base, whose length can be determined by the distance it travels in the gel. An experienced worker can interpret the DNA sequence from the gel pattern.

The Du Pont system also uses DNA polymerase and chain terminators to make a family of partial complementary copies of the DNA to be sequenced. Du Pont's dideoxy chain terminators, however, are tagged with fluorescein dyes. Each emits light of a slightly different wavelength when excited by an argon laser.

Because the chain terminators can be distinguished by their emission spectra, the Du Pont system combines all four in one pot rather than using separate reaction chambers. The resulting mixture of DNA fragments is separated on a single lane of a polyacrylamide gel. The identity of the nucleotide terminating each band on the gel is then determined by its characteristic fluorescent emission.

Using fluorescence rather than autoradiography to visualize the bands allows the electrophoresis gels to be read as soon as they are run. The Du Pont sequencer employs a scanning system that can read up to 12 lanes of a gel at a time - that is, 12 different DNA chains can be sequenced at once. The data are fed to a microcomputer that reconstructs the DNA sequences according to the order of appearance of each fluorescence signal.

The ABI instrument also makes use of fluorescent tags - not in the chain terminators, like Du Pont's, but in the short primer oligonucleotides needed to initiate DNA synthesis. Du Pont asserts its system allows more flexibility and minimizes errors. None the less, ABI's system also capitalizes on computer-controlled data acquisition and analysis for speed. Indeed, both firms claim their sequencers can identify about 10,000 nucleotides per day. In contrast to the average of about 50,000 nucleotides per year that the National Research Council estimates a skilled worker could identify using the established Sanger methods, that speed is remarkable.



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Instrument for faster testing

A new instrument has been patented (US 4,721,335) to run simultaneous tests on 60 human tissue specimens by pathologist D.J. Brigati of Pennsylvania State University's medical centre (Hershey, PA) for Fisher Scientific (Pittsburgh, PA). Stained slides are produced for diagnostic examination much faster than using current manual methods (1.5-2.5 hours, versus days). (Extracted from New York Times, 19 March 1988)

General

Enzymic catalysis in supercritical fluids

The rate of enzymic oxidation of cholesterol in supercritical carbon dioxide is increased by co-solvents that enhance cholesterol aggregation, according to a team of researchers from the department of chemical engineering at the University of California, Berkeley. T.W. Randolph, Douglas S. Clark, Harvey W. Blanch, and John M. Prausnitz note that experiments using supercritical fluids can offer insight into the interactions between enzymes and solvent because small changes in pressure or temperature near the critical point can result in large changes in solvent properties. They used electron paramagnetic resonance spectroscopy with spin-labeled enzyme and cholesterol to study the conformation of the enzyme. The rate of reaction increases when cholesterol is more tightly aggregated, as it becomes when isobutyl or tert-butyl alcohol is used as a cosolvent. (Reprinted with permission from Chemical and Engineering News, 25 January 1988. Copyright (1988) American Chemical Society.)

Picture of HIV infection in US

At the request of the White House, a team of epidemiologists from the Centres for Disease Control (CDC) recently performed an intense review of the numerous studies that measure rates of infection for human immunodeficiency virus (HIV) in the United States. CDC concluded that the AIDS epidemic continues to focus on the established risk groups, whose ranks are filled by homosexual men and needle-sharing drug abusers and their sexual partners. As for heterosexuals in the so-called "general population", the rate of infection remains remarkably low, or a fraction of 1 per cent. How long this lull in the AIDS storm will last is not known.

The CDC report is the first to pull together all the surveys that are complete or currently under way, published or unpublished. Indeed, the phrase "personal communication" is the most frequent reference citation in the report. In an attempt to be truly comprehensive, hundreds of sources were canvassed during October 1987. The data come from local health departments, federal agencies, and medical research institutes.

However, CDC warns the White House that large gaps in knowledge still exist. The report correctly states: "The various surveys and studies differ in sampling, inclusion and exclusion criteria for subjects, rigour of ascertaining risk information, and

resulting bias. The results, therefore, cannot always be validly compared". Regardless, the CDC report does paint a picture, or rather a montage, of current HIV infection in the United States, and as such it is a useful document even though the image may be a bit impressionistic. (Extracted from Science, Vol. 239, 15 January 1988, p. 253 by W. Booth. Copyright 1988 by the AAAS.)

Fixing nitrogen

Nitrogen accounts for roughly 78 per cent of the air that we breathe. But this nitrogen is useless to the living cells of almost all plants and animals, which rely on a select group of organisms - most notably blue-green algae and the bacteria on the roots of alfalfa and peanuts - that can "fix" nitrogen, or combine it with other elements into a biologically useful form. Traditionally, atmospheric scientists have thought that these organisms were the major source of fixed nitrogen but one group of researchers has found that lightning may be doing as much as half of the job.

Edward Franzblau and his colleagues at the New Mexico Institute of Mining and Technology in Socorro, measured the nitrogen compounds produced by lightning and found that each lightning flash fixed more nitrogen than had been previously predicted. By multiplying the molecules fixed per flash by the average number of lightning flashes on earth - approximately 100 per second - they calculated that lightning produces about half the score of fixed atmospheric nitrogen.

The measurements are difficult and even dangerous. Because these measurements are unconfirmed and contradict airborne measurements of nitrogen compounds produced by lightning, some scientists question the new conclusions, but others believe the findings warrant attention. (Source: Science News, Vol. 133, 2 January 1988)

Gold-filled discovery in transplants

Tissue transplantation may have a shining future - if gold proves to be as precious as recent research on neural transplants suggests. By filling envelopes made of viruses with colloidal gold and fusing them with nerve cells, scientists at the University of South Florida in Tampa have been able to track the migration of transplanted cells and measure their survival.

Used for years as a cell marker, the gelatin-like colloidal gold is easily distinguished by its yellow or bright white appearance through a microscope. Gary W. Arendash and his co-workers took advantage of gold's shining qualities and devised a model system applicable to transplantation science. The researchers mixed gold with a solution of harmless Sendai viruses that had been broken apart by a detergent. Pieces of the viral envelopes spontaneously regrouped as detergent was removed, forming whole envelopes that contained the gold colloid. Made from a virus that avidly fuses to vertebrate cells, the gold-filled Sendai virus envelopes attached to neural cells that were later transplanted into rats.

By scanning transplanted tissue for signs of gold, the scientists were able to follow the migration of transplanted cells through areas of the rats' brains, and to determine that the transplanted cells survived at least three months. Both location and viability are crucial to understanding the fate of nerve-tissue transplants, which have attracted attention and controversy as potential treatments for conditions like Parkinson's disease. It should be possible to similarly label other types of cells used for transplants and that the gold/Sendai system might settle the debate over whether adrenal cells transplanted into the brain for treating Parkinson's actually survive, or instead release nerve-cell-stimulating factors before their death. (Source: Science News, Vol. 133, 20 February 1988)

D. APPLICATIONS

Pharmaceutical and medical applications

First trials for a malaria vaccine

A new and potentially cheap vaccine against malaria has been tested successfully in humans for the first time. Not only is it the first vaccine against the blood stage of the parasite to have been tested in humans, but it was isolated and synthesized at a laboratory in a developing country.

Much of the parasite's life cycle is spent inside cells and the best hope for the immune system is to catch it outside. The first chance comes when the so-called sporozoite stage is injected by the mosquito. But that only circulates in the blood for a few minutes before invading liver cells. It breaks out of the liver in the merozoite stage and invades red blood cells, where it multiplies many times and causes fever. In the third, or gametocyte stage, a biting mosquito sucks in the parasite and goes on to infect another person.

Teams around the world are trying to develop vaccines against all three stages. Gametocyte vaccines are under development, but they would not protect the individual; they would only prevent the parasites being transmitted.

Most work has concentrated on the merozoite stage in the blood, and that is the target of Manuel Patarroyo and his team at the Institute of Immunology at the Hospital San Juan de Dios in Bogota. They have spent several years chemically dissecting the malaria parasite and have produced and tested 60 per cent of all the proteins in the merozoite stage from Aotus monkeys. They identified four peptides that seemed to offer protection when given as a vaccine to the monkeys. Two of them seemed to delay the onset of malaria by about a week, the other two seemed to offer almost complete protection.

The researchers have recently produced a candidate for a human vaccine based on three of these chemicals and tested it in 13 volunteers from the Colombian armed forces. They were young and healthy, and were allowed to withdraw from the trials at any stage.

The results of the trial, though not conclusive, are hopeful. The three controls came off by far the worst, but three people given one particular combination of vaccine doses were completely clear of the disease within 21 days.

There is still a long way to go before a vaccine can be available for widespread use. The trials, both in monkeys and people, will have to be repeated by independent researchers. The formulation and dose will have to be perfected. It would cost under 20 pence a dose if produced on a large scale. (Source: New Scientist, 10 March 1988)

Vaccine fights malaria without antibodies

Researchers in the US and Switzerland have developed an experimental malaria vaccine that does not induce an antibody response, but rather concentrates on the cell-mediated aspects of immunity

to the disease. The new vaccine stimulates a completely different part of the immune response and is directed against a different stage in the parasite's life-cycle.

The malaria parasite, which infects more than 200 million people and threatens 800 million more, is increasingly resistant to the drugs currently used. The need for a vaccine is urgent.

During the past year, researchers have tested three vaccines on humans. All employed antigens known to stimulate the production of antibodies against various stages of the malaria parasite. The most recent advance was reported in March, when Colombian researchers tested the world's first vaccine against a blood stage of the malaria parasite and conferred partial immunity on three volunteers. The other two trials were also only partially successful.

Many scientists have pointed to a lack of correlation between levels of antibodies and immunity. At the end of last year, Louis Schofield and his colleagues at New York University Medical School showed that substances could kill malarial parasites in the liver itself without involving antibodies at all. They implicated a substance called gamma-interferon, which acts by stimulating cells to secrete substances that are lethal to parasites. The latest vaccine is also active against the liver stages and does not involve antibodies.

Jerald Sadoff and his colleagues at the Walter Reed Army Institute of Research in Washington have developed such a vaccine, working with scientists from Praxis Biologics, of Rochester, New York, SmithKline and French in Swedeland, Philadelphia, and the Swiss Serum and Vaccine Institute in Berne. They inserted the genes for malaria antigen, called the CS protein, into a harmless strain of the bacterium Salmonella typhimurium which then expressed the antigen. When animals take the antigen orally, macrophages take up these bacteria which then colonize the liver and induce a response to both the Salmonella and the liver stage of the malaria parasite. The researchers tried the vaccine experimentally on mice. The vaccine protected two thirds of the mice.

Although these experiments were carried out on mice, there is every reason to be optimistic about a similar vaccine for humans. The CS protein used in the vaccine has been shown to be safe and partially protective in humans, as have the Salmonella bacteria. The scientists have already shown that they can insert the gene for the CS protein of the human parasite Plasmodium falciparum into Salmonella and that it then expresses the malaria antigen.

Any really effective vaccine against an organism as complex as the malaria parasite is likely to have to contain components that elicit both antibody and cellular immune responses. This experimental vaccine may have brought this possibility a stage nearer. (Source: New Scientist, 5 May 1988)

Artemisia joins the antimalarial arsenal

A Chinese weed may provide doctors with a new, potent drug to treat malaria. The drug, called arteether, has proved effective against the malaria parasite, Plasmodium falciparum, both in vitro and in animal experiments. Doctors hope to begin clinical trials by the end of the year.

A committee of the World Health Organization that is responsible for developing antimalarial drugs instigated the work by American, Chinese, Swiss and British scientists in 1985.

Arteether is effective against the blood stages of the malaria parasite (the merozoites). So far, the drug does not look promising as a preventative measure. "To be practical," Cranfield says "for prevention, an antimalarial must stay in the blood for, say, a week, as chloroquine does, and continue to suppress the parasite as it enters the blood. All that we know so far about arteether suggests that it is shortlived and needs to be taken several times a day."

Arteether is a classic case of a drug developed because scientists noticed the medicinal effect of a natural product. For centuries the Chinese have treated people suffering from malaria with a preparation of the weed Artemisia annua. In 1972, Chinese scientists isolated the plant's active ingredient - a molecule they called qinghaosu, which contains a peroxide bridge. Arnold Brossi, the leader of the research, says that the peroxide group is essential to the drug's antimalarial activity, although scientists do not know exactly why.

Brossi, deputy director of the laboratory of analytical chemistry at one of the US's National Institutes of Health, and his colleagues have concentrated on producing a chemically very similar derivative of qinghaosu that is more potent and which the body assimilates more easily than the natural drug. Brossi's search for an analogue builds on work by Chinese chemists. Qinghaosu is only sparingly soluble in oil or water so the gut does not absorb it well. The arteether molecule retains the active peroxide group, but an ethyl ether group replaces an oxygen atom, making the molecule more lipophilic. The molecule is soluble in oil and can be administered as an intramuscular injection.

Scientsts assessed arteether's antimalarial activity in vitro against clones of two strains of the malaria parasite. One, which is common in Indochina, is resistant to the usual antimalarial drugs - chloroquine, pyrimethamine, sulfadoxine and quinine - but is susceptible to mefloquine. The other strain, prevalent in Sierra Leone, is also susceptible to mefloquine and resistant to chloroquine, pyrimethamine and sulfadoxine. In both cases, arteether proved twice as potent as the natural drug qinghaosu.

In tests on groups of mice carrying a range of strains of the parasites variously resistant to antimalarial drugs, arteether proved more potent than the natural drug. Scientists at the London School of Hygiene and Tropical Medicine are now running toxicity studies in mice, rats and dogs. The first clinical tests on people will be against cerebral malaria, the most deadly form of the disease.

If developing coutries are to buy arteether, it will have to be cheap. Currently, says Cranfield, the drug is expensive. SAPEC, a Swiss chemicals company, is participating in WHO's work and produces the relatively small quantities needed for experiments. Cranfield says that the producers of the weed in China need to team up with a large pharmaceuticals company to produce an affordable drug. Synthesis of the drug from scratch, says Cranfield, is cumbersome and difficult. (Source: New Scientist, 31 March 1988)

Recombinant vaccine shows promise against dengue fever

Scientists have reported progress in genetically engineering a vaccine for dengue fever, a severe viral disease of global significance that is beginning to spread to North America. Public health officials have expressed increasing concern about the mosquito-borne disease, which is endemic to much of Asia, Africa and

South and Central America. Development of a vaccine has been hampered, however, by a peculiar characteristic of the dengue virus: Antibodies against dengue tend to promote rather than prevent reinfection with closely related strains of the dengue virus.

Ching-Juh Lai, a researcher with the National Institute of Allergy and Infectious Diseases in Bethesda, MD., reported at a National Institutes of Health seminar that a novel approach to vaccine development has so far conferred complete protection against dengue in mice. The vaccine is now being tested on rhesus monkeys.

Most viral antibodies - whether naturally occurring or vaccine induced - recognize and bind to the outer envelope of a target virus. But strains of the dengue virus can bind to such antibodies and subvert them to enhance the virus's ability to infect human monocytes. Antibody-enhanced infection can lead to a potentially fatal syndrome involving internal bleeding, severe dehydration and shock.

Lai's approach is based on work by scientists at the University of Rochester (NY), who found that antibodies against a so-called non-structural protein, produced inside the monocytes to help assemble new viruses, can protect against dengue without enhancing re-infection later. The non-structural protein, dubbed NS-1, is produced in monocytes after a dengue virus "hijacks" the cells' genetic machinery. It is critical to virus replication but is never actually incorporated into new viral offspring. Although the mechanism of protection is not well understood, there is evidence that NS-1 antibodies recognize dengue-infected monocytes and destroy them before the virus has a chance to reproduce.

More than 100 million cases of dengue fever and its more severe form, dengue haemorrhagic fever, are estimated to occur each year worldwide. Concern about its spread to the North American continent was spurred by the recent introduction into 17 states of Aedes albopictus, a mosquito that can transmit the disease very efficiently. (Extracted from Science News, Vol. 133, 26 March 1988)

Enzyme to fight an immune disease

Enzon (South Plainfield, NJ) has filed its first new drug application with the Food and Drug Administration. The application involves the drug polyethylene glycol (PEG)-adenosine deaminase, which treats severe combined immunodeficiency disease (SCID). The disease - which affects children and is caused by a deficiency of the enzyme adenosine deaminase - is fatal unless children are kept in protective isolation or undergo bone marrow transplantation, an operation that is not always successful. SCID treatment with PEG-adenosine deaminase replaces the missing enzyme, which is essential for the differentiation of white blood cells that are critical to the immune system's function. Enzon's process involves attaching PEG to an enzyme, thereby disguising it from the body's immune system. That minimizes adverse side effects and allows the enzyme to remain in the body longer. (Source: Chemical Week, 3 February 1988)

GM-CSF to treat bone-marrow disorder

Immunex (Seattle, WA) has achieved good results using a blood protein to treat patients with a bone-marrow disorder. The naturally occurring hormone granulocyte-macrophage colony stimulating factor (GM-CSF) is said to boost growth of white blood cells, and was created by the biotechnology company using gene-splicing techniques. In an Immunex study, eight sufferers of myelodysplastic syndrome - a condition which stunts production of white blood cells by the bone marrow - were given constant intravenous GM-CSF on a two-week on, 2-week off schedule. Test results showed a raised white-cell count and reduced chances of infection. None of the patients in the tests progressed to leukemia.

Meanwhile, Australian researchers, at the Royal Melbourne Hospital and Ludwig Institute for Cancer Research, believe it could have applications in other areas where the immune system flags, such as in bone marrow transplants, leukaemia, burns, cancer and possibly AIDS. The hormone also protects patients against the side-effects of anti-cancer drugs. It ameliorates the usual decrease in white blood cells which follows the administration of the anti-cancer drug, melphalan. The hormone not only elevates the level of white blood cells, it also activates them to become better protectors against infection.

The hormone was originally isolated a decade ago by researchers from the Walter and Eliza Hall Institute of Medical Research and Melbourne University.

The researchers now plan to embark on clinical trials. (Extracted from Wall Street Journal, 17 December 1987 and New Scientist, 7 April 1988)

Diagnostic test for sickle-cell anaemia

Scientists in California have developed a simple and highly sensitive test to detect sickle-cell anaemia, an inherited disease of the blood that frequently affects people of African, Mediterranean and Asian descent. The test, called Joshua, for Joint Sickling Haemoglobin Universal Assay, is based on a monoclonal antibody specific for sickle-cell anaemia.

Gordon Longerbeam, of the Lawrence Livermore National Laboratory, says that developing countries could use the test to screen for sickle cell anaemia. Unlike the current diagnostic technique, electrophoresis, Joshua does not require trained technicians and expensive equipment that needs electrical power.

According to the World Health Organization, about 200,000 babies are born each year with sickle-cell anaemia. Many sufferers die in childhood and few live longer than 40 years.

A recent study by the National Institutes of Health (NIH) in the US found that 15 per cent fewer babies with sickle cell anaemia die if doctors diagnose the disease before the infants reach the age of four months, and treat them with prophylactic penicillin. A panel at the NIH recently recommended that all newborn babies should be screened for sickle-cell anaemia. Eleven states in the US have already made such screening mandatory.

Longerbeam says that the simplicity of the test means that it could be used in parts of the developing world where screening for sickle-cell disease might not otherwise take place. However, the new test is designed to complement electrophoresis, not replace it. Electrophoresis will still be necessary after a positive result from the Joshua test, to determine whether a patient has the disease or is only a carrier. (Source: New Scientist, 31 March 1988)

Insulin pill a boon for diabetics

A group of Israeli researchers at Hadassah Hospital in Jerusalem has developed an insulin preparation that diabetes sufferers can take by mouth instead of by injection.

The new method of taking insulin is in early clinical trials. It could be an alternative to the existing one-off injections, subcutaneous injection pumps and nasal sprays, which are still mainly experimental.

The Israeli group started working on the idea of emulating the natural flow of insulin from the pancreas to the liver, by making it absorbable through the intestine.

They had to overcome two problems: the insulin molecule is too large to pass through the intestinal wall, and insulin cannot be taken by mouth in its normal form, because the digestive system would break it down.

The group discovered, however, that insulin could pass through the intestinal wall into the bloodstream if it was mixed with a detergent. Unfortunately, the detergent used was toxic. But once the principle was established, Ziv found that natural bile salts did the same job, allowing up to 10 per cent of the insulin (injected directly into the gut of laboratory rats and dogs) to be absorbed. The insulin could also be protected from digestive attack by adding a substance derived from soybeans or chick peas that inhibits the enzymes that would break the insulin down.

They also had to ensure that it would be absorbed gradually, rather than naturally emptying into the small intestine. (Source: New Scientist, 25 February 1988)

Japan produces first alpha-interferon drug

Takeda Chemical Industries and Nippon Roche of Japan will introduce recombinant alpha-interferon as the first recombinant DNA-produced drug in Japan. The jointly-developed drug will be marketed independently by Takeda as Canferon-A and by Nippon Roche as Roferon. Alpha interferon produced by a cell fusion process is already available from Sumitomo Pharmaceuticals and Toray Industries. The new alpha interferon is produced by E. coli into which the proper gene has been inserted. The interferon so produced has 165 amino acids and a molecular weight of 19,237. Approval was granted in November 1987 and marketing will start in early 1988. The drug is approved for treatment of hepatitis B, kidney cancer and multiple myeloma. (Extracted from Japanese Chemistry, 28 January 1988)

Joint development of cancer treatment

Joint development of a new procedure using interleukin-2 (IL-2) to treat certain types of cancer is the aim of a research collaboration between Hoffmann-La Roche and Du Pont. The companies will use Du Pont's SteriCell family of products to conduct clinical trials with Roche's genetically engineered IL-2, a lymphokine that plays a major role in immune system function. The SteriCell products allow rapid processing of a patient's blood cells, which are then mixed with IL-2 to make lymphokine-activated killer (LAK) cells. In some patients, cancer cells have been attacked, leaving normal tissue virtually unharmed when LAK cells are administered back to the patient with additional IL-2. The treatment has led to regression of various kinds of tumors, including malignant melanoma and kidney cancer. (Source: Chemical Week, 3 February 1988)

Uses of alpha interferon in variety of cancers

Alpha interferon is finding use in treating a variety of cancers, according to a variety of studies on chronic myelogenous leukemia, mycosis fungoides and Kaposi's sarcoma. Low-grade nodular non-Hodgkin's lymphoma responds well to the drug, according to K.A. Foon of Roswell Par Memorial Institute. Side-effects from the necessary high dosages can frequently be controlled. Multiple myeloma patients are also showing some response to the drug, according to studies at M.D. Anderson Hospital & Tumor Institute and the University of Wisconsin (Madison). The University of California at Los Angeles scientist R. Figlin says the drug produced a 15-20 per cent response rate in patients with renal cell carcinoma. Bladder carcinoma responded well to alpha interferon in 20-30 per cent of cases, according to N. Vogelzang of the University of Chicago. Side-effects such as high fevers, hypertension and cardiac arrhythmia can be modified by taking the drug so side-effects occur during sleep or by taking acetaminophen before taking the interferon. Gradually increasing dosage can also reduce side-effects, although this may also reduce therapeutic benefits. (Extracted from Medical World, 8 February 1988)

Albumin may take the toxicity out of cancer treatment

A research team from the pharmaceutical department of Strathclyde University and the Glasgow Royal Infirmary has developed a new approach to dealing with the problem of toxicity in chemotherapy treatment for cancer. The technique relies on the fact that blood vessels develop abnormally in cancer tumours. The results in animal tests and human studies are said to be promising.

Tumours produce chemicals that stimulate blood vessels to grow rapidly into tumours and supply them with food and oxygen. The walls of such blood vessels, however, do not have the same muscular structure of those that supply normal organs. When drugs are used to reduce blood flow to organs, by making the muscular walls of the arteries contract so the arteries constrict, the flow of blood into tumours is unaffected, thereby increasing the blood flow relative to normal organs.

Neville Willmott and his colleagues at the infirmary have encapsulated the anticancer drug adriamycin into microspheres of human albumin. These measure only about 40 micrometres in diameter when loaded with the drug. The microspheres are small enough to flow freely through arteries and veins but jam in the networks of capillaries found in organs such as the liver, lungs and kidneys. Capillaries are only 7 micrometres in diameter on average.

When drug-loaded microspheres are injected into arteries leading to target organs in rats, tests show that the spheres become jammed in the capillary beds in the organs. Studies in human cancer patients show that when similar drug-loaded microspheres are injected into the circulation, while the patients are being given synthesized angiotensin II, a potent artery constrictor, the effect is to concentrate the microspheres in the tumour, where they are needed. Clinical tests to assess the value of the technique are now being planned. (Source: New Scientist, 14 April 1988)

Drug reduces chances of breast cancer recurring

Treatment with bromocriptine, a drug that lowers levels of the hormone prolactin in the body, might reduce the chances of breast cancer recurring after surgery.

A team led by Ian Fentiman at the Clinical Oncology Unit at Guy's Hospital, London, has shown that giving bromocriptine to women substantially reduced the numbers of dividing malignant cells present in the breast at the time of surgery. The drug probably also reduces the risk of cancer cells spreading from the site of the primary tumour and forming new growths elsewhere in the body.

Bromocriptine blocks the production of prolactin by the pituitary gland. Fentiman's team gave either bromocriptine or an inert placebo to 38 women with early breast cancer for five days before surgery and for several days afterwards. The doctors measured the amount of DNA, which depends on the proportion of dividing cells, in a sample of tissue from the tumour. They found that samples from the women given bromocriptine contained far fewer dividing cells than those from the women given the placebo.

These results suggest that bromocriptine, which appears to have no side effects when used in this way, could at least partially replace chemotherapy aimed at preventing the spread of cancer. The toxic drugs used in chemotherapy might be carcinogenic, and often have unpleasant side-effects. Bromocriptine might reduce the risk of recurrence more effectively, as well as being more pleasant for the patient. (Source: New Scientist, 14 April 1988)

TGF-alpha against breast cancer cells

A technique to nullify growth factors secreted by breast cancer cells could be ready for testing by early 1989, according to M. Lippman of the US National Cancer Institute. The strategy apparently works in both estrogen-dependent and estrogen-independent cancers. All solid tumours produce transforming growth factor alpha (TGF-alpha). Antibodies to TGF-alpha inhibit in vitro cancer cells. Growth factor secretion and tumour growth are inhibited by antiestrogens such as glucocorticoids and tamoxifen, which induce production of TGF-beta instead. TGF-beta appears to act as a negative autocrine growth factor. TGF-beta itself is not an acceptable anticancer drug because it also inhibits the growth of skin and bronchial epithelium. Antibodies are able to counteract TGF-alpha, however, which the body does not ordinarily produce. Animal and toxicology studies on TGF-alpha antibodies must be conducted before clinical trials can begin. (Extracted from Medical World, 25 January 1988)

New leukemia treatment

Lederle Laboratories' new treatment for acute non-lymphocytic leukemia "Novantrone" (mixtoxantrone hydrochloride), is the first anticancer chemotherapeutic agent to be approved for marketing in the US since 1983, Lederle officials say.

"Novantrone," according to Lederle officials, has been shown as effective as daunorubican a leading anticancer drug in the field. "Novantrone" is said to have fewer side effects, however, thus shortening patients' stays in the hospital and often allowing them to receive cancer treatment on an out-patient basis. Company representatives say that the drug is believed to interrupt the function of DNA in tumour cells by forming a bridge between DNA strands and preventing cell division and replication and by other mechanisms including external electrostatic disruption of the DNA helix.

"Once in the body," 'Novatrone' undergoes what we call three-compartment distribution. Following distribution, the drug is rapidly removed from the blood, sequestered in the deeper tissues of the body and slowly released back into the bloodstream. This three-phase distribution prolongs the drug's half-life," says Dr. Denneth Cartwright, vice-president of clinical research for the medical research division of American Cyanamid's Lederle Laboratories. (Extracted from Chemical Marketing Reporter, 18 April 1988)

Diagnostic test for urinary tract cancers

Researchers at Nippon Kayaku (Tokyo), working in collaboration with Katsushi Ishii at the Saitama Prefectural Research Center, have developed a new enzyme-linked immuno-assay for early detection of cancers of the urinary tract and reproductive organs. The test uses a monoclonal antibody that binds to basic fetal protein (BFP). BFP, which Ishii discovered in 1974, is produced by many cells of the developing foetus but not by normal adult cells. The protein is made by certain tumour cells, however, and the presence of BFP in the serum is a good early predictor for stomach, colon, bladder, urinary tract, prostate gland, and uterus cancers. Nippon Kayaku plans to apply to the Japanese Government soon for permission to manufacture the test and hopes to offer a diagnostic kit by next summer. (Source: Bio/Technology, Vol. 6, February 1988)

Commercial production of EPO

Ortho-Cilag (UK) will begin commercial production of EPO, an erythropoietin preparation. Its parent Johnson & Johnson (US) will produce the hormone in the US. This is the first commercial scale production of erythropoietin worldwide, and involves the use of the gene that controls erythropoetin levels in the human body. Erythropoietin stimulates production of red blood cells, and thus has major potential in the treatment of anaemia, particularly in haemodialysis patients. Its side-effects can include arterial hypertension and vascular complications. The firms have applied for marketing approval in the US and parts of Western Europe. (Extracted from Le Monde, 29 January 1988)

Down's syndrome detection

Testing pregnant women's blood oestriol levels is more effective than alpha-foetoprotein level screening in Down's syndrome detection, according to H. Cuckle of St. Bartholomew's Hospital, London. The blood oestriol levels of mothers carrying Down's syndrome children is unusually low. Some 45 per cent of Down's syndrome foetuses can be detected by combining variables on blood oestriol levels, alpha-foetoprotein and maternal age. (Extracted from Clinica, 20 January 1988)

A safer method to detect blood clots

Doctors are hoping that by injecting a radioactive, genetically-engineered antibody into a patient's bloodstream, they can detect blood clots more quickly, safely and accurately. Called antifibrin antibody imaging, the method may revolutionize the diagnosis of blood clots, according to Dr. Abass S. Alavi, chief of nuclear medicine and professor of radiology at the Hospital of the University of Pennsylvania.

Blood clots can cause strokes or heart attacks when they travel to the brain or pulmonary arteries. However, once a clot is pinpointed it can be dissolved with drugs. The method involves the injection of the radioactive antibody that travels to the blood clot and emits radiation. The blood clot can then be detected within an hour by a special camera.

The new method of imaging, combined with a lung scan, may eliminate the need for commonly used tests such as venograms, in which dye is injected into the veins. While venograms are effective in finding clots, the dye can cause unwanted reaction, and the injection itself can trigger a clotting response. (Source: International Herald Tribune, 10 March 1988)

Enzyme offers brighter future

Clinical trials start next year of a dipstick which can indicate in just 10 minutes whether a patient has a bacterial infection. Instead of waiting days for a result from the laboratory, the doctor dips the stick first into a urine sample and then into a mixture including an enzyme extracted from fireflies. The mixture lights up if the test is positive.

It is the latest application of bioluminescence which promises to turn the pathology laboratories of the 1990s into while-you-wait units at health centres.

All living cells use adenosine triphosphate (ATP) to carry energy if ATP is mixed with two compounds extracted from fireflies - luciferin and the enzyme luciferase - the energy is released as light. The amount of light given off is directly proportional to the amount of ATP, which shows how many micro-organisms were in the original sample.

In practice, a sample is mixed with a reagent, such as apyrase, which degrades any non-microbial ATP. Then the ATP which is contained in the bacteria cells is extracted with trichloraetic acid and mixed with the luciferin and luciferase. The light is measured by a luminometer.

Robert Brown of the Royal Signals and Radar Establishment believes that switching to techniques that use solid-state devices to pick up the light could "reduce the price of the detector from a few thousand to a few hundred pounds".

Equipment manufacturers are already discussing such a move, which would make ATP assaying even more competitive. By using specific reagents or treating samples with antibiotics which kill off particular strains of bacteria, it is possible to develop tests for specific infections. Amersham International is using a simplified version of the technique for its dipstick, which will be used initially to detect infections of the urinary tract.

The food and drink industry is also very interested in ATP because ATP testing makes it easy to check every batch of a product and the results are delivered before the goods leave the factory. (Extracted from New Scientist, 28 April 1988)

New therapy blocks newborn jaundice

A novel technique for managing jaundice in newborn infants is proving successful in clinical trials, researchers report. The experimental procedure, which involves injecting a synthetic blood protein into affected babies soon after birth, may greatly simplify treatment of one of the most frequent and troubling complications to occur during an infant's first few days of life.

Newborn jaundice is the result of an abnormal accumulation of bilirubin, a yellow pigment that is one of the breakdown products of haemoglobin, the oxygen-carrying component of blood. It occurs when unusually large amounts of a newborn's red blood cells are destroyed, such as when the newborn's blood type is incompatible with its mother's. It also occurs frequently in normal premature infants, and in some full-term babies, because the immature liver is incapable of clearing even normal levels of bilirubin from the blood. If not treated promptly, newborn jaundice, or hyperbilirubinemia, can result in permanent brain damage.

Working under the direction of Attallah Kappas, physician-in-chief at Rockefeller University Hospital in New York City, a research team designed a synthetic protein, called Sn-protoporphyrin, that mimics haemoglobin in the blood but that contains tin instead of iron as its central metal atom. The pseudo-haemoglobin binds to the enzyme that normally converts haemoglobin to bilirubin, preventing real haemoglobin from interacting with the enzyme. Thus haemoglobin is excreted without ever getting converted to bilirubin.

After years of studies on animals and on adults suffering jaundice due to liver disease, the researchers recently treated 53 newborn, full-term infants with jaundice due to blood-group incompatibility. Those trials, performed in Greece, reduced bilirubin levels by as much as 34 per cent and cut the need for ultraviolet therapy more than 40 per cent.

The only side-effects reported were transient redness of the skin in two infants who received the bilirubin enzyme inhibitor and light treatment concurrently. The researchers say those effects may be eliminated by changing slightly the wavelengths of ultraviolet light used in those cases. (Extracted from Science News, Vol. 133, 16 April 1988)

AIDS drugs research focus for more than fifty companies

Fifty-five companies are researching or have developed a total of 77 products to diagnose, prevent or treat AIDS, says Pharmaceutical Manufacturers Association. However, not all the products currently in development will be approved, but other products will be discovered and developed as research continues.

Pharmaceutical industry scientists express "cautious optimism" that while there is yet no cure for HIV infection, effective treatments will be found to prolong life, restore immune function and halt the progress of the disease once it is diagnosed.

Products already approved include nine diagnostic tests to detect the presence of antibodies to the virus, the drug "Retrovir" (AZT) to arrest the development of AIDS, and "Pentam 300" for Pneumocystis carinii pneumonia.

Other products being developed include 15 antiviral drugs, 22 immunomodulators (to strengthen the immune system), two anti-infectives, 17 diagnostics and 10 vaccines. (Extracted from Chemical and Engineering News, 29 February 1988)

Second AIDS trial

The US National Institutes of Health (NIH) and the biotechnology company MicroGeneSys have announced another clinical trial of their jointly developed vaccine against AIDS. The vaccine, which consists of the gp 160 envelope protein from HIV, the virus causing AIDS, is to be administered to 72 healthy seronegative male and female volunteers at six federally sponsored Vaccine Evaluation Units.

The first clinical trial of the vaccine that began in October involving homosexual men will continue. But so far only 31 volunteers out of the 81 required have been found.

The six Vaccine Evaluation Units - at Baylor College of Medicine in Houston, Texas; Johns Hopkins University and the University of Maryland in Baltimore, Maryland; Vanderbilt University in Nashville, Tennessee; Marshall University in Huntington, West Virginia; and the University of Rochester in Rochester, New York - will recruit volunteers locally. Two test groups will receive differing dosages of the actual vaccine, and control groups will receive either recombinant hepatitis B vaccine or the adjuvant alum. (Source: Nature, Vol. 331, 28 January 1988)

AIDS: glimmer of hope

As promising results of a small clinical trial on the AIDS drug AZT were reported from the Netherlands, testing of another drug for combating the pneumonia associated with AIDS received a boost from the US Government, and a new improved diagnostic test for the disease was launched in the USA.

The Dutch study, although limited in size and not placebo controlled, appears to give a glimmer of hope that AZT may be able to prevent people infected with the HIV virus from developing the full blown disease. US scientists, however, have cautioned against over-interpreting the new results.

The scientists at the University of Amsterdam medical centre and two Dutch health services have reported that AZT, also known as zidovudine, significantly reduced the blood levels of the HIV virus in 13 out of 18 men infected but not showing overt symptoms. Swollen lymph nodes shrank and the levels of the particular white blood cells - CD4+lymphocytes - attacked by the virus rose slightly.

A larger trial, in 1,600 overtly healthy patients with HIV antibodies, is being undertaken in the USA to see if AZT can prevent or at least slow down the development of the disease.

Meanwhile, the US Government has given a Warner-Lambert drug, trimetrexate, special status to allow it to be given to patients with pneumonia carinii even though testing and approval of the drug are not complete.

SmithKline Beckman's Bioscience Laboratories subsidiary has launched a new test for antibodies to HIV, called Hivagen, which in trials gave no "false positive" or indeterminate results. It will be used by blood banks and other laboratories instead of the Western blot test, which is currently used as a confirmatory test following an initial ELISA test. (Source: Chemistry and Industry, 7 March 1988)

Extension of zidovudine trials in children

In early April, doctors in the US began trials to find out how effective the drug zidovudine is in the treatment of AIDS in children. The National Institute of Allergy and Infectious Diseases in Bethesda, Maryland, has named eight centres to take part in tests on children with AIDS or other symptoms related to infection with the human immunodeficiency virus (HIV).

Doctors need to conduct trials on children independently to those on adults, because HIV attacks children at a time when their immune systems are still developing. John Modlin, associate professor of paediatrics at Johns Hopkins Medical Institutions, one of the eight centres participating in the study, says: "Children and adults are different hosts to the AIDS virus, and the age when the child encounters the virus may affect the course of the disease."

Catherine Wilfert, a doctor at Duke University in North Carolina, who is co-ordinating the study, says that a "phase one trial" to examine the toxicity of the drug in children is already in progress. This study involved 36 children aged between three months and 12 years attending three different centres in the US. Some have taken the drug since the trial began in October 1986. Others joined the study only three months ago.

The researchers hope to publish results of that study at the beginning of May, but Wilfert says: "In general terms, the toxicity is at least as well tolerated as it is in adults." In adults, zidovudine can cause anaemia severe enough to warrant repeated blood transfusions. Not all patients can tolerate it.

Wilfert also says that doctors participating in the toxicity trial noted improvements in children suffering from neurological complications. None of the children has died. However, the study is relatively small, and some children have participated for only a short time. (Source: New Scientist, 31 March 1988)

AIMS Biotech develops direct test for AIDS

In the race to discover a more accurate, faster, and cheaper test for AIDS detection, Canada's AIMS Biotech Corp. is clearly leaving the 25-some other AIDS research companies behind in a wake of breakthrough discoveries.

AIMS Biotech through the company's wholly-owned subsidiary, AIMS Research Corp., and its licensed affiliate, Virunostics Inc., has started commercial testing for the AIDS virus through viral culturing.

Until now, diagnosis of an AIDS viral infection was made through the detection of antibodies, an indirect method based on inference. For the first time in the fight against AIDS AIMS Biotech is able to offer a direct test for the virus itself.

AIMS' viral culturing method comes at a time when every scientific breakthrough is vital in combating the spread of AIDS.

The disease is spreading at a shocking 79 per cent infection growth rate, say officials at Atlanta's Center for Disease Control (CDC). With current antibody testing procedures providing inconclusive results, and failing under the increasing demand from the public for faster and more accurate testing, AIMS Biotech is poised as a medical innovator and as a market leader in the fight against AIDS.

For those who go for voluntary testing, the period spent waiting for testing is as high as three months in New York City and seven weeks in Los Angeles. Jumping in with a four-week wait in San Francisco, its health officials warn that waiting times will only increase if more effective testing means are not implemented.

Currently, it takes from four to six weeks after testing to provide results. Even then the results are only 95 per cent accurate and valid for some six months. In some cases, when a person tests positive for the presence of antibodies, an entire battery of tests must then be administered, involving increased time and expense in confirming the initial result.

Working with researchers in Canada at the University of Saskatchewan, in Saskatoon, Saskatchewan, and at the Armand-Frappler Institute in Montreal, Quebec, and with US researchers at the Biskind Pathology Research Laboratory of the Mount Zion Medical Center and Hospital in San Francisco, AIMS has developed a viral testing system which has the capabilities to process 100 tests per day and should be readily available on a commercial basis in late 1988.

Until the FDA grants approval for the testing, AIMS will conduct commercial testing on a physician referral basis only through its licensed Virunostics affiliate at the company's Sutter Street laboratory, adjacent to Mount Zion hospital in San Francisco. The company does not need FDA approval to offer the service in a clinical laboratory but will need the Government's approval when licensing the system to other laboratories.

AIMS Biotech will apply for investigational new drug status for its testing system, the precursor to getting formal approval, in the beginning of 1988. For more information contact: AIMS Biotech Corp., 21st Floor, 1176 Georgia Street, Vancouver, British Columbia, V6E 4A2 (604) 688-0671. (Extracted from PennyStock News, Vol. 9, No. 1, 22 January 1988)

New AIDS test

Cetus (US) is developing a test than can detect AIDS virus genes in patients with negative viral culture tests. It gives results in under four days as against four weeks to assess current infection by culturing a virus. Antibody tests successfully indicate whether or not people have been infected by the virus but fail to indicate whether they still carry the virus or its genes. The new test uses Cetus proprietary polymerase chain reaction gene amplification technology. (Extracted from European Chemical News, 1 February 1988)

Another AIDS blood test

SmithKline Bio-Science Laboratories (SKBL) of Philadelphia, a unit of SmithKline Beckman, is making an entry in the already crowded field of AIDS blood tests. SKBL expects its new test, Hivagen, to replace the Western blot test, the current standard for confirming the presence of antibodies to the AIDS virus, HIV, in a blood sample. The test, according to an SKBL spokesman, has shown no false-positive results in clinical trials and has reduced indeterminate results 5-fold to 10-fold, compared with the Western blot assay. Western blot tests, he adds, can falsely identify up to 5 per cent of those tested as infected with the AIDS virus. The Hivagen assay contains six pure, genetically engineered fragments of the HIV virus. If HIV antibodies are present in a blood sample and bind to at least two types of those fragments, the sample is considered positive for AIDS. On the other hand, the Western blot test uses antigens that are only partly purified, sometimes leading to incorrect results. In addition, Hivagen is automated and requires no interpretation whereas the Western blot test is manual and subjective. The test is available immediately. SmithKline Beckman is also working on AIDS vaccines and drugs for use in AIDS therapy. (Source: Chemical Week, 2 March 1988)

HIV-2 diagnostic test

French biotechnology helped American doctors detect the first person in the United States infected with HIV-2, the second AIDS virus, which had been discovered less than two years earlier.

The patient, a woman from a West African country, did not have any of the known risk factors associated with AIDS. The presence of the virus had also not been detected by tests used since 1985 to screen out the more common HIV-1 virus.

Theoretically, it was possible for this woman to donate her blood and thereby infect many others with AIDS without ever being detected.

The HIV-2 test, currently marketed in several European and African countries, has yet to be approved by the US Food and Drug Administration.

Diagnostics Pasteur the company that developed the test - a joint venture between the Pasteur Institute and France's second largest pharmaceutical company, Sanofi - is optimistic that this woman's case will help it receive quick approval to distribute the test, Elavia HIV-2, in the United States. As yet, Elavia HIV-2 is the only commercially available test for the HIV-2 virus.

The product's rapid creation resulted from the successful blend of commercial demands and the company's proximity to a storehouse of AIDS-related research at the Pasteur Institute. The institute first identified the HIV-2 virus and shared credit with US researchers for the discovery of the HIV-1 virus.

The test kit is composed of a plastic strip with two wells. One well is coated with a biochemical solution that includes an extract of lymphocytes, or white blood cells, bearing the lab-cultured HIV-2 virus. The other well, designed as a control, is coated with identical cells that have not been infected with the virus.

In a test, part of the blood sample is poured in both wells. If the blood is carrying the HIV-2 virus and, therefore, its antibodies, those antibodies will begin reacting with antigens of the lab-produced virus in the first well. The reaction, aided by certain enzymes, causes the well to turn a yellow-orange within three hours.

If the blood sample is healthy, there would normally be no color change. However, up to 3 per cent of normal blood samples may carry non-specific antibodies not linked to the AIDS virus. These antibodies could react with the lymphocyte cells themselves, also causing a yellowish coloration.

To prevent misreading this result as positive, the control well is used. The non-specific antibodies would cause the same coloration in the control well, indicating that they, not the HIV-2 antibodies, caused the reaction.

Only if there were a significant difference in the color density in the two wells could doctors conclude that the blood sample actually was carrying the HIV-2 AIDS antibodies and, therefore, the AIDS virus.

The control well reduces the chance of false positive readings from 0.5 to 0.15 per cent.

Patents are pending on all facets of the manufacturing process, including a patent on the HIV-2 virus itself. (Extracted from International Herald Tribune, 16 March 1988)

New test will simplify syphilis detection

A new test for the diagnosis of syphilis, a venereal disease that is re-emerging in North America and which has been linked by some to the spread of AIDS, will make detection of primary and secondary infections much easier and faster. For the first time, one simple test using skin lesion samples will quickly and accurately diagnose the disease during the infectious stages.

Development of the test comes at a crucial time. Even though syphilis is treatable, a five-year trend to lower rates has recently reversed. The test is being developed by Allelix Diagnostics, a spin-off from Allelix Inc., in collaboration with Serex International Inc. of California, and is due on the market next year.

The number of syphilis cases reported in the US in the first 46 weeks of 1987 increased 32 per cent over the same period in 1986. Many of its victims are newborns who die before their first birthday.

The increased spread is partly because the disease is "under-tested", as it is very difficult to obtain a viable organism required for a definitive diagnosis of a syphilitic lesion using darkfield

microscopy. In addition, some of the tests are laborious, time-consuming, often inaccurate, and require technical expertise and special instrumentation.

Over 90 per cent of current tests are performed to detect antibodies to Treponema pallidum but they indicate only that a person has, at some time in the past, been exposed to T. pallidum. Allelix's new test will accurately detect the bacteria themselves, proving that a person is presently infected.

The collaboration gives Allelix Diagnostics exclusive worldwide marketing rights to the patented test and improvements. Much of the preliminary research was funded by Serex and conducted by the University of Texas Health Science Center and the University of California, Los Angeles (UCLA) - two of the world's most prestigious syphilis research centres. UCLA is a World Health Organization reference laboratory for syphilis.

The first of several products to arise from the agreement is expected on the market in 1989 and is intended for professional use. Allelix predicts that with the introduction of a rapid, accurate test, the world market for syphilis tests could grow from $US 25 million to over $150 million in the next five years.

For more information contact: Jeff Greenberg, Commercial Director, or Dr. John Hurrell, Vice President, R & D and Scientific Affairs. Telephone (416) 677-0831. (Source: Company News Release, 30 March 1988)

Ten-minute test could be ideal for developing countries

Laboratories in Britain will soon be able to buy a simple test for antibodies to HIV which takes only 10 minutes to carry out. The test, called the HIV-Chek, which has been developed by the American company Du Pont, may find its greatest application in developing countries. It needs no specialized equipment to read the result, has a long shelf life, and neither the kit nor the reagents need refrigeration.

The HIV-Chek is much faster than the standard ELISA test which can take two to three hours. Du Pont claims that the test is as accurate as an ELISA. William Burns, marketing manager, says that in trials the test had "a specificity of 100 per cent" - in other words, it produced no false-positive results. The test's sensitivity was about 99 per cent, so it has a very low false-negative rate, too, he says.

Du Pont's original idea was to produce a test which needed only the addition of a drop of diluted blood. Such a test could pose problems if its distribution were not carefully controlled. People attempting to test themselves may produce a wrong finding or be unable to deal with the consequences of a positive result without help, and doctors may start testing people without good reason - for instance, on behalf of employers or insurance companies.

In the US the Food and Drug Administration licenses all tests because blood is considered a pharmaceutical product there. In Britain there is no regulatory framework for tests, though guidelines issued by the Department of Health and Social Security specify, for example, that people having tests must be adequately counselled.

Du Pont hopes that it has skirted this problem by designing the test for use with serum or plasma rather than whole blood. This would make it slightly more difficult for the lay person to use. The HIV-Chek involves adding either serum or plasma to the well in the middle of the capsule, followed by a series of solutions for washing and rinsing. The central well contains a membrane impregnated with genetically engineered antigen (protein) from HIV-1. If antibodies to HIV-1 are present in the added serum or plasma, these will bind to the antigen on the membrane.

The next step is to add a reagent containing colloidal gold. If antigen-antibody complexes are present, the gold will attach itself to them, and a red spot will appear in the middle of the membrane.

The test has its flaws. One problem is that the antigen incorporated in the membrane is the envelope protein of HIV-1. Some people infected with HIV-1 never produce antibodies to this particular protein, perhaps because they are genetically incapable of doing so. In addition, people who have recently been infected with HIV may produce antibodies to other viral proteins before they produce antibodies to the envelope protein. HIV-Chek will fail to diagnose infection at this time.

The second difficulty is that the test works best on fresh serum or plasma, rather than that which has been stored frozen and thawed. (Source: New Scientist, 14 April 1988)

Celltech's gastric lipase agreement

Work by Celltech (UK) scientists may lead to the development and marketing of a new therapeutic for sufferers from cystic fibrosis and chronic pancreatitis. They have succeeded in isolating human gastric lipase, an enzyme produced in the stomach and in cloning and expressing it. Patients with the genetic disorder cystic fibrosis and also those with pancreatitis (which may be brought on by alcohol abuse) are unable to digest nutritional fats and as a result suffer from malnutrition and the unpleasant presence of undigested fat in their faeces.

Current therapy is by oral ingestion of a lipase enzyme preparation derived from the pancreas of pigs. The challenge was to identify a naturally occurring enzyme which is acid stable and so capable of oral administration in low dosage. The existence of human gastric lipase (secreted in the stomach rather than the pancreas) had been a matter of controversy for many years, but the Celltech programme has been successful in isolating it, proving its acid stability and bringing it to the stage where bulk production is possible. (Source: Biotechnology Bulletin, Vol. 7, No. 2, March 1988)

Will 1988 be 'the year of the liposome'?

In some ways, the maturation of liposomes has typified the development of biotechnology: crests of hype and expectation followed by troughs of disappointment and disillusion. Now, however, armed with a much clearer understanding of the technology's limitations - as well as how to better design and manufacture these phospholipid-based microspheres - companies are marching impressive numbers of liposome-encapsulated drugs into human trials. In fact, more than 15 liposome products are scheduled to be in US clinicals during the upcoming year (see table).

LIPOSOME PRODUCTS LIKELY TO BE IN THE US CLINIC IN 1988

Sponsor	Therapeutic	Application	US States
The Liposome Co.	Doxorubicin	Cancer	Clinic early 1988
The Liposome Co.	Platinum (L-NDDP)	Cancer	Clinic early 1988
The Liposome Co.	Gentamicin	Gram negative infections	Probably clinic in 1988
Squibb (with TLC)	Amphotericin B	Fungal infections	Probably clinic in 1988
Ortho (with TLC)	Miconazole	Vaginal antifungal	Possible clinic in 1988
Barnes-Hind (with LTI)	Water	Dry eyes	Completing phase II
Barnes-Hind (with LTI)	Undisclosed	Glaucoma	Probably clinic in 1988
Cooper (with LTI)	Metaproterenol sulfate	Asthma	In phase I
Upjohn (with LTI)	Minoxidil	Hair growth (topical)	Clinic early 1988
Vestar	Indium	Tumor imaging	In phase II/III
Vestar	Daunorubicin	Cancer	Probably clinic in 1988
LyphoMed (with Vestar)	Doxorubicin	Cancer	In phase II
LyphoMed (with Vestar)	Amphotericin B	Fungal infections	Probably clinic in 1988
Ethicon (with Vestar)	Non-steroidal anti-inflammatory drug	Post-surgical healing	Probably clinic in 1988
Technology Unlimited Inc. (partner undisclosed)	Insulin	Diabetes	Probably clinic in 1988
Technology Unlimited Inc. (partner undisclosed)	Undisclosed	Cancer	Probably clinic in 1988
Ciba-Geigy	Muramyl tripeptide	Cancer	In phase I

During 1988, The Liposome Company (TLC, Princeton, NJ) expects that two of its partners will test anti-fungal products on humans, and will produce a pair of anti-cancer formulations and one against Gram negative infections. The firm is also developing non-steroidal anti-inflammatory drugs, vaccines, topical ophthalmics, and sustained-release systems for injectable proteins and peptides.

Through its partners, LTI's liposomes are already in the clinic for treating dry-eye and asthma, while glaucoma and hair-growth formulations are scheduled to begin trials in 1988. In the UK and Israel, LTI is running its own tests of a doxorubicin liposome against cancer, and the firm has also developed an anti-fungal preparation of amphotericin B.

Once liposomes could be designed to meet various specifications, researchers set out to optimize them. This kind of approach has allowed Vestar to increase the shelf-life of its liposomes from weeks to years.

Vestar's proprietary, targeted daunorubicin formulation is scheduled to go into clinical trials this year, as are partner-sponsored products against cancer, fungal infections, and post-surgical healing. The company's indium-based tumor imaging product is already in phase II/III trials, and Vestar's magnetic resonance imaging enhancer might make it to the clinic in 1988.

The three publicly traded liposome specialists - TLC, LTI, and Vestar - have succeeded in raising the impressive total of $120-150 million over the last five years. But the potential payback of liposomes - with their ability to increase potency while decreasing toxicity - is enormous. For example, TLC reports that the current markets for the three anti-cancer drugs that it intends to have in the clinic this year total some $575 million. (Extracted from Bio/Technology, Vol.6, January 1988)

Test for alcoholism

A test for platelet enzymes monoamine oxidase and adenylate cyclase could determine if a person is alcoholic, even if the person has abstained from drinking for up to four years, according to B. Tabakoff of the US National Institute on Alcohol Abuse & Alcoholism. Monoamine oxidase activity declines significantly more when platelets of alcoholics are subjected to alcohol than when platelets of non-alcoholics are subject to the same test. Adenylate cyclase activity in the platelets of alcoholics is less stimulated by cesium fluoride than the same enzyme from non-alcoholics. Combining the two tests correctly identified 75 per cent of alcoholics. The test may indicate an inherent predisposition to alcohol abuse. A new study will investigate enzyme activity in children of alcoholics with Type II alcoholism. Persons in the completed study generally had Type I alcoholism. The role of the enzymes in related disorders such as depression will also be investigated. Such biochemical markers eventually may prove a basis for tests to identify problem drinkers or even individuals genetically susceptible to alcoholism. Intriguingly, recovering alcoholics who had not drunk for up to four years

resemble alcoholics rather than non-alcoholics in the enzyme assays. That may be the consequence of long-term heavy drinking or it may reflect an innate underlying genetic difference in people predisposed to alcoholism. The researchers have begun studying children of alcoholics to see if their enzymes share the pattern seen in problem drinkers.

"Such a test may prove a helpful tool to physicians with patients who exhibit symptoms of alcoholism but deny it," says George Marcelle, a representative of the National Council on Alcoholism. "And a blood test might help identify children at risk so they can be targeted for special intervention."

Nevertheless, Marcelle worries that such a test would be perceived as a panacea for society's struggle with alcohol. "The focus on biologic aspects of alcoholism may be placing undue emphasis on the physical aspects of the disease and neglecting psycho-social aspects," he says.

Marcelle is also concerned about the accuracy of the test and how the results would be interpreted - especially for recovering alcoholics - because of the stigma society still attaches to the disease. (Extracted from Science News, 30 January 1988 and Chemical and Engineering News, 1 February 1988)

Dental drug via biotechnology

Vipont Pharmaceutical, Inc., Fort Collins, Colo., says its subsidiary, Vipont Research Laboratories, Inc., has signed an exclusive research agreement with the Plant Biotechnology Institute of Canada to develop a commercial production process for the compound, sanguinarine. Sanguinarine is the base compound in "Viadent" dental products.

According to Vipont officials, the potential for extracting pure sanguinarine by this new biotechnology allows Vipont to greatly increase production of the compound for use in therapeutic drugs for dental and medical applications.

The new technology is based on a discovery by PBI scientists that utilizes an advanced process for producing sanguinarine by secondary elicitation (extraction) from plant cell culture. A natural compound of the bloodroot plant, sanguinarine has antimicrobial properties and has been shown to be effective in reducing and preventing dental plaque and gingivitis in numerous clinical studies. VRLI scientists say the compound has potential in other dental and medical applications based on additional properties discovered through clinical research. Meanwhile, Biotechnica Diagnostics (Cambridge, MA) has introduced a diagnostic test for periodontitis, a gum and tooth disease affecting more than 50 million Americans. The DMDX test uses enzyme or DNA coated paper points that are inserted at the base of the tooth to detect active bacteria. Four teeth can be tested for three types of bacteria, after which the points are sent to Biotechnica for analysis. Biotechnica is currently developing an in-office analysis test. Colgate Palmolive and Xytronix (San Diego, CA) will be applying for FDA approval on an in-office kit that adds a reagent to the paper points that causes them to change colour to indicate active disease. (Source: Chemical Marketing Reporter, 1 February 1988)

Aspirin increases effect of heart-attack treatment

Marketing was approved in November for tissue plasminogen activator, or TPA, that some experts think may work better and with fewer side effects than streptokinase.

Recently, in what heart doctors called the most pleasant surprise of all, a study found that plain aspirin could double the effectiveness of streptokinase and presumably TPA as well.

A new study, not yet published but reported at a scientific meeting in Atlanta, found that a 50 per cent reduction occurred in the death rate among patients who were given aspirin together with streptokinase immediately after the onset of a heart attack.

Administered as soon as possible after a heart attack begins, streptokinase and TPA break up blood clots after they have formed. The scientists theorize that aspirin inhibits the formation of new clots, which frequently occur after an old clot is broken up.

Because of its anti-clotting property, aspirin taken over the long term has previously been shown to help prevent heart attacks. But the new study is the first to show a benefit in taking aspirin while a heart attack is occurring and just afterward.

The new study, which involved 17,000 heart attack patients from North America, Europe and Australia, is the largest study of the treatment of heart disease.

In addition to reducing the death rate among heart attack patients, aspirin also reduced the incidence of non-fatal heart attack by 50 per cent and reduce the risk of non-fatal stroke by one third. Streptokinase had no such effects, the researchers found.

The same study that showed the aspirin effect also showed that streptokinase is effective as long as 24 hours after a heart attack starts.

TPA was recently approved by the Food and Drug Administration, and many doctors in the United States consider it the drug of choice because it does not elicit the allergic reactions that afflict 10 to 15 per cent of patients who receive streptokinase. (Extracted from International Herald Tribune, 11 April 1988)

Novel chimeric MAbs developed

International Genetic Engineering (Santa Monica, CA) will jointly develop novel chimeric monoclonal antibodies for use in products to diagnose and treat human cancers with Eastman Pharmaceuticals, which will provide a mouse hybridoma cell line producing a mouse monclonal antibody. International Genetic (Ingene) will develop cell lines to produce theraMAbs, a part human, part mouse antibody specific to certain cancer cells, using proprietary technology. It will receive payments for developing specific theraMAbs and royalties on sales of resulting products, and will retain some manufacturing rights. Eastman will have exclusive worldwide rights to any products resulting from the collaboration. (Abstracted with permission from Chemical and Engineering News, 29 February 1988, p. 13. Copyright (1988) American Chemical Society)

Second generation monoclonals

With an array of more than 100 products, monoclonal technology - involving production of antibodies from cell clones - racks up revenues estimated at $300 million/year now and projected to reach $2 billion/year by 1990, and the stakes could jump even higher if second-generation monoclonals become a commercial reality.

First-generation monoclonals - which have found application mainly in diagnosing and treating disease - are used for their ability to bind

antigens. The role of second-generation monoclonals, known as anti-idiotypes (anti-ids), would be to mimic the shape of a variety of molecules. Anti-ids could serve in a wide range of important applications - with possible uses in improved vaccines, drugs and enzymes.

Numerous companies are active in anti-id research. Ortho Pharmaceutical, Merck and Hoffmann-La Roche have mounted research programmes and at least a dozen biotechnology companies are involved, including Eli Lilly's Hybritech and Centocor, Biotherapy Systems and Biotherapeutics. Synbiotics is developing two anti-id animal vaccines that it expects to market in 1991, one against feline infectious peritonitis, another against canine heartworm disease.

So far, most anti-id research programmes have been low profile, but industry insiders say that the lion's share of work is focused on development of vaccines, especially those that might be effective against the AIDS virus.

The anti-id technology that could spur such products boils down to the mating of a monoclonal with a monoclonal. Antibodies, including monoclonals, are made by white blood cells called B lymphocytes, which are part of the immune system. Antibodies bind to antigens on such disease-causing organisms, or pathogens, as viruses, marking those organisms for destruction. Conventional vaccines make use of actual pathogens which are either killed or genetically weakened so that they will not cause disease. When a vaccine is introduced into the body, it triggers a response from the immune system, which then produces antibodies to the disease. Those antibodies then serve as protection against future exposure to the disease. The problem with conventional vaccines is that they sometimes fail, either because the pathogen has not been killed or has not been sufficiently weakened. By introducing a disease organism into the system, the vaccine can actually cause the disease it is meant to prevent.

Use of anti-ids might solve that problem. Since the anti-ids only mimic the antigen of a disease-causing organism, it could cause antibody production but not cause inadvertent infection.

Anti-ids are also being studied for use in fighting autoimmune diseases, which are caused when the immune system erroneously makes antibodies against its own cells, leading to the attack of those cells. There is conjecture, for instance, that rheumatoid arthritis may result from antibodies attacking connective tissue of the joints. In theory, autoimmune antibodies could be isolated and anti-ids made against them. The anti-ids would then bind to the autoimmune antibodies, rendering them harmless.

Cancer also could be a target of anti-ids. For example, Idec (San Diego) and Biotherapy Systems (Mountain View, Calif.) are developing anti-ids to fight B-cell lymphoma, a cancer of the B lymphocytes. Those cells not only make antibodies but also place a copy of those antibodies on their outer membrane. Antibodies could be isolated and anti-ids raised against them. Then, bound to the antibodies, anti-ids could mark cancer cells for destruction.

The design of drugs that interact with cell membrane receptors is another possible use of anti-id know-how. Such receptors bind natural compounds, like hormones, causing a cellular response. Drugs often mimic those natural compounds by binding to a receptor, causing the same cellular response as the natural compound. Researchers use receptors in the laboratory to screen for new drugs, but receptors cannot always be isolated from cell membranes. With anti-id technology, an antibody could be made to a receptor. An anti-id to that antibody would mimic the receptor and screen drugs. (Source: Chemical Week, 24 February 1988)

The effects of serotonin on sleep, appetite, depression and aggression

Michael Stanley is convinced that he has an important clue to why people commit suicide. A key factor, says the Columbia University psychopharmacologist who has analyzed the spinal fluids of some who have tried and the brains of some who have succeeded, is the inability of some people's brains to make normal use of a vital chemical called serotonin.

In the past, it was all but impossible to correct this problem, but a new family of drugs that can regulate serotonin in the body is becoming available. Researchers who are studying the substance, one of a family of so-called neurotransmitters that help pass messages through the nervous system, are hopeful that their work will lead to new treatments for a variety of conditions.

The first such drug to reach the market was Eli Lilly & Co.'s Prozac, which at the end of last year won Food and Drug Administration approval for use in treating depression, but researchers have also linked serotonin to sleep, appetite, aggression and other shifts in mood.

It was serotonin's impact on mood - specifically, depression - that first attracted drug developers. The chemical is secreted in the brain when an impulse jumps between two nerve endings. Most is then reabsorbed by the nerves. But some serotonin remains, and it improves mood. That is exactly what Prozac and the other drugs in development achieve. Called serotonin uptake blockers, they slow the process and reduce the ability of the nerves to sop up serotinin.

Unlike other antidepressants, which have a broad effect on the brain's other chemical systems, serotonin uptake blockers seem to leave other neurotransmitters alone. Fewer side-effects are one reason analysts who follow the pharmaceutical industry predict that Prozac could take 10 per cent or even 20 per cent of the US antidepressant market.

Many researchers, too, are intrigued by the absence of one potentially very important side effect. Some other antidepressants stimulate appetite, but the new drugs seem to spur weight loss instead. So a number of researchers are convinced that serotonin regulators could help treat certain forms of obesity.

The drugs may also hold promise for some people with anorexia, a serious eating disorder in which patients starve themselves. In particular, the drugs might help bulimics, those with a form of anorexia who punctuate their self-deprivation with binges of gorging. Early research shows that bulimics suffer from diminished serotonin activity.

The link between reduced serotonin levels and binge eating comes as no surprise to Sarah F. Leibowitz, a Rockefeller University neuropharmacologist who has done pioneering work on neurotransmitters' role in appetite. Serotonin turns off the appetite once hunger is satisfied, says Leibowitz, who has studied the eating habits of rats "bite by bite" and correlated the changes in neurotransmitter activity caused by different foods. Specifically, eating carbohydrates stimulates the production of serotonin in the brain. It paves the

way for other neurotransmitters that stimulate an appetite for protein and fat. At the same time the serotonin promotes a feeling of well-being.

But what of people who cannot produce enough serotonin? As their serotonin level drops and they become depressed, says Judith Wurtman, a nutritional biochemist at the Massachusetts Institute of Technology, they develop a craving for foods that trigger production of the substance. People who overindulge on pasta and pastry may be "using carbohydrate as an edible antidepressant," she says.

This is just one cause of overeating, says Wurtman, who cautions that no one drug will treat all kinds of obesity. So there is no reason to expect serotonin uptake blockers to end weight problems that arise from overindulging in protein or fatty foods. And it could be downright risky to give the drugs to people whose appetites disappear when they get depressed.

New discoveries about serotonin's many roles are also helping scientists understand problems ranging far beyond depression and appetite disorders. Most dramatic, psychopharmacologist Markku Linnoila of the National Institute on Alcohol Abuse & Alcoholism has found a link between reduced serotonin levels and unpremeditated crimes. Linnoila studied the spinal fluids of a group of people who had either attempted or committed murder "out of the blue". He found that their levels of serotonin were diminished. Similarly, Linnoila found reduced serotonin activity among a group of convicted arsonists, who had not planned their crimes ahead of time to collect insurance on the property. As a result, Linnoila is convinced that low serotonin levels play a role in spontaneous acts of violence.

It is not likely that drugs will be prescribed to potential murderers. But Columbia's Stanley believes that simply identifying low serotonin activity in troubled people will help, particularly as more drugs become available. Psychological treatment alone cannot counteract biochemical imbalances that contribute to impulsive acts, he maintains.

Researchers admit that they are just beginning to try to find out what causes low serotonin levels in the first place. (Source: Business Week, 22 February 1988)

Livestock applications

Bark extract amplifies vaccines

Bror Morein of the department of veterinary microbiology of the Swedish University of Agricultural Sciences has evidence that the immunogenicity of viral proteins can be greatly increased if they are in the form of an ISCOM - his term for the Immuno Stimulating COMplex formed by a protein antigen and Quil A, which is derived from the bark of the South American tree Quillaja saponaria Molina.

Quil A, a known adjuvant for foot-and-mouth disease vaccines, is an incompletely characterized glycoside that is semipurified from a saponin extract of the bark. Morein has found that mixing low concentrations of Quil A with a detergent extract of a viral membrane, followed by removal of the excess detergent (via density-gradient centrifugation, ultrafiltration, or dialysis), results in the formation of cage-like micellar structures - the ISCOMs - in which the viral proteins are attached by hydrophobic interactions to a Quil A matrix. If the starting material is a purified protein or synthetic peptide, rather than a membrane extract, a small quantity of lipid must be supplied to enable the ISCOMs to form.

The first ISCOM-based vaccine was marketed in 1987. Manufactured by Iscotec (Lulea, Sweden), which holds patents on ISCOM technology, the vaccine protects against equine influenza virus. Product sales rocketed last year when an outbreak of the disease took a much greater toll on stables using conventional vaccines as compared to one where the ISCOM vaccine was being tested.

ISCOM products against several other viruses, including rabies and pseudorabies viruses, have already been shown to be protective, but a feline leukemia virus vaccine is likely to be the next ISCOM prophylactic to reach the market.

Coopers Animal Health (Berkhamsted, UK) is developing the feline leukemia virus ISCOM vaccine in collaboration with Iscotec and is also further refining the equine influenza virus vaccine. The major effort concerns scaling up the production process and maximizing the incorporation of viral proteins into ISCOMs. (Source: Bio/Technology, Vol. 6, January 1988)

New anti-mycoplasma drug

A new drug developed at Dainippon Pharmaceuticals (Osaka) rids animal cell cultures of contaminating mycoplasma within one week. Mycoplasma - small, wall-less cells that invade and colonize larger eukaryotic cells - are common contaminants. For example, an estimated 30 per cent of all cells stored in the Japanese cell bank may be infected. The new anti-mycoplasma drug, designated MC-110, is a derivative of quinolonecarboxylic acid. It clears a wide range of mycoplasma types from cells and, when added to the culture medium, can prevent re-infection. MC-110 is anticipated to sell for about 15,000 yen ($120) per 50 milliliter bottle. Although drugs that prevent infection by mycoplasma are already available, this is the first to clear these organisms from already-infected cell lines. (Source: Bio/Technology, Vol. 6, February 1988)

Sheep produce more wool on a bioengineered diet

The Commonwealth Scientific and Industrial Research Organization (Australia) will develop genetically-engineered sheep feeds to boost wool growth. The work is based on research showing that wool growth is critically dependent on the amount of sulphur-rich amino acids that make it past the sheep's rumen and are digested by its main stomach. Under laboratory conditions adding sulphur-rich compounds to feed can boost wool growth by up to 30 per cent. The team are now working on genetically altering sheep feeds. Initial successes include the isolation of a gene from a pea seed, reconstruction of the gene, and transferral of it into lucerne, where it produces a leaf protein rich in sulphur that is not broken down in the sheep's rumen. The team is now working on a similar technique for the more widely used subterranean clover. The work could have significant value, particularly as wool has now overtaken coal as Australia's primary export good.

The research opens up the possibility of increasing wool production by up to 5 per cent. This could add an extra A$300 million to the value of Australia's annual wool clip. The researchers are planning full field trials by early 1989, but it will be five to eight years before the genetically engineered alfalfa can be marketed commercially.

The researchers, led by Jon Spenser and Thomas Higgins, have been working on the project for 10 years. They started by transferring the gene to the leaves of tobacco, because the plants regenerate easily from tissue culture. In the long run, the gene could be transferred to white clover or tropical legumes. (Extracted from The Financial Times, 11 February 1988 and New Scientist, 10 March 1988)

Fowlpox virus may be key to rabies vaccine

A virus that infects poultry may one day become the basis of an effective vaccine against rabies in humans.

Enzo Paoletti, from the New York State Department of Health in the US, has made a rabies vaccine from the fowlpox virus by inserting into the fowl virus a copy of a gene taken from the rabies virus. The gene codes for a glycoprotein found in the membrane of the cells infected with the rabies virus. The glycoprotein stimulates the production of antibodies in animals inoculated with the genetically engineered fowlpox virus.

Paoletti told a conference in Cardiff on the release of genetically engineered organisms that early studies on animals have shown that the vaccine is good at protecting animals against live rabies virus. He inoculated seven species of animals with the vaccine, and tested their immunity by introducing or challenging them with live rabies. He compared the results against a similar challenge in unvaccinated animals.

"All non-vaccinated animals died in 12 to 16 days post challenge," he said. "All animals vaccinated with the fowlpox-rabies recombinant survivied the challenge. Researchers observed all the animals for 21 days after the death of the last unvaccinated animal and all remained without symptoms and healthy."

Paoletti said the discovery was an unexpected bonus from work on the virus. He knew that fowlpox virus did not replicate in non-avian species, but did not know whether it would express foreign proteins. It turns out that it does express proteins and they are expressed at a level that causes serological activity - that is, when antibodies are produced in response to antigens.

Other scientists are working on different ways to make a genetically engineered vaccine against rabies. One approach is to use vaccinia, or cowpox virus used as the basis of the vaccine against smallpox in humans. But Paoletti said a fowlpox-based vaccine would be safer than ones based on vaccinia, especially for people whose immune systems are compromised.

Paoletti's experiments showed that the rabies glycoprotein was produced in high levels in cells grown in vitro. He then inoculated chicken, mouse, rat, rabbit, cat, dog and cattle, with the genetically engineered fowlpox virus. "All animals responded by the production of anti-rabies antibody detectable by one to two weeks post inoculation," Paoletti said. He intends to publish his results in the next few months.

Paoletti believes that the fowlpox vaccine needs to be tested still further to demonstrate that it provides full protective immunity against rabies. The first practical use, he says, will most likely be in the veterinary field, although he sees no reason why fowlpox may not one day provide humans with immunity from rabies. (Source: New Scientist, 14 April 1988)

Scotland takes its salmon farms out to sea

A new company called Stirling Aquatic Technology, set up by the University of Stirling, has taken the first steps in establishing the feasibility of offshore fish farming. The first of two cages for its experimental farm is in Oban harbour, waiting to be taken to Camus-Rubha-Na-Liathaig, in the Firth of Lorn. Although this site is only about a kilometre from the nearest shore, it is as exposed as most offshore sites.

The tubular steel cages, supplied by the Swedish company Farmocean, are 25 metres in diameter and are moored half-submerged. The top part of the cage is a food store, holding 3 tonnes of commercial feed. A computer controls the release of food so that in bad weather the fish will not starve if no one attends them.

Stirling Aquatic Technology will introduce 40,000 smolts to each cage. Derek Robertson, managing director of the company, estimates that each cage should produce 105 tonnes of salmon each year.

Offshore fish farming has many advantages. The circulation of water is better so the water is cleaner and does not suffer the dramatic changes in salinity of some inshore sites. Waste from the fish is quickly swept away so that pollution is not a problem. Fish grown in such conditions will be healthier and more efficient at converting food into fish meat.

At inshore sites, the waste food and faeces from fish often accumulate around cages, leading to population explosions of bacteria, which deplete the water of oxygen.

Farms offshore are also less of an eyesore in tourist areas and they do not interfere with pleasure craft. However, no one is sure how bad weather will affect the fish. The cages are designed to withstand waves 6 metres high but violent storms might damage the fish and reduce productivity.

Robertson and his colleagues will be monitoring their experimental farm carefully. Environmental data, collected automatically, will be transmitted through underwater cables to a base on shore. Cameras in the cage will record the behaviour of the salmon. Researchers from the University of Stirling, from the Scottish Marine Biological Association and from other interested groups will study the engineering aspects of the cage, fouling by marine organisms and the effect the farm will have on its local environment.

If the experiment is successful, it will open the way for a great expansion of the salmon industry in Scotland, not only offshore but also in some of the more exposed coastal sites previously thought too dangerous for caged fish. (Source: New Scientist, 3 March 1988)

Patent application for fast-growing pig

A research team has applied for a patent on another new genetically engineered animal - a fast-growing transgenic pig. Farmers should be able to buy the pig within five years.

Researchers at the University of Adelaide, led by Bob Seamark, have inserted an extra growth hormone into the pig. The hormone makes it 30 per cent more efficient at converting its food, and brings it to market seven weeks earlier than a normal pig.

The team produced the first transgenic pig in 1985. Since then, the researchers have refined the technique and the experimental transgenic pigs are now in their seventh generation.

A group from the Commonwealth Scientific and Industrial Research Organization (CSIRO) has also considered applying for a patent for a transgenic sheep. This animal, developed by the CSIRO's Division of Animal Production, grows 30 per cent more quickly than a normal sheep.

The move by the two Australian teams follows a decision earlier this month by the US Patent Office to grant a patent for a transgenic mouse, developed at Harvard University which has led to protests from members of Congress, who are considering legislation to halt the patenting of transgenic animals until they have debated the ethical, moral and economic issues.

In Australia, there is no legislation and the Australian Patent Office will grant a patent for the transgenic pigs and sheep if it finds the animals represent a unique invention, irrespective of the technique used.

The university has formed a joint venture company called Metrotech with a local pig production company. They are building a piggery for 500 sows to produce transgenic animals for the Australian pig industry. The pigs should be on sale in five years. (Source: New Scientist, 28 April 1988)

Oyster epidemic

A parasite with a voracious appetite for oyster flesh has invaded Chesapeake Bay, the USA's largest estuary and most famous oyster fishery. The bivalve mollusc, Crassostrea virginica, could disappear unless marine biologists find a way to stem the infestation.

The parasite, a protozoan called Haplosporidium nelsoni, has existed in the bay for almost 30 years. In the past three years, however, it has grown increasingly virulent. While harmless to humans, the parasite has killed 90 per cent of the oysters in some beds. A decade ago, Chesapeake watermen took five or six million oysters each year. Last year they took only a few hundred thousand.

Biologists first encountered Haplosporidium in 1957. The parasite invaded Delaware Bay, less than 100 kilometres to the east of the Chesapeake. In two years, the disease wiped out 95 per cent of Delaware's oysters. Biologists never discovered where it came from, nor exactly how it kills the oyster. They called it multinucleated sphere X, or MSX for short - the X is for "unknown". This "epizootic" - a disease that affects many animals of one kind in one region simultaneously - now extends over most of the eastern seaboard. The parasite does most damage when water in the estuary is saltier than usual, for example, after a drought, with salinity reaching 15 parts of salt per thousand or more.

Stories of oyster epidemics date back to 1877, when "maladie du pied" infested oysters in France. Over the past few decades, however, the number of parasitic attacks has increased. For example, in 1969 another sporozoan parasite, Marteilia refringens, infested the European native oyster, Ostrea edulis, in northern France. A large proportion of the oysters died. Ten years later, apparently carried by stocks imported from California, the protozoan parasite Bonamia ostrea attacked the native oyster along the west coast of Europe and in Britain and reduced its numbers still further.

Southwestern France had the good fortune to have cultivated a different species of oyster, as the result of a freak accident in 1868, but in the 1960s, the Iridovirus, a virus that causes gill disease, appeared and almost wiped them out. The local oyster growers have brought in Pacific oysters, Crassostrea gigas, to replace them.

Oysters are prone to outbreaks of disease partly because growers trade freely in different species and varieties for cultivation. In almost every infestation, either an "introduced" species of oyster has fallen victim to a local parasite or a new strain of oyster has brought in a parasite to which indigenous oysters had no resistance. Mussels, which have not travelled so widely, have suffered far fewer epizootics.

MSX is the latest and among the most potent of oyster killers. No one knows for certain where it came from, although it has a close cousin in Korea. The parasite measures between 5 and 50 micrometres in diameter, increasing the number of its nuclei as it grows in size. Scientists still do not know exactly how the parasite kills its host, but it does not seem to secrete a toxin. Some researchers believe that the parasite competes with its host for nutrition. Infected oysters almost always lose weight; by the time they die they are small and shrunken. Another possibility is that MSX damages the oyster's tissue just by its presence. Whatever the cause, MSX kill some oysters in weeks. Others survive for two or three years, isolating the infection in their gills. No one has been able to isolate and culture MSX outside the oyster; and researchers cannot transmit MSX from one oyster to another. Even infected tissue from one oyster, when injected into another, will not transmit the parasite. Haplosporidia normally produce spores as a part of their life cycle, but none has been found associated with MSX.

Biologists suspect that an intermediate host might carry MSX. There are scores of candidates. One possibility is the bright yellow boring sponge Cliona, which envelopes the oyster's shell and breaks it down. A variety of worms also colonises the outer surface of the shell. Another unlikely boarder is a type of pea crab, so called because of its pea-like proportions. The oyster crab, Pinnotheres ostreum, could carry MSX. The female crab lives permanently in an oyster's gills. Male oyster crabs leave their hosts when they need to find a female.

Some biologists speculate that in the past native oysters resisted these parasites but that pollution has weakened their immune systems. Oysters feed by filtering particles suspended in the water. They are not very discriminating in their filtration and collect and concentrate harmful substances as well as edible ones. Biologists at the University of Maryland, at Solomans, near Chesapeake Bay, found that chemicals weakened the oyster's defences against invading organisms. Pollutants destablized membranes within the immune cells that normally digest foreign particles. The chemicals also crippled phagocytes, cells that engulf foreign materials in the host. Much as the pollution theory will appeal to environmentalists, despite the damage pollutants do, healthy, unstressed oysters die as quickly from MSX as those in polluted water.

The Chesapeake's oysters need help now. Overfishing since the 19th century paved the way for the current desperate situation. Fewer oysters also means murkier water and harmful blooms of algae - because too few bivalves are feeding on them. When the algae die, bacteria break down the plant cells, consuming oxygen in the process. The more algae there are, the more oxygen the bacteria consume, which sometimes makes the water uninhabitable for other animals. Roger Newell of the Horn Point laboratory calculates that a century ago, the bay harboured 76 billion oysters, each filtering water at a rate of about 5 litres an hour. All the water in Maryland's part of the bay, roughly half, filtered through the oysters in about four days. By the 1970s, the diminished oyster population required almost 100 days to do the job. Now, the few remaining need 480 days to filter Maryland's waters.

But saving the oyster in America's east coast demands a completely new approach to oystering. Raising resistant oysters requires hatcheries, something unpopular in the Chesapeake Bay. And resistant oysters must be kept separate from the wild type, or they will interbreed and begin to lose their resistance. In France, this type of aquaculture is well known. In much of Chesapeake Bay, however, the state owns the oyster beds. Watermen simply sail out to the beds and take what they can. To discourage overfishing, Maryland requires watermen to bring up oysters with hand tongs, essentially hand-operated pincers 10 metres long. Anyone who prefers the more efficient motor-operated dredges must operate under sail. Watermen cherish these traditions and regard aquaculture as farming.

Aquaculture is more advanced in Virginia. Most of the oyster beds are privately owned and operators have adopted hatchery techniques. Scientists are considering growing "triploid" oysters. Normally animals have a paired set of chromosomes, that is, they are diploid. Standish Allen, a marine biologist at the University of Maryland, has learnt that, by subjecting newly fertilized, one-celled larvae to unusually cold temperatures and high pressure, he can create oysters that have a triple set of chromosomes. These triploid oysters, like commercially bred triploid trout, are sterile. They do not "waste" energy on manufacturing gametes or spawning, and so grow bigger and more succulent. Triploid oysters may be able to survive infection with MSX longer than normal diploid oysters.

Even with tricks like this, scientists will probably solve the MSX problem too late to save oystering in Chesapeake Bay. Even if resistant species thrive, the waterman's tradition of sailing freely from bed to bed will disappear. Already, the state of Maryland invests millions of dollars to haul young seed oysters from water of low salinity, where they are less likely to succumb to MSX, into public beds so that the few hundred watermen still in business can reach them. Besides costing a small fortune to keep the tradition alive, the practice exposes susceptible oysters to MSX for the first time, and many die before they mature.

Eventually, consumers will eat oysters from hatcheries where technicians have carefully mixed sperm and eggs in tubs, nursed the larvae and then farmed the adults in well tended beds in the shallows. The romance will have gone. As for consumers, they will probably be none the wiser. (Source: New Scientist, 7 January 1988)

Agricultural applications

Enter the supertomato

The US firm Monsanto will publish results of the world's first trials of a genetically engineered tomato, in 1988. Monsanto's tomatoes resist tobacco mosaic virus, which costs millions in lost yields every year. Other Monsanto varieties are resistant to glyphosphate, the active ingredient in the herbicide Roundup, and a third group produces a protein that kills insect pests, including tomato worm and fruitworm.

The genes that code for the protein were taken from Bacterium thuringiensis (Bt) which has been used for years as a spray-on insecticide. By having the crop produce its own insecticide, Monsanto scientists hope to be able to do away with the need to apply Bt sprays.

The supertomatoes open the way for similar feats with plants from the broad-leafed dicotyledon group, which includes sugar beet, tobacco and potatoes, the last two of great importance to developing countries. Scientists at the biotechnology research centre in Beijing are trying to improve the nutritional content of amino acids in potatoes and soya beans using genetic engineering. Results are expected within two years.

It will not be an easy task. Molecular Genetics in the US has a patent for a strain of corn with enhanced content of the essential amino acid tryptophan, but the yields with this strain have been much lower than from ordinary varieties of corn, which contain only limited amounts of the amino acids tryptophan and lysine.

Biochemist Alan Goldhammer, director of technical affairs at the International Biotechnology Association in Washington DC, says the earliest application of agricultural biotechnology will be pest control agents, which should be available within two years. Herbicide-resistant plants are two to four years off. The broad-leafed group are more amenable to foreign genes placed by infectious agents such as viruses or bacteria. The plants of the narrow-leafed monocotyledon group, such as rice, wheat, oats and barley, have proved more resistant.

The effects of the revolution ushered in by genetic engineering techniques will be felt first in industrialized nations. However, it holds greatest promise for the third world. Impoverished economies without the expertise to apply sophisticated cultivation techniques, nor the foreign exchange to buy expensive machinery to maximize crop yields, can look forward to crops that thrive on little water, without herbicides or insecticides, and under unfavourable climatic and soil conditions.

More than 1,000 companies around the world have begun to apply gene-splicing techniques to plant agriculture. Large agricultural chemical companies have joined the legion of lesser-known biotechnology firms. In addition, land-grant agricultural universities in the US and research institutions like the FRG's Max Planck Institute have research programmes in agricultural biotechnology.

Plant biotechnology has lagged behind animal biotechnology, however, mainly because gene-splicing methods developed for biomedical science transfer far more easily to the latter and plant genetics is a far less advanced science than animal genetics. Moreover, genetically engineered crop varieties are considered by many to be less saleable than, say, genetically engineered pharmaceuticals. (Source: South, January 1988)

Salt bushes to fight salinity

An estimated 7 per cent of the world's land area is badly affected by salt; in particular, millions of hectares in Africa and in North, Central and South Asia are unusable because of rising salt.

Western Australia has substantial areas with sterile topsoil, the result of clearing the bush and planting the land to wheat. State Department of Agriculture scientists have been seeking ways to reverse the process and make the land useful again. First they researched salt-tolerant forage plants, tested them and identified those most suitable for various saline conditions. One problem was that even highly salt-tolerant salt bushes, such as the Atriplex species and Maireana brevifolia, are salt-sensitive in the germination stage. A method had to be found to create a mini-environment in which seeds could germinate and grow until mature enough to tolerate the salt in the soil.

A special machine cultivated the ground, made a mound and pressed a V-shaped niche to concentrate water. The seeds were placed at 1-2 metre intervals

and covered with mulch. The bottom of the niche is above ground level to improve drainage and help leach the salt out of the soil.

Once a good stand of bush is established, grazing from that land can go on more or less indefinitely. Sometimes production from salt-tolerant forages equals, in dollar terms, wheat production on non-saline land in the same district.

The ecology has also improved. Within a year of planting the bushes, there are birds nesting in them. Mice, lizards, insects and spiders colonize the stands. Grasses and other plants start to grow under the bushes. And the soil on the surface becomes less saline. (Source: Development Forum, March-April 1988)

New process to extract compounds from plant roots

Lion (Japan) has developed technology for extracting compounds from plant roots. The process has already been used to obtain a thousand times more shikonin from gromwell roots than can be extracted with conventional techniques. The new process generates hairy roots by treating the roots with Agrobacterium rhizogenes. These secondary roots produce the same metabolites as the natural roots, and they grow very quickly in culture media. The shikonin pigment is excreted into the culture medium and is removed from it by an adsorbent column. Although the process will not be used commercially for shikonin production, it could be adapted for producing other plant root metabolites for use in pharmaceuticals, perfumes or pigments. (Extracted from Japanese Chemistry, 4 February 1988)

Asparagus plants from tissue calluses

Researchers at Jujo Paper (Tokyo) have developed a method for producing large numbers of asparagus plants from tissue calluses grown in culture. The technique allows asparagus to be harvested in two years, as compared to three years with current cultivation methods. Asparagus tissue calluses are conventionally produced from cells isolated from the growing tips of young shoots. The culture medium usually includes the plant hormones benzyladenine and naphthaleneacetic acid, but these hormones also induce the formation of abnormal, transparent sprouts that fail to develop. Jujo researchers determined, however, that they can increase the production of healthy, white sprouts by including a special (undisclosed) hormone in the culture medium. (Source: Bio/Technology, Vol. 6, January 1988)

Vegetable production factory using artificial light

A vegetable production factory, which began operations in Kushiro City, Hokkaido in April 1986 is currently shipping out about 300 lettuce plants/day.

The factory was developed by Toyo Engineering Corp. as a vegetable production system using artificial light for operation in frigid regions.

The vegetable factory is literally a system for industrially producing vegetables. It is designed to continuously and efficiently produce a fixed quantity of vegetables daily and uniformly without being influenced by external environmental conditions.

Since it represents a technology that produces vegetables without insolation and soil, the technology is actually applicable not only to frigid regions but also hot climates such as deserts or urban building tops, and in the future to marine cities and space cities. As long as its economic feasibility can be demonstrated, the technology will be applicable virtually anywhere. Thus the vegetable factory presently in operation may be regarded as an experimental facility with great future potential.

The factory is made of a steel skeleton construction and its installation area is 333.04 m². The culture chamber is equipped with a plant germination tank, a seedling culturing tank and two growth tanks. The plants are transplanted from the first to the second and third tanks depending on their stages of growth.

More specifically, when producing lettuce, for example, the coated seeds are first sown on an urethane foam sheeting provided in sleeve pots made of plastic. Then they are lined up on the plant germination tank's floor for germination under white incandescent lamps. The germinated plants are next placed in the seedling culturing tank which contains a nutritive liquid to grow bigger under fluorescent lamps. Subsequently, in the first growth tank, the plants are grown even bigger and stronger under high-pressure sodium lamps and metal halide lamps having a combined light intensity of 20,000 lux. After they are grown to designated size, they are shifted to the second growth tank, provided with ample space between each plant to expedite their growth.

From the time of seed germination to harvesting, a computer is employed for centralized control of internal conditions such as the temperature, humidity, carbon dioxide concentration, lighting time, fertilizer concentration and pH of the nutritive liquid. Meanwhile, filters are used to prevent infiltration of insects into the factory. The culturing chambers are constantly maintained in a germ-free condition, so no chemical herbicides or pesticides are used.

When the plants grow to a weight of about 100 g each, they are uprooted from their sleeve pots for shipment. Lettuce is shipped out about 30 days after the seeds are sown. The growth rate is roughly 2.5-3 times faster compared with culturing on farmlands. Since the plants are not influenced by external meteorological conditions or insects, the yield rate is constant and the plant quality very uniform. The mineral and vitamin contents of the vegetables grown by this method have been confirmed to be 1.4-1.5 times higher than those of their farmland counterparts.

Besides lettuce, the factory also engages in the growing of about 10 other plant types such as celery, herbs, and Chinese vegetables. Determining the environmental conditions for culturing these plants is very difficult. Environmental conditions are being changed in various ways experimentally at present in order to acquire reliable data and ascertain optimum growing conditions.

The vegetable factory plans to start producing new kinds of plant by the end of this year with the aim of not only establishing the conditions for the factory's economic feasibility but also to expand the utility value of the facilities themselves. Further information may be had from Toyo Engineering Corp., 2-5, Kasumigaseki 3-chome, Chiyoda-ku, Tokyo. Tel: 03-581-6331, Telex: 2223344 TEC. (Source: JETRO, December 1987)

Crop protection

Crop Genetics International, of Hanover, Maryland, wants to bypass the problem of crop protection by putting new genes into a group of little-known bacteria called endophytes, and then putting the endophytes into the plants.

The victim of this cunning ploy will be the European corn borer which causes more than $400 million-worth of damage in America each year and it recently turned Kenya's unexpected corn surplus into a suspected health hazard. Field testing could begin soon.

Dr. Peter Carlson of Crop Genetics International decided that the genetic engineering of bacteria was a relatively simple procedure, and getting the endophytes into the plants did not look difficult.

The first hurdle was choosing the best endophyte for the job but there was little information to go on. The benign endophytes had been largely ignored by scientists, who preferred bacteria with obvious propensities for good or ill. Dr. Carlson persevered, and now has a list of some 1,000 different endophytes. He selected one called Cxc, which normally lives in Bermuda grass, as a candidate for conveying pest-resistance to corn. Cxc, it seems, is harmless to virtually all living things; furthermore, it thrives only within the plants, so it will not stray too far from its hosts. Cxc does not normally live in corn, but will happily, if put there, multiply in its sap.

Having chosen Cxc, the scientists at Crop Genetics then had to choose a gene to put in it. They decided on a gene from Bacillus thuringiensis, another bacterium, which describes a toxin. The toxin is popular because it is safe and selective, so much so that it has been in use since 1938 as a garden and forest pesticide.

At the end of last year toxin accounted for 0.1 per cent of the proteins produced by Crop Genetics' best genetically engineered endophytes. Crop Genetics believes that yields of around 1 per cent are needed to control insect pests. It hopes to achieve that by the end of this year - by linking more efficient promoters, stretches of DNA responsible for switching on genes, to the toxin gene.

The next step is to perfect a process that can introduce the altered endophytes into corn seed. Crop Genetics is working on a system which throws bacteria at the seed so hard that they can get into the tiny cracks that form in the seeds' coats while they dry. The bacteria then rapidly reproduce within the growing corn plant. But since the bacteria cannot get into the next generation of seeds without such help, the pesticide dies with the plant.

Crop Genetics wants to try out its product in three open one-acre sites (two in Maryland and one in Montfavet, France). Young corn plants will be injected with the recombinant endophytes and then exposed to the destructive caterpillars.

Crop Genetics reckons, after $50,000 of research, that people will be perfectly safe. The bacterium is contained within the plants, and unlikely to get out. Anyway, other species of caterpillar living on weeds near corn in Maryland are not affected by the toxin. The toxin is in common use, so more testing seems unnecessary. Cows have eaten the wild Cxc endophyte in Bermuda grass for centuries without any untoward effects. As for the consumer, since the endophytes cannot get into the seed kernel without help the corn eaten should be bacteria-free. If some toxin did get through, or the method was used on other crops, the gut's digestive juices could deal with it. (Source: The Economist, 16 April 1988)

Biotechnology tricks generate environmentally 'safe' insecticide

Public concern about the safety of releasing live, genetically engineered bacteria into the environment has led one biotechnology company to invent a new kind of genetically engineered produce made from dead bacteria.

Dr. Jerry D. Caulder, president of Mycogen Corporation of San Diego, explained the process used to kill the bacteria that turns them into tiny capsules containing an environmentally safe insecticide, or biotoxin.

The capsule, analogous to the gelatin capsule used to protect human drugs until they reach the stomach, protects the biotoxin until it is eaten by an insect pest.

Mycogen received two US patents for the invention in September 1987. Called the "MCap" biopesticide delivery system, the invention enabled Mycogen to become the first company to get Environmental Protection Agency approval to field test genetically engineered bacterial pesticides.

Several biotechnology companies are working on genetically engineered bacteria for use as alternatives to chemical pesticides. Such bacteria can be engineered to produce natural toxins that kill crop-eating insects but are safe for humans, beneficial insects, or other living things. If effective, these biopesticides could help to eliminate the health and environmental risks caused by chemical pesticides.

EPA has been slow to approve field tests of live genetically engineered bacteria because of concern that the microbes might multiply and spread, causing unforeseen environmental problems. The first such tests were approved in 1987, after delays as long as four years.

A staff chemical engineer at Mycogen suggested that they kill its genetically engineered bacteria. Then the company could get quick EPA approval for field tests since dead bacteria cannot hurt the environment. Initially the idea was dismissed as killing the bacteria would destroy the cell wall and deactivate the insect toxin within, but company scientists eventually developed a process combining heat and chemical treatments that killed the bacteria while cross-linking the molecules of the cell wall.

The researchers had not only solved the problem of containment of experimental organisms in the environment, they also had invented a tiny, natural capsule that prolongs the effectiveness of the toxin.

By killing the bacteria, Mycogen was able to start field tests of its first genetically engineered biopesticide in 1985, two years before the much-publicized initial field test of live genetically engineered bacteria. A similar technique is being used to carry hundreds of microscopic, parasitic worms. The worms, a variety of nematode, are the "active ingredient" in a newly patented agricultural pest-control system. Although not yet commercially available, the "pills" have been shown in preliminary tests to be effective against such pests as fire ants, termites and corn rootworm.

It has been known for years that parasitic nematodes can be useful as biological controls. When consumed by an insect pest, the nematode releases a variety of bacteria that are deadly to the insect. But with 2 to 3 billion nematodes required per acre for control, distributing them is a problem. The new method, according to Robert J. DeDominic of Plant Genetics, the Davis, Calif.-based biotechnology company that developed the system, has great potential "if we ever get people to start producing these nematodes in great enough quantities".

Indeed, the friendly nematode is in short supply. According to Art Kushner, a vice president of Biosis, a Palo Alto, Calif. mass-producer of nematodes, it is difficult to grow nematodes in large quantities. The company is experimenting with growing them in a 7,500-litre fermentation container, with hopes of producing 100,000 nematodes per millilitre.

He adds that partly dried, living nematodes may prove more useful than the gelatinized ones, as the latter need to be refrigerated. (Source: Science News, Vol. 132, 12 December 1987 and Chemical Marketing Reporter, 1 February 1988)

Protein in bean thwarts weevils' feast

Researchers in the UK and USA have found out what enables some wild strains of bean to resist attacks by weevils.

The common bean, Phaseolus vulgaris, is the preferred diet of two bruchids, the common bean weevil, Acanthoselides obtectus, and the Mexican bean weevil, Zabrotes subfasciatus. These two pests are responsible for the loss of between 5 and 15 per cent of the stored beans in Latin America. In Africa the weevils account for losses of up to 35 per cent. Such damage is often devastating to small farmers in Latin America and parts of Africa where the common bean is a staple food.

Between 1978 and 1981 researchers at the International Centre for Tropical Agriculture in Cali, Colombia screened more than 8,000 varieties of cultivated beans for resistance to the bruchids without success. Then, in 1981, they received 350 varieties of wild bean from Mexico, 10 per cent of which proved highly resistant to both species of bruchid. Fortunately, the wild varieties could be crossed with cultivated varieties, and the segregation of characters followed the principles of simple Mendelian inheritance.

Researchers at the University of Wisconsin showed that a previously unknown protein was present only in those beans that were resistant to bruchids. They named the protein arcelin after Arcelia, the town in Mexico where the wild varieties came from. Researchers in Cali later showed that beans which produce arcelin are resistant to Z. subfasciatus but not to A. obtectus. They then made a flour of beans that are susceptible to Z. subfasciatus and added increasing amounts of arcelin. The "fake" beans containing the highest concentrations of arcelin were damaged the least. As the level of arcelin increased, so the life cycle of the Mexican bean weevil was prolonged and the proportion of emerging adults drastically reduced. Researchers can now detect arcelin by electrophoresis, serological tests and, quickest of all, by an ELISA test.

At the University of Durham and the Overseas Development Natural Resource Institute, researchers set about investigating what, if not arcelin, is responsible for resistance to A. obtectus. The resistance factor turned out to be a carbohydrate, and investigators are now attempting to isolate and characterize the substance in the hope of finding a simple test to detect it.

Once the carbohydrate can be detected quickly and simply, plant breeders can speed up development of resistant beans. Breeders would screen the progeny of each generation for resistance and so could make subsequent crosses more quickly. Toxicity tests of arcelin on mice and rats have so far revealed no adverse effects. Toxicity tests are to continue for another year. (Source: New Scientist, 7 April 1988)

Biopesticide against Colorado potato beetle

This year, farmers in the Northeast of the USA should be able to use a bacterium as a new, environmentally safe pesticide against the Colorado potato beetle, a pest that has resisted decades of chemical onslaughts.

Pending registration by the Environmental Protection Agency, the bacterium will be marketed this spring, under the tradename "M-One" bioinsecticide. The earliest applications could take place in May on the Delmarva Peninsula, comprising Delaware and parts of Maryland and Virginia.

"M-One" bio-insecticide provides crop protection without harming health or the environment, but it will cost about the same as chemical pesticides," says Dr. Jerry D. Caulder, president of Mycogen Corporation.

Scientists at the San Diego-based biotechnology company discovered the bacterium to be effective against the Colorado potato beetle.

Known to scientists as Bacillus thuringiensis (B.t.) variety san diego, "M-One" bioinsecticide is a newly discovered variety of the bacterium.

The natural toxins in many varieties of B.t. kill crop-eating insects but are safe for human beings, beneficial insects, and other living things. B.t. has been used to control caterpillars for more than 50 years, but until now, none of the commercial varieties of B.t. have been effective against the Colorado potato beetle.

Mycogen has tested "M-One" bioinsecticide for Colorado potato beetle on several hundred acres of potatoes, tomatoes, and eggplants. The tests indicate that the product provides more than 90 per cent protection from insect damage.

Through the process of natural selection, insect pests often evolve resistance to pesticides. In this way, the Colorado potato beetle has become resistant to most of the chemical pesticides that have been used against it, but Dr. Caulder believes that insects may not develop resistance to "M-One" as quickly as they have developed resistance to chemical pesticides. (Extracted from Chemical Marketing Reporter, 8 February 1988)

New insecticide from arrestant

A new insecticide could be made from the lethal crystals with which a tiny parasitic wasp injects its caterpillar victims, according to US Department of Agriculture scientists. The female Euplectrus plathypenae wasp stings its host and injects an arrestant into the insect's bloodstream to prevent it from moulting. The host insect stops growing and, unable to shed its skin, dies, according to T.A. Coudron of ARS. In laboratory experiments, the substance was effective against growth in bollworm, cabbage looper, armyworm, common green lacewing and asparagus beetle. Coudron says that the chemical arrestant affects larvae before the fifth and sixth instar (stage), when they do 90 per cent of their feeding damage to crop plants. (Extracted from Chemical Marketing Reporter, 18 January 1988)

Automated plant propagation

Developers of an automated plant micropropagation system claim hundredfold increases in plant tissue culture productivity. Concomitant price reductions could expand commercial micropropagation beyond low-volume, high-value ornamentals into such bread-and-butter crops as tubers, bulbs, vegetables and woody species. Micropropagated seedlings might even compete with relatively expensive seeds.

Plant Biotech Industries of Ashrat (Israel) has automated the entire process of micropropagation, without ever being touched by human hands. This

virtual elimination of manual labour not only saves operating costs, it also ensures that seedlings are pathogen-free when delivered to customers.

The automated micropropagation system eliminates time-consuming plating of plant cells onto gel media. Instead, growth to the propagule stage takes place inside the bioreactor. A pilot facility being built in Israel as a joint venture with Primerica (Greenwich, CT) will produce 15 million plants per year, according to a consultant for the company. (Source: Bio/Technology, Vol. 6, April 1988)

AGC and Stirling Diagnostics to focus on aquaculture and agricultural markets

The Agricultural Genetics Company (AGC) is setting its sights on a new market opportunity, expected to be worth in excess of £200 million by 1992, following its involvement in the formation of Sterling Diagnostics Ltd.

Stirling Diagnostics plans to launch a first series of kits later in the spring. These kits will enable vets and fish farmers to rapidly diagnose bacterial diseases which currently cause major losses to the salmon and trout farming industries worldwide. Subsequent kits will tackle the problem of the identification of viral, bacterial and fungal pathogens in arable and horticultural crops. It is anticipated that full field trials will begin in the spring for cereal fungi. In addition, the first kits will address potato, flowering plant and sugar beet viruses, including rhizomania.

Initial efforts will focus on establishing a rapid and reliable testing service for farmers and fish farmers. The service will be offered from a purpose-built laboratory on the Stirling Innovation Park. One of the first services will be a virus testing service for mushroom spawn producers. Details from: Dr. Roger Gilmour, Chief Executive, Agricultural Genetics Co., Unit 154-155, Cambridge Science Park, Milton Road, Cambridge CB4 4GG or on 0223 312882. At Stirling Diagnostics, talk to Dr. Michael Horne on 0786 73171 or to Dr. James MacAskill on 031 228 2281. (Source: Biotechnology Bulletin, Vol. 7, No. 2, March 1988)

New system for plant tissue culturing

Toyobo Co., Ltd. (Japan) has developed a new system for plant tissue culturing that uses polyester fibre and has started full-scale marketing of the system.

Called "Plantex", the new culturing system features high-culturing efficiency and ease of operation. It consists of a plastic vessel and a supporting polyester fibre mat for liquid media as an alternative to agar, which is most commonly used today. The new mat has a special composition that is capable of rapid transfer of oxygen and nutrients, realizing a few times higher cell growth efficiency than when using agar.

If one desires to supplement a new medium and/or add a special ingredient or drug, this can be carried out while the cultivation is proceeding. Culture conditions can readily be modified by changing the old medium with a new one without transplanting the cells growing on the mat.

Since all the vessels and fibre mats are thoroughly sterilized with ethylene oxide gas, sterilization processes such as autoclaving are not required. This simplifies operations.

Plantex can be applied to various kinds of experiments in the field of plant tissue culture, including micropropagation, callus culture, cell aggregate selection and embryo culture. Forecasting an accelerated demand in the field of biotechnology R&D, the company will commercialize the application of the system for animal and insect cell culturing. Further information may be obtained from Toyobo Co., Ltd., 2-8, Dojimahama 2-chome, Kita-ku, Osaka. Tel: 06-348-3191. (Source: JETRO, April 1988)

Ornamental plants commercialized

Mitsui Petrochemical Industries Ltd. (Japan) has developed new types of ornamental plants, using applied biotechnology, named "Bio Green Interior plants" and will begin distributing samples.

The new plants include ornamentals such as Vriesea carinata, Pachiras and Syngonium whose breeds have been improved and miniaturized. They are meristem cultured by virus-free cultivation and then sealed in compact, transparent and hermetically sealed containers together with acrylate resin particles.

The resin particles contain water 30-50 times their self-weight and provide the plants with the necessary nutrition and water so that the sealed plants remain healthy and beautiful for months and sometimes years on end without watering.

The firm has so far established technologies for the miniaturization, virus-free nurturing and mass production of over 20 plant varieties. Experiments have corroborated that there is hardly any water vaporization from the sealed containers and that the plants can be preserved maintenance-free for at least three months and at times for as long as two years.

The container vessels come in three models and are priced according to their size.

Incidentally, the company has been engaged in the full-scale tank cultivation of white trumpet lilies since last year. They have succeeded in the mass culture of about 400,000 grafts at its Iwakuni Plant and plan to distribute samples transplanted in pots within the year. Further information may be obtained from Mitsui Petrochemical Industries Ltd., 2-5, Kasumigaseki 3-chome, Chiyoda-ku, Tokyo. Tel: 03-580-3611. Telex: J22984. (Source: JETRO, April 1988)

Food production and processing

Biogas algae could feed the world

A volunteer group in Switzerland has developed a way of using blue-green algae (cyanobacteria) to turn a major problem with biogas generators into a cheap source of protein.

In a biogas generator, organic material such as vegetable scraps, weeds or manure, are fermented by bacteria in a tank. This produces a sludge that can be used for fertilizer, and so-called biogas that can be used for heating and lighting.

The fuel in the gas is methane. But the biogas flame burns red rather than blue, and gives off soot, because it contains up to 40 per cent carbon dioxide. It also adds to the burden of greenhouse gases in the atmosphere. With seven million biogas generators providing power in China alone, the contribution is substantial.

The Swiss group calls itself Green Flamingo, after the bird that lives on the blue-green algae that thrive in alkaline lakes in Africa. (Flamingos are actually pink because of the beta-carotene pigment in the algae.) They have devised a way to bubble the biogas coming out of the fermentation tank through water, where the carbon dioxide dissolves. The methane is then drawn off and can be burned cleanly.

The carbon dioxide solution is, in turn, fed to blue-green algae, Spirulina. The solution would be too acid to feed to most micro-organisms, but Spirulina lives at such high natural levels of alkalinity, up to pH 11, that the acid makes little difference. Francois Baumann, of Green Flamingo, says the Spirulina can be grown under sunlight in troughs containing sea salt, at one fifth the strength of sea water, with phosphorus, iron salts and nitrogen from the biogas fermenter.

This makes it possible to use biogas and Spirulina in an integrated system. The fermenter supplies carbon dioxide and nitrogen for the Spirulina, and methane for the village; the Spirulina provides food for people directly, or is fed to fish.

Spirulina is good food, says Baumann. It contains up to 70 per cent protein dry weight, and its efficiency in turning raw input into protein is 25 times that of maize, and 300 times that of beef. The tanks of water may seem an inappropriate farming method for desert areas, but Baumann says that it produces more nutrients for a given investment of water than any other food.

For human nutrition, Spirulina's protein is equivalent to that of eggs, being slightly deficient only in cystine and tryptophan. It contains little saturated fat, says Baumann, but all the essential fatty acids, including gamma-linoleic acid, a scarce nutrient in some traditional diets. The algae contain vitamins A and B complex, including B12, otherwise found only in animal sources.

Spirulina is grown commercially in the US and France to provide blue food colouring, health foods, and cosmetics. It is used to purify waste water in Israel, animal food in India, and is being studied as a way of producing oxygen on submarines and spaceships.

Green Flamingo has set up prototypes of their integrated biogas/Spirulina system, called Flamingo One, in India, Togo, and Peru. The algae have mostly been used as a food supplement for babies and nursing mothers. Baumann says an unexpected observation has been the ease with which babies digest the algae, which are primitive organisms without complex cell walls. Babies on the edge of starvation, he says, respond to Spirulina after they have ceased to respond to any other emergency food.

The group wants to establish its integrated systems in areas of the Sahel in West Africa that are becoming deserts. The idea, says Baumann, is to set up a green belt along water courses based on the humus added to the soil by the biogas fermenters, and to save trees by substituting biogas fuel for wood. In the long term it could alter the climate and halt the advance of the desert.

Meanwhile, the Chinese are impressed with the system, and are trying it out on 300 biogas installations.

Recently, the group won the top award in an EEC competition for its work. (Source: New Scientist, 31 March 1988)

Enzyme against food contamination

Prodotti Antibiotici (Italy) researchers are extracting an enzyme from egg whites that may be used to prevent food poisoning. Scientists have recently noted an increase in food contamination from the bacteria listeria monocytogenes. Listeria has been found in vegetables, cheeses and sausage products. Though it usually does not lead to serious illness, it can produce influenza-like symptoms and be deadly to the elderly and foetuses who contract it from their mothers. A University of Wisconsin researcher found that listeria can be killed with an enzyme called lysozome, a natural bacteria-fighter in the eyes and nasal passages. Lysozome has been shown to destroy listeria grown in cole slaw without affecting the quality of the food. The enzyme has also been found effective against certain kinds of botulism. Prodotti Antibiotici has produced lysozome from egg whites, and in collaboration with Miles Laboratories is trying to determine which commercial foods can use the enzyme. (Extracted from Wall Street Journal, 22 February 1988)

Food-grade yeast process

Provesta's fermenter-based food-grade yeast process provides high production rates and simplified downstream protein processing. A high-performance fermenter developed by Fluor Daniel is the core of the process, which produces a high-cell-density broth that is spray-dried without intermediate dewatering. Provesta, the marketing arm of Phillips Petroleum, will start a three-four million pounds per year protein production plant at Bartlesville, OK, by July 1988. Fluor Daniel has been licensed by Phillips to produce and sell the design of vessels under 30 kL.

Three variants of the Provesteen high-quality protein product, which has successfully substituted 50-75 per cent of protein requirements in animal feed and has been approved for human consumption in the US, are available using feedstocks of alcohols, sugars or whey - methanol or ethanol from oil and natural gas; sugars from sugar cane, sugar beet, sorghum, sweet potatoes, bananas or corn. Using whey permeate as a carbon energy source provides lower protein content but adds value to material otherwise wasted.

The high growth rate provided creates a heat output (1.6 kW for a 25 kL reactor) that requires efficient cooling; a liquid ammonia refrigeration system minimizes risk of contamination because ammonia is one feedstock. The internal heat transfer surface is of a proprietary material that minimizes fouling and reduces resistance to heat transfer. (Extracted from Process Engineering, January 1988)

New enzymes for food processing

Imperial Biotech (UK) has introduced aminopeptidases, a range of enzymes for food processing. Aminopeptidases are proteolytic enzymes that hydrolyze proteins, subtly altering protein structures by causing a change in functional and organoleptic properties. This improves the proteins' nutritional values and makes them suitable for many applications including acceleration of cheese ripening, production of low-fat dairy products, and development of high-nutrition foods for use in hospital patient recovery. Unlike previous attempts at protein hydrolysis, the new enzymes do not give foods a bitter taste or off flavours. This gives them great potential to develop new enzyme applications in the food industry, following on from the success of enzymes to hydrolyze carbohydrates over the last 15 years. (Extracted from Food-Processing (UK), December 1987)

Alternative sweetener

Erythritol can be produced by fermenting grape sugar via Aureobasidium yeast, according to the Japanese National Food Research Institute. The process can yield 47 grams of erythritol from 100 grams of sugramsar. The yeast strain can live under high osmotic pressure, so grape sugar solutions as high as 35 per cent can be used. Erythritol might be used as a noncaloric sweetener, since it is not metabolized by the human body or enteric bacteria. Its sweetness is 80 per cent that of sugar. Some foods already contain tiny amounts of erythritol.

Nikken Chemicals plans to commercialize the compound in about three years. (Extracted from Japanese Chemistry, 28 January 1988)

Synthesis of diet sweetener from inulin

Japan's National Food Research Institute, Ministry of Agriculture, Forestry and Fisheries, and Ninon Starch Co., Ltd. have jointly succeeded in synthesizing, at a high yield rate, a diet sweetener agent from the Jerusalem artichoke (Helianthus tuberosus).

This sweetener, "difructose", has a structure in which two fructose molecules are bonded together. Its sweetness is rather low, only about one half that of sugar. However, since it does not promote insulin secretion, it can be used as a sweetener for diabetics.

Difructose is produced from a polysaccharide known as inulin that has a construction in which one glucose molecule combines with 30-40 fructose molecules. Reacting inulin with a refined inulin decomposing enzyme, obtained from a certain type of soil bacteria, enables difructose to be produced at a rate as high as 85 per cent.

The percentage of inulin in the Jerusalem artichoke tuber is as high as 15-17 per cent, and can be cultivated with ease even on barren land since it is highly reproductive. Further information may be obtained from National Food Research Institute, Ministry of Agriculture, Forestry and Fisheries, 1-2, Kannondai 2-chome, Yatabe-machi, Tsukuba-gun, Ibaraki Pref. Tel: 02975-6-7971. (Source: JETRO, January 1988)

Low-calorie fat substitute developed

An all-protein substitute for fat in certain foods has been developed by NutraSweet Co., a subsidiary of Monsanto. Use of the additive will reduce the calorie count and unsaturated fat and cholesterol contents of such foods as ice cream, yoghurt, butter, cheese spreads, dips, sour cream, salad dressings, and mayonnaise. The product is unsuitable for frying or baking, however. Trade-named Simplesse, it is scheduled for introduction in 12 to 18 months.

The fat substitute is made from milk and egg white proteins by a proprietary combination of heating and shearing called microparticulation. The technique results in spherical particles 0.1 to 2 μm in diameter. In this shape and size range, the particles roll smoothly over one another to produce a rich taste and texture associated with fats.

Because the additive is made by mere mechanical processing of natural protein, NutraSweet spokesmen say that it requires no approval from the Food and Drug Administration for marketing. However, the company has agreed to file a petition with the Food and Drug Administration to seek "generally recognized as safe" (GRAS) status for the substance, after meeting with FDA Commissioner Frank E. Young, who said he was "perplexed" by the decision to announce the product without consulting FDA.

One of the key questions concerning Simplesse will be whether extracting the protein and altering it will change its toxicity and nutritional value, says Theodore Labuza, incoming president of the Institute of Food Technologists and professor of food science and technology at the University of Minnesota in St. Paul.

Labuza says NutraSweet was within legal limits when it commissioned an expert panel to determine whether Simplesse was GRAS. The Flavor Extracts Manufacturers Association (FEMA), for example, also has an expert panel to determine the GRAS status of artificial flavours made from natural products.

But Gerard McCowin, director of FDA's division of food and color additives, says the FEMA situation is different because it deals with minute amounts, compared with the potentially large Simplesse market.

Although NutraSweet, a division of the St. Louis-based Monsanto Co., has done nothing illegal, some believe the company made a public relations blunder.

NutraSweet has said it went through proper legal channels, and would not comment further on the Simplesse issue.

Once NutraSweet submits a GRAS petition, FDA's review process should take about 12 to 18 months, which would coincide with NutraSweet's marketing goal.

Meanwhile, Procter & Gamble is planning to introduce its own fat substitute, called Olestra, but it involves new chemical configurations and thus will require FDA approval.

In many blended foods, 1 gram of Simplesse containing 4 calories will replace 3 grams of fat containing 27 calories. And as a protein, it has no unsaturated fat or cholesterol. Excessive consumption of saturated fat as in some animal fats and hydrogenated vegetable oils has been linked to elevated concentrations of low-density lipoprotein (LDL) in blood serum.

Future projects at NutraSweet will aim at incorporating Simplesse into various food types. The company also will seek partnerships with other firms that will bring Simplesse to market as soon as possible. (Source: Chemical and Engineering News, 1 February 1988 and Science News, Vol. 133, 6 February 1988)

Salmonella bacterium test

Vitek Systems Inc., the Hazelwood (Mo.) subsidiary of McDonnell Douglas Corp. is developing a test for salmonella, using a modified horseradish enzyme that attaches itself to the dangerous bacteria. The tagged bugs are then captured on a filter, where they become visible as a brown spot. The test can reveal as few as 10 organisms, far less than the 1 million detected by conventional tests.

Because the new test will take two days to run instead of five, Vitek says food processors can reduce inventories substantially and ship food sooner. Some 2.5 million salmonella tests are conducted in the US annually at a cost of $7 each, and the market is likely to grow at some 10 per cent per year for the next few years. The salmonella test may be marketed first in the UK during 1988. (Source: Business Week, 22 February 1988)

The taste of food research

The UK's Institute of Food Research, the largest institute within the Agricultural and Food Research Council, covers a wide variety of subjects in its programme of basic food science. Grouped into three main areas - food processing, food safety and food quality - the IFR's research includes everything from relatively exotic work on plant root cultures, robotic meat carving and the theoretical physics of food structure, to more mundane but no less valuable work on cooking and chilling processes, nutrient composition, and the texture of frozen french fries. In this article on the IFR, Andrew Miller samples a limited selection of items from the institute's menu of research.

Pathogenic bacteria and natural toxicants feature prominently among the IFR's work on food safety.

Rapid bacterial detection and counting methods are being developed at Reading, where scientists have already produced the so-called DEFT test for counting bacterial numbers, now being used on a commercial basis by the dairy and meat industries. According to microbiologist Ronan Kroll, this method has been recently modified to get a crude selective count of various types of bacteria, and further work will be done to allow the test to be used with heat-treated food.

One new method, for determining the keeping quality of pasteurised milk by counting spoilage bacteria involves a colour change when a bacterial enzyme, cytochrome oxidase, binds to a fluorescent dye. The test still needs some improvement, and has not yet entered field trials.

An electrical detection method, based on predicted voltage changes when antibodies bind to bacterial surfaces, is the subject of another new project. Although at a very early stage, the method could have advantages in linking up with computers, Kroll believes.

The use of harmless bacteria as protection against harmful bacteria is being studied with poultry, to help counter the spread of Salmonella in flocks, by Geoff Mead at Bristol, and with premature babies, who are vulnerable to infection, by Roy Fuller at Reading. In both the cases, the idea is to keep pathogenic species from colonising the gut by populating it with 'friendly' ones.

Dr. Terry Roberts at Bristol is working on predictive modelling of microbial growth in meats, as a potential way of avoiding a lot of microbiological measurement when processed products are reformulated, for example by changing water or nitrate content.

Bristol microbiologists are also studying whether volatile compounds released by bacteria, such as tyramine and acetoin, can be used as the basis for small chemical sensors in sealed packs of meat. These sensors would enable retailers and their customers to easily see whether pre-packed meats were about to go off.

At Reading, the factors affecting the microbiological susceptibility of beverages - including alcoholic and carbonated drinks - are being studied by Don Stead. Among other things, he is looking for synergistic effects between natural and added preservatives, and it is hoped the project will enable predictive modelling to be carried out.

The food industry, especially the dairy and meat sectors, are fond of using natural enzymes to help them process raw ingredients. The IFR's enzymology is centred on Reading, under Barry Law. The unit is perhaps best known for its work on cheese-ripening enzymes.

Current work includes protein engineering on papain aimed at modifying the natural enzyme to make it more stable at low pH. Law's team hope to make it more active at pH 3 by tinkering with the ionic environment of amino acids at the active site using site-directed mutagenesis based on molecular modelling studies.

One new project is aimed at similarly modifying the specificity of phospholipase A_2, which is used for interesterification of fats, to make it better at upgrading cheap fats like palm oil into expensive cocoa butter equivalents. Another new project, on improving peptidases for use in organic solvents, is aimed ultimately at producing bioactive peptides and flavours.

Meanwhile, work on microbial genetics, under Mike Gasson at Norwich, is focused mainly on the lactic acid bacteria used in the dairy industry, though research on yeast and filamentous fungi is growing. In the last year or so, the group have developed their genetic engineering technology and have perfected the use of protoplasts and electroporation for putting DNA into these bacteria, as well as plasmid vectors for gene cloning, and are now concentrating on the expression and export of materials out of the cells.

Greater understanding of the genetics underlying the metabolism of these bacteria should eventually allow their key industrial traits to be manipulated. For example, citrate metabolism, which results in the carbon dioxide that creates the holes in some cheeses and influences flavour, could be tinkered with by genetic means to give specifically desired characteristics. Gasson's group have been looking at this, in addition to the genes involved in production of proteinase, lactose catabolism, and resistance to bacteriophages.

With the planned disbandment of nutritionists at Reading, nutritional research at the IFR will be concentrated at Norwich, where Professor David Southgate heads a department investigating nutritional composition, nutrient bioavailability, food choice and mineral nutrition.

For example, Ian Johnson and others have examined the way in which a soluble polysaccharide like guar gum can influence the absorption of glucose by making the gut content very viscous. They are now investigating the effect of these dietary components on gut growth, and thus on bioavailability of nutrients, given that these polysaccharides have been shown to cause the release of the gut growth hormone, enteroglucagon.

At Reading meanwhile, nutritionists have studied the ability of some types of fibre to reduce blood cholesterol levels. In pigs with high levels, a diet containing 90 per cent rye was able to keep levels low, though barley and wheat were less effective.

For those humans who would find a high-rye diet more than a little hard to swallow, the Reading group has found that baked beans will do the trick nicely in both pigs and university students. However, the students taking part in the study ate a pound of beans a day: too much for more sensitive bowels, perhaps.

With an eye on how food components interact to affect the texture and other properties of processed foods, IFR scientists study the structure of foods and the biopolymers they are made of, and then try to see how variations can affect the appearance and texture of processed food.

At Bristol, much work has been done on the structure of muscle proteins and interconnective tissue, and this now includes studying the nature of protein gels, such as those used to bind pieces of meat together in processed meat products. Work at Reading includes studies of casein micelles in milk, and the way in which foams such as whipped cream are created.

The extrusion properties of various foods and food components are studied at Norwich along with the structure and properties of protein and polysaccharide gels, and the stability of emulsions.

Last year, Vic Morris and others, in collaboration with scientists at Cambridge University, were able to determine the hexagonal structure of the vicilin molecule. Vicilin is a pea storage protein which, if modified using protein engineering, might one day come to replace imported soya as a cheap source of protein.

Although limited by space, the selection of research projects above indicates that the Institute of Food Research can still draw on a wide range of scientific skills and expertise among its staff, despite some of the financial worries it has faced. It remains to be seen whether the Government's attempt to persuade industry to pay for more of it will be successful. (Source: Chemistry and Industry, 21 March 1988)

Low temperature protein decomposition enzyme

Associate Professor H. Murakami and his group of researchers of the Department of Food Science and Technology, Faculty of Agriculture, Kyushu University (Japan), have succeeded in extracting a new type of protein decomposing enzyme (protease) from krill, a shrimp-like planktonic crustacens. It is characterized by a strong activity in temperatures as low as 20°C, and high hopes are placed on the application to the field of food processing at low temperatures.

The group, alert to the krill's characteristic to mist itself spontaneously when left as it is after being caught, attempted to extract the protein decomposing enzyme responsible for this phenomenon. In their experiments, the krill was minced into an aqueous solution to extract the enzyme. They confirmed that two kinds of enzymes having molecular weights of roughly 30,000 and 50,000, respectively, possess this decomposition attribute.

It was also confirmed that these enzymes display protein decomposition capabilities more than a dozen times higher at 20°C compared with tripsine, a typical protein decomposing enzyme. Even when the temperature was lowered to 10°C, their decomposition capacities were maintained at about 50 per cent of their respective values at 20°C.

In general, protein decomposing enzymes are the most active at about 37°C, but the new enzymes display their peak activities at around 20°C, and even at 10°C display an activity several times stronger than tripsine. True, a few protein decomposing enzymes working at low temperatures have been confirmed in the past, but the intensities of their activities have not been analyzed in detail.

In meat processing, an enzyme process for making the meat tender is necessary, and if protein decomposing enzymes which can be used at low temperatures are available, then processing will be possible without any hazard of spoilage. Also, when manufacturing shoyu (soy sauce), a large quantity of salt is currently used to prevent spoiling in the process of soybean or barley fermentation. However, if low-temperature protein decomposing enzymes are available, then the amount of salt can be reduced. Thus these enzymes also feature a salt-decreasing effect, in addition to permitting detergent enzymes to be used in water, without having to use hot water.

Kyushu University has already succeeded in obtaining an enzyme with a molecular weight of 30,000 in a 100 per cent purified state, and future plans are to conduct structural analysis of the enzyme, including an elucidation of its amino acid arrangement. Further information may be obtained from Kyushu University, Department of Food Science and Technology, Faculty of Agriculture, 10-1, Hakozaki 6-chome, Higashi-ku, Fukuoka City, Fukuoka Pref. Tel: 092-641-1101. (Source: JETRO, March 1988)

Chemical applications

Novo mass-produces enzyme for low temperatures

Novo Industri A/S, an enzyme and insulin producer based in Bagsvaerd, Denmark, has commercialized a genetically-engineered enzyme and plans to market the product as an effective "fat-splitting" component for laundry detergents, the company says. The enzyme, "Lipolase", both dissolves fatty stains at low temperatures and is available to industry in commercial quantities, making it a breakthrough in the detergent industry, according to Novo.

Novo has high hopes for eventual demand for "Lipolase" but must first contend with the regulatory labyrinths surrounding genetically-engineered materials. The regulatory environment is one of the reasons Novo started producing "Lipolase" in Japan before entering either the US or Danish markets. "Frankly, the environment is more favourable for bacteria-related products in Japan than it is here," says Sarah Bayles, investor relations representative.

Though it is difficult to predict when major domestic soapers will become interested, "Lipolase" will probably undergo a three to six year period before the product obtains significant worldwide market penetration.

Part of the marketing appeal to the Japanese detergent industry is the waning popularity of an aggressive cellulose enzyme incorporated into a product named "Attack". The more specific and less harsh action of "Lipolase" puts it in a position to benefit from soapers dissatisfied with the cellulose product. (Source: Chemical Marketing Reporter, 8 February 1988)

Synergen's first commercial product

Coors Biotech Products Co. has opened a plant for the commercial production of riboflavin, also known as vitamin B2, using an improved micro-organism developed by Synergen. The vitamin will be used for human health care applications and in animal feed as a nutritional supplement. First commercial sales are expected by the end of the first quarter of 1988. Coors and Synergen are also nearing completion of a second project in which they are developing a natural food colouring agent. Details from:
Dr. Jane MacQueen, director of corporate communications, Synergen Inc., 1885 3rd Street, Boulder, CO 80301, USA or on (303) 938-6200.
(Source: Biotechnology Bulletin, Vol. 6, No. 12, January 1988)

Purple dye produced by biotechnology

Mitsui Petrochemical Industries, Ltd. has developed and plans to put on the market soon a purple fibre dye produced by the application of biotechnology. This dye is based on a mass production technology using a shikonin plant cell culture technology developed by the company earlier. It follows the firm's commercialization of a biotechnology soap called "Murasaki" (purple) and a lipstick raw material.

Shikonin is a purple [illegible] the root of the natural gromwell (Li[illegible]orhizon) and has been used in Japan fo[illegible]ars for dyeing

kimono purple. However, the plant is very rarely found in natural environments today, so chemically synthesized dyes are being used today for dyeing fabrics purple.

The company established a technology for mass producing shikonin as an "ancient Japanese colour" by applying their plant cell culture technology.

The company is presently conducting pre-market research, and having confirmed that the dye is optimal for silk fabrics, it plans to agressively enter this market. The dye has been highly evaluated by users particularly in the sectors in which existing dyes fail to provide fabrics with the desirable gloss and elegance. Further information may be obtained from Mitsui Petrochemical Industries, Ltd., 2-5, Kasumigaseki 3-chome, Chiyoda-ku, Tokyo. Tel: 03-580-3611. Telex: J22984. (Source: JETRO, April 1988)

Energy and environmental applications

Hydrogen sulphide treatment system using bioreactor

Nippon Kokan K.K. and Dowa Mining Co., Ltd. of Japan have jointly developed and started accepting orders for a hydrogen sulphide treatment system using a bioreactor for treating hydrogen sulphide gases discharged by chemical plants.

The new treatment system uses bacteria called Thiobacillus ferro-oxidans to treat hydrogen sulphide gases, and its operating costs are one half to one third that of systems using the conventional caustic soda process.

In the system's basic process, hydrogen sulphide gas and ferrous sulphate, a hydrogen sulphide absorbing liquid, are mutually reacted to reduce the gas to ferric sulphate and to generate simple sulfur. Simple sulfur is solid-liquid separated and recovered, while the ferrous sulphate solution is oxidized with Thiobacillus ferro-oxidans inside the bioreactor to regenerate it into a ferric sulphate solution for recirculation and re-utilization in the hydrogen sulphide absorption process.

A distinct characteristic is that this system is free of side reaction. Therefore, the absorption liquid is not deteriorated and there is no need whatsoever of using catalyst or chemical drugs. Also since the reaction occurs at normal temperature and pressure, there are also the advantages that the energy cost is minimal, maintenance is accomplished with ease, waste liquid treatment is unnecessary and an excellent selective absorbance with carbon dioxide gas is displayed. Consequently, the system's treatment cost is decreased signficantly.

Various applications are possible with this treatment system such as the treatment of various kinds of gases containing hydrogen sulphide, also for the recovery of sulphur from amine offgas, desulphurization of sludge digestion gas in sewage treatment plants, and the treatment of sour and acidic gases in oil refineries. Further information may be obtained from Nippon Kokan K.K., Public Relations Department, 1-2, Marunouchi 1-chome, Chiyoda-ku, Tokyo. Tel: 03-212-7111. Telex: J22578 NKK. (Source: JETRO, December 1987)

Cornstarch may protect groundwater for pesticides

The US Agriculture Department says cornstarch may be used to protect groundwater from pesticides. If pesticides are released too quickly, they can soak 60 inches into soil and contaminate groundwater. Cornstarch is being tested to encapsulate various weedkillers and insecticides. When cornstarch gets wet, it releases the chemicals slowly, allowing them to stay close to the surface where they are effective. Microbes on the soil's surface are then also be able to aid in breaking down pesticides before they can move deeply into the ground. Illinois Cereal Mills (Paris, IL) and Stauffer Chemical (Westport, CT) are co-licensees for the process. (Extracted from Business Week, 15 February 1988)

Microbes 'could break down dioxin'

Chemicals from mutant microbes could solve one of the world's fastest-growing problems: what to do with toxic wastes and land contaminated by persistent pesticides. Ananda Chakrabarty, a microbiologist at the University of Illinois at Chicago, has developed a strain of soil bacterium that has the potential to break down such serious environmental contaminants as DDT, dioxins and polychlorinated buphenyls (PCBs).

He has also produced from the bacterium Pseudomonas, an emulsifying agent that will save oil companies millions of pounds a year in treating their hydrocarbon wastes.

Chakrabarty selected a strain of Pseudomonas that could grow in the presence of hydrocarbons. Hydrocarbons are hydrophobic and the bacteria live in water, or in a film around soil particles. Normally a bacterium surrounded by water cannot get close enough to a hydrocarbon compound to take it in and digest it. Chakrabarty's strain of Pseudomonas has a mutant gene that codes for an emulsifying agent which enables the solution of bacteria and the oil to mix, allowing the bacteria to break down the hydrocarbons.

In field trials in the Middle East, Petrogen, the Illinois company, granted a licence to manufacture the chemical, added the emulsifier to large oil storage tanks and left the mix for four days. Each tank contained about 6,200 barrels of sludge - waste that the oil company must dispose of. Addition of the chemical released another 5,600 barrels of oil that would normally have been lost, and reduced the amount of waste.

The success of the oil-recovery experiments gives fresh impetus to the search for micro-organisms that break down highly toxic substances such as the persistent organic pesticides. The worst of these linger in the environment because there are no organisms that can break them down. This is because they are among the few organic compounds containing chlorine.

Chakrabarty had earlier isolated a strain of Pseudomonas that could break down chlorobenzoic acid, a very simple chlorinated compound. This strain had developed the necessary enzymes to act on chlorine that are missing from normal pseudomonas.

Already, Chakrabarty has had some success in breaking down the notorious dioxin defoliant 2,4,5-trichlorophenoxyacetic acid, one of the compounds in Agent Orange. When he added this strain of Pseudomonas to samples of contaminated soil containing 1,000 parts per million of the toxin, the microbe reduced the level to 7 ppm within a week. Moreover, seeds in the soil germinated and grew, although not as well as in soil free of the herbicide. At some sites, around American army bases for example, the soil contains more than 30,000 ppm of the compound. The microbe removed 90 per cent of the toxin from such highly contaminated soil.

Chakrabarty is convinced that "eventually there will be success in breeding micro-organisms that will degrade many of the most toxic chemicals".

But there are many legal and ethical difficulties surrounding the release of genetically engineered organisms. (Source: New Scientist, 25 February 1988)

Anaerobic waste water treatment system

Japan Organo Co., Ltd. has developed an anaerobic waste water treatment system named "Meta Rapid", which uses pelletized microbe granules for treating organic substances in waste water by methane fermentation while recovering the generated methane gas.

Normally, waste water of high concentration of organic substances is treated by an aerobic biological treatment process, such as the activated sludge process, but this type of treatment is disadvantageous in that it requires a large quantity of electricity in order to supply the required amounts of oxygen. This treatment process also tends to generate secondary pollution, such as offensive odours.

By contrast, the standard anaerobic treatment (methane fermentation) process demands less energy than aerobic biological treatment, enables utilization of recovered methane gas, and generates less excess sludge than the aerobic process. However, the conventional anaerobic treatment process is also accompanied by disadvantages, such as the need for longer treatment times, a poor adaptability to load fluctuations, and difficulties in system maintenance and control. Therefore, its application had usually been limited to the anaerobic treatment of night soil, the anaerobic digestion of sewage sludge, and slightly to the treatment of fermentation waste liquid.

With the newly developed anaerobic processing system, waste water is fed from underneath the reaction tank, which contains microbe granules having particle diameters of 0.5-2.0/mm. Here the microbes are made to come into contact with the upward flow of waste water in order to begin the treatment process. The generated methane gas is piped into a storage tank, and then the treated water is removed of its oil content while its biological oxygen demand (BOD) is reduced by a factor of ten.

The microbe granules, differing from the conventional flotation type microbes (which have particle diameters of 0.1-0.5 mm), have a netted form and comprise aggregations that contain large numbers of these microbes. They are therefore capable of withstanding 5-10 times the loads of conventional microbes, or loads as large as 5-30 kg BOD/m^3/day. Therefore, these microbe granules can be used for treating high-strength waste water having BOD ratings of over 2,000 mg/litre.

In addition, in comparison with the aerobic treatment system, the newly developed anaerobic treatment system's power consumption is as low as one fifth to one tenth, its reaction tank is much more compact, the recovered methane gas can be reutilized, and the quantity of generated excess sludge is significantly smaller.

The system is being marketed at a domestic price of ¥150-200 million, depending on its ancillary equipment. Further information may be obtained from Japan Organo Co., Ltd., 28-23, Hongo 1-chome, Bunkyo-ku, Tokyo. Tel: 03-815-7111. (Source: JETRO, January 1988)

Microbial detoxification at the source

By the year 2000, chemical producers will no longer have to build chemical treatment plants to detoxify hazardous organic waste streams: colonies of microbes in special bioreactors will do the job instead. That is the future as seen by Alan S. Michaels, distinguished Professor of Chemical Engineering at North Carolina State University (NCS) in Raleigh, and three of his colleagues at NCS and Duke University (Durham, NC). Michaels' group is working on the design and development of a bioreactor that uses what they call a "wild or genetically transformed microbial culture" to convert hazardous organics into harmless substances. They have applied to the US Geological Survey for a $750,000 grant to carry out their project. Their test waste: a representative polychlorinated biphenyl (PCB).

Michaels' group hopes to create an immobilized-microbial-cell bioreactor that will: keep a high-density population of specific micro-organisms or organisms alive and stationary for extended periods of time; prevent the bugs from being killed or mutated by the PCB stream or the organisms it might contain; and, at the same time, maximize the detoxification of the waste. Michaels and his colleagues' purpose to evaluate three types of continuous bioreactors that might do the job. The first is a fluidized-bed, solid-phase-supported culture reactor. The second bioreactor is a free-suspension-culture, feed-and-bleed system that utilizes a cross-flow membrane microfiltration unit to remove the toxics. The third system uses tubular membrane filters composed of hollow fibres.

The Michaels team anticipates that the micro-organisms most suitable for these processes will be "solid-substrate-dependent bacteria" - that is, nonaqueous - that will adhere to solid surfaces. Finding the right type or combination of microbes to undo toxicants will be the first major hurdle of the project. The naturally occurring microbes that consume and microbiologically transform or decompose hazardous organics are relatively rare and tend to thrive only in abnormal, hard-to-duplicate environments, such as porous, water-filled subterranean strata. Also, the microbes are unlikely to survive in competition with others that consume and transform organics. Thus, they must be maintained under highly specialized conditions and be isolated from contamination by competing bacteria. In addition, the rare bugs that Michaels and his colleagues are working with will be difficult to keep alive once the microbes are applied to real waste streams.

Another problem will be how to keep the membranes containing the microbes from becoming gummed up by oils and solids that are almost always present in PCB-laden liquids or any waste stream.

Michaels and his team say that they are nowhere near the breakthrough point yet.

Already, researchers at Stanford University (Palo Alto, Calif.) have successfully enhanced the organics-eating activity of bacteria for partial detoxification of a Silicon Valley site. It is being used on groundwater contaminated by trichloroethylene.

Other university researchers also are looking into point-of-generation bioreclamation. For instance, Steven D. Aust, director of biotechnology at Utah State University in Logan, says that his school hopes to reach an agreement soon with one of four waste reclamation companies to develop the use of white rot fungus in biological treatment of hazardous waste.

Environmental organizations, trade groups and other research organizations are lining up in support of the NCS/Duke project. A point-of-generation system, combined with process plant changes to funnel certain types of waste through certain bacteria-filled filters, "are two of the most important steps that

could be taken" to make the biological approach to hazardous waste cleanup work. (Extracted from Chemical Week, 3 February 1988)

Making motor fuels from microalgae

Despite budget cuts, one promising biomass project has moved forward during the past six years. Its object is to make gasoline and diesel fuels from microalgae ponds. The project, which is being carried out by US Department of Energy (DOE), Solar Energy Research Institute (SERI) in Golden, Colo., could by 2010 produce 150-400 bbl of liquid fuel per acre per year. The gasoline that is produced would be priced at $1.60-2.00/gal, says Paul G. Roessler, a SERI staff scientist.

Microalgae, the most primitive members of the plant kingdom, are single-celled and small: they range in size from 1 to 200 micrometers. Yet they can double their biomass 3-5 times a day; and in microalgae ponds, they can produce 12,500 grams/m/year, which makes microalgae - in terms of biomass production - five times more productive than a tropical rain forest. Microalgae also are unique in that they can thrive in highly saline water and can accumulate large quantities of lipids, up to 70 per cent of their biomass. It is the lipids, in fact, that are converted into gasoline and diesel fuels.

The microalgae project involves growing algae in big outdoor ponds. After a rapid growth phase in one set of ponds, the algae are moved into a second set. In their new home, nutrients are limited, growth and cell division stop, and the algae use all their energy to make lipids as storage products for survival. When the algae have accumulated enough lipids, they are harvested. The lipids are then extracted and converted into fuels.

The algae project is concentrating in four major areas. The first, which receives about 60 per cent of total funding, is the study of microalgae growth and production.

Researchers have collected more than 3,000 strains of microalgae and are currently narrowing those down to the best 10-25 strains. Selection criteria include tolerance to temperature and salinity fluctuations, high growth rate and high lipid production. Thus far, Chaetoceros and Navicula strains have been found most suitable. They tolerate temperatures of 10-35°C and salinity of 10-85 millimho/cm. The strains have attained growth rates of 35 g/m/day; the targeted growth rate is 50 g/m/day.

Researchers have found that removing nitrogen or silicon from the media induces the microalgae to accumulate lipids, primarily triglycerides, with fractions of isoprenoids, phospholipids, glycolipids and hydrocarbons. A silicon deficiency, for instance, causes carbon to be partitioned into lipids instead of storage carbohydrates because silicon decreases the activity of a key enzyme involved in storage carbohydrate synthesis while at the same time increasing activity of an enzyme key to lipid synthesis.

Researchers do not believe that a single strain of algae will exhibit the necessary environmental tolerance, high growth and high lipid yield. So desirable traits from different strains will most likely have to be combined, which has led to work in such methods of genetic engineering as mutation selection and protoplast fusion. The search for a virus that can act as a vector injecting desirable DNA into microalgae has also begun. Moreover, researchers have discovered that genetic diversity in microalgae is higher than it is in terrestrial plants. That indicates the algae have a big collective genome, which bodes well for future genetic engineering efforts.

The project's second major area of focus is engineering the microalgae ponds. An open pond system costing $76,000/hectare to construct was chosen because the system is cheaper than raceways or enclosed tubes.

Microalgae harvesting is the third area of focus. Currently, harvesting represents about 25 per cent of total capital cost of a microalgae facility. High-molecular-weight cationic polymers, acting as flocculants, allow microalgae removal efficiences of 85-95 per cent at a polymer cost of 0.5-1.5cents/kg. Such polymer costs are not economical, however.

Converstion of algae lipids into fuels is the fourth area of interest. The lipids contain about 10 per cent oxygen and therefore cannot be blended with crude petroleum, which contains essentially no oxygen. Blending is not possible because at the high temperatures used in crude distillation, the lipid oxygenates would cause polymerization or undesirable reaction. Transesterification now seems the most promising means of producing fuels similar to diesel fuels, while zeolite catalysts could be used to produce gasoline. (Source: Chemical Week, 13 April 1988)

Industrial microbiology

Technology for reforming wool with papaya enzyme

Nakajima Spinning Co., Ltd. of Japan has come out with a technology for reforming animal fibres, such as wool, by using papain, an enzyme obtained by extracting and refining papaya fruit essence. The company has started marketing a thread named "protecorte" which is the product reformed with this new technology.

Not only does the reformed thread retain the intrinsic properties of animal wool much better than threads processed by the conventional chemical reforming method, it also eliminates various kinds of defects.

The trunk (cortex) parts of animal fibres such as wool are covered with cilium-like scales resembling those of fishes. If these fibres were processed intact into thread, these threads would cause diverse irregularities such as shrinkage when washed, stimulation of the fabric wearer's skin, loss of pliancy and lustre, degradation of dyeability and undergo elongation with ease.

To cope with this situation, these fibres have traditionally been reformed using chemicals like chlorine, but this process removes too many scales depriving the fibres of their intrinsic properties such as fluffy feel, heat retention attribute and resistance to pilling (generation of wool balls).

The company discovered that papain, a proteolytic enzyme obtained from papaya fruit essence, that is normally used primarily as a food ingredient, has the effect of selectively removing only a certain layer of fibre scales. Therefore, the company mass-produced the substance and applied it to wool reforming. The thread produced by this new reforming process retains some of the scales in almost their natural state and is also reformed to the same degree as by conventional

processes. Further information may be obtained from Nakajima Spinning Co., Ltd., 370, Itabara, Izumiohtsu City, Osaka. Tel: 0725-33-1101. Telex: 220727. (Source: JETRO, December 1987)

Kenaf: a cheaper pulp for newsprint

A partial solution to the problem of a projected rise in newsprint demand of 25 per cent during the next 10 years may be kenaf, an annual fibre crop that has been grown for cordage in Asia and Africa for centuries. Kenaf International (McAllen, Tex.) hopes to bring onstream in 1991 a kenaf mill that will produce about 200,000 metric tons of newsprint annually, equal to less than 2 per cent of the current US newsprint demand of 12 million tons.

However, the kenaf mill is in need of funding. Kenaf International plans to raise $380 million from its own equity and from nearby newspaper publishers.

Government and industry representatives are backing the effort to develop kenaf. The US Department of Agriculture, which has long supported kenaf research, has granted Kenaf International $300,000 this year for harvesting studies and seed development. And CIP (Montreal), Canada's second-biggest newsprint maker, behind Abitibi-Price (Toronto), last year entered a joint venture with Kenaf International. Known as Kenaf Technologies Group, the venture is separate from the kenaf mill and is described as a "repository for kenaf know-how".

Among kenaf's touted advantages:

- It is cheaper than wood. Kenaf grows from a seedling to a 14-ft, mature plant in five months and yields about 12 tons of dry plant per acre. That is roughly nine times the yield of wood on a per-acre, per-year basis, as trees can take 35 years to mature. That, in turn, translates to a 12-20 per cent lower fibre cost for kenaf than for wood. However, kenaf must be grown within 20 miles of a kenaf mill because the plant is bulky and transportation costs are high. Moreover, because kenaf is a tropical plant, in the US it can be grown only in the South.

- Kenaf requires 20 per cent less energy to pulp than wood because it has only half the lignin of wood. Lignin, together with cellulose, forms the woody cell walls of plants and cements the cells together. Hence, less lignin means that kenaf cellulose fibres are easier to separate from the plant before reforming into newsprint.

- Kenaf makes a high-quality newsprint. Newsprint industry research has found that kenaf newsprint is superior in both tear and tensile strength to thermal mechanical pulping (TMP) newsprint from southern pine and comparable to TMP newsprint from northern spruce.

Kenaf International's proposed mill would use the conventional technology: a two-stage chemical TMP process with a washing stage between the primary and secondary pulping stages. The mill's front end is modified, however, because kenaf is only a fourth as dense as wood, and conventional handling equipment for wood chips does not work well with kenaf. (Source: Chemical Week, 10 February 1988)

High-efficiency process for fermenting L-tryptophan

Sanraku, Inc. (Japan) has established a crystallization fermentation process using microbes for manufacturing L-tryptophan at more than four times the efficiency of existing fermentation processes.

The company has already succeeded in culturing a high-production strain for producing L-tryptophan by using a gene recombinant plasmid. However, after the degree of concentration of accumulated L-tryptophan produced and stored in the fermentation tank exceeds about 20 grams/litre, the process productivity deteriorates rapidly. To cope with this situation, the company devised a method for crystallizing the produced L-tryptophan and lowering its degree of accumulation in solution, by which process productivity can be maintained at a high level.

In its experiments, the company used high-productivity bacilli that have the characteristic of effectively retaining a gene recombinant plasmid developed earlier, to which was added a non-ionic surfactant "Pluronic L-61" as a medium for promoting crystallization, and conducted semi-batch culturing.

As a result, crystallization started only at a point where the degree of L-tryptophan concentration exceeded 30 grams/litre, and subsequently the fermentation was maintained in a state in which the bacilli and crystals coexisted while maintaining the dissolved substance's concentration at about 20 grams/litre.

In the primary stage experiments, about 40 grams/litre of fermenting solution was accumulated as a whole, but with subsequent improvements, together with the development of better high-productivity bacilli, the degree of accumulation was increased to permit high-productivity manufacture of L-tryptophan at about four times the productivity of conventional processes.

L-tryptophan is regarded as having the effect of invigorating the brain's activities, and is therefore being sold on the market partly as a health food. In addition to this, the company plans to commercialize L-tryptophan as a food additive, whose market demand is expected to be as brisk as that for L-lysine. Further information may be obtained from Sanraku, Inc., 15-1, Kyobashi 1-chome, Chuo-ku, Tokyo. Tel: 03-566-5811. Telex: 2522761. (Source: JETRO, March 1988)

Industrial equipment

High-efficiency bio-reactor for producing cellobiose

Japan's National Food Research Institute of the Ministry of Agriculture, Forestry and Fisheries has developed a bioreactor that decomposes cellulose and enables cellobiose to be manufactured at a high efficiency rate.

Cellobio[illegible] kind of sugar that is not metabolized [illegible]en into the body and is therefore expected to [illegible] a highly effective additive for low-calorie [illegible] constitutes a raw material of high added va[illegible]

The sugar has until now been manufactured by the inorganic synthesis process, but since it cannot be mass produced at low cost, it has been used only as a biochemical reagent. The newly developed bioreactor paves the way for the utilization of cellulose as a convenient raw material for producing foods, which had up to now been an untapped field of application.

The new bioreactor uses a cellobiose-producing enzyme as the reacting material in combination with a membrane reactor that passes only cellobiose with a molecular weight of 20,000. The bioreactor is mixed with powdered cellulose and cellobiose producing enzymes at a ratio of 10:1. It is reacted at 30°C and at a pH value of 6.5.

Then, cellulose fibres with long chain structures are decomposed and converted into cellobiose with a

short molecular structure. Only cellobiose with this short molecular structure is passed through the micron-sized holes of the membrane reactor for recovery.

In the field of food processing, roughly two-thirds of cellulose is constantly being thrown away. The research institute developed the new bioreactor to utilize this cellulose by-product more effectively.

Bioreactors for producing glucose from cellulose have already been developed. However, since it is more economical to produce glucose from starch, there has been a need to produce products of high-added values other than glucose by applying the bioreactor. Further information may be obtained from:
The National Food Research Institute,
Ministry of Agriculture, Forestry and Fisheries,
P.O. Box 11, Tsukuba Science City, Ibaraki Pref.
Tel: 02975-6-8015. (Source: JETRO, April 1988)

A cheaper way to dry almost anything

Precision Drying Systems (PDS) in Princeton, N.J., is marketing a continuous, low-temperature drier that is said to have advantages over other drying technologies.

The PDS drier is not brand new. It has been used commercially in Scandinavia and Ireland for almost five years to dry blood plasma. But PDS - which holds exclusive rights to manufacture and market the drier - has been working to expand applications. Indeed, the range of products that PDS has dried includes eggs, fruits, vegetables and fish, as well as enzymes, vitamins, yeasts and antibiotics.

PDS will focus on food and pharmaceutical applications. The company plans to sell driers directly to food and drug companies. It also plans to provide driers in joint-venture arrangements close to large agricultural growers and food processors. PDS is currently in the final stage of negotiating sales of several driers, which, depending on size and application, cost from $400,000 to $3 million. Operation of its first commercial machine, for an unidentified customer, will begin in August for drying such culture products as yoghurt.

Estimated manufacturing cost for the PDS drier is 8-11 cents/lb of water-removal capacity. That includes labour, utilities and maintenance, as well as depreciation and overheads. Such costs are about one-third of those for freeze drying, which costs 25-30 cents/lb of water-removal capacity. A vacuum drier is double the cost of the PDS drier, at 16-21 cents/lb of water-removal capacity. However, a spray drier - at 7-10 cents/lb of water-removal capacity - is slightly cheaper than the PDS drier.

The principle of the PDS drier is simple. The product is applied to drying balls in the application zone. As the drying balls and product move continuously downward at an adjustable speed through the drying zone, they pass a counter current stream of temperature-controlled drying air. In the separation zone at the bottom of the drier, the drying balls and product meet a co-current flow of air for final drying and separation of product and drying balls. The drying balls are recyled to the application zone, where the process continues. The co-current stream of air carries the dried product to additional processing or packaging machinery.

The advantages. The PDS drier is said to have several advantages over other driers:

- The system is versatile. It dries liquids, slurries and particulates, as well as high-viscosity and low-viscosity materials. The key is the drying balls, which can be made of stainless steel, plastic or ceramic. For instance, a sticky product, like cheese, would require drying balls made of a slippery plastic resin. The size of the drying balls can vary, as well. The biggest balls have a diameter of one and a half inches. Such large sizes are needed for drying particulates made of large pieces, such as banana slices. Also, the dried product can take many diverse forms, from a crystalline powder to flakes of different size and thickness.

- The drier operates at low temperatures. Most products are dried in a PDS drier below 160°F, which preserves nutrients, cell structure, flavour and colour. Water content is reduced 75-95 per cent, moreover. That cuts weight, and shipping and storage costs significantly.

- The process is continuous, which is generally more convenient and cheaper than batch processing. The continuous process also allows precise control of air flow, dwell time, temperature and moisture content. Dwell time, for instance, can vary from 1 minute to 100 minutes.

- The drier is compact. Drying balls greatly enlarge the drying surface area. As an example, 1 cu ft of balls with a diameter of 5/8 in. create a drying surface of 60 sq ft. Moreover, the drier requires less than one third the space needed for conventional freeze or spray driers.

The drier's versatility shows off in drying potatoes. Potato slices with a thickness of 1/8-1/4 in. can be dried. And when the slices are rehydrated, it is possible to distinguish between the Idaho, Maine and New Jersey potatoes because of the high flavour retention. What is more, because of the low temperature that is involved in drying, browning - common in conventional drying of potatoes, which is done from 250 to 300°F - does not occur. Another example of versatility: the drying of cauliflower and broccoli. Both are fed into the drier in 1/4-1/2 in. pieces. Although the pieces shrink slightly during drying, upon rehydration they regain most of their original colour and shape. The "bite-feel" of rehydrated vegetables is "very close" to their fresh counterparts. (Source: Chemical Week, 3 February 1988)

Freeze drying stirs new interest

Freeze drying's potential is being more widely exploited than hitherto.

Indeed, some companies are factoring freeze drying into a variety of chemical and biological processes that turn out products such as microbials, superconducting powders, drugs and bacteria. Eastman Kodak, for example, is relying on freeze drying as a preservative finishing step.

As companies become more aware of freeze drying's potential, more use will open up. Freeze drying involves the rapid freezing of a porous material followed by rapid dehydration by sublimation in a high vaccum. In certain applications, for example, with biologicals, that method of dehydration has some advantages over other drying technologies, including vacuum drying and spray drying, in that the driving force of the dehydration is not heat but rather the difference between the vapour pressure of the porous material and the condenser plate.

The freeze drying of ceramics, also an expensive process, has been done on a laboratory scale for more than 20 years, but now Oregon Freeze Dry (Albany, Oregon) is working on a commercial process.

In some cases, the benefits of freeze drying are worth the expense. One such application is in making a homogenous material for ceramics, including superconductors. Freeze drying is finding uses elsewhere in chemical processing. For one, it can be used to separate solvents and solutes. In another new application, an Oregon Freeze Dry client is developing a way to remove water from a water-based latex polymer to render it miscible with other materials.

Outside the chemical processing arena, freeze drying is being more widely used. For example, freeze drying has been used for a long time to preserve sensitive biologicals, which also can be be preserved for shipment or storage in a cold liquid medium or as frozen solids. Among the problems in storing a live organism in liquid media are that over time the nutrient level drops, and that type of storage is bulky and costly to ship, as both shipper and end-user must keep the liquid cold. Frozen shipments of organisms are also costly to ship and store. Freeze drying is easier on the organism and bypasses those problems but is more costly at the front end. Still, freeze drying, is the method of choice of microbiologists for preserving cultures.

Micro-organisms, for example, have been freeze-dried since about 1940 on a small scale and for the past 15 years on a semicommercial scale by the American Type Culture Collection (ATCC), a Rockville, Md.-based, non-profit organization that maintains a collection of starter cultures, including cell lines, viruses and genetic materials for use by researchers. Freeze drying is the preferred method of preservation for many organisms, says Frank Simione, who heads ATCC's Applied Sciences and Workshops Dept., because it stops an organism's metabolism for many years, holding it "in a kind of suspended animation".

With the increasing emergence of biological products, particularly genetically engineered materials, freeze drying is being used to process large quantities.

One of a few companies devoted to contract freeze drying is Bell-More Laboratories (Hampstead, Md.), which processes diagnostic reagents and drugs. Bell-More's niche in the growing market is freeze drying for larger companies on a pilot scale. In Japan, for instance, Takeda Chemical Industries (Osaka), a leading drug maker, notes that if it decides to produce its interleukin-2 product, which is still in clinical trials, in a powdered, freeze-dried form, it would do the drying in-house.

A drug company can bypass rigid Food and Drug Administration regulations on freeze drying by contracting the process out. Freeze driers must offer custom packaging technology that is effective in keeping out oxygen and moisture.

Bug marketers have exploited packaging and freeze-drying technologies. For instance, Eastman Kodak's Snowmax, the snow-making bacteria Pseudomonas syringae, is extremely heat-sensitive, and freeze drying is the only way to protect it before shipment to customers. Kodak ships Snowmax as frozen pellets to a small upstate New York freeze drier, Ontario Foods, which freeze dries and packages the product.

Freeze drying is crucial to the effectiveness and extended life of two types of feed additives produced by Xeroferm Laboratories (Portland, Ore.): probiotics and silage inoculants. Probiotics are living lactic acid bacteria, used in place of antibiotics in feed to correct intestinal bacteria in animals. Silage inoculants are starter cultures of lactic acid bacteria used to control the rate of fermentation of silage to keep forage from spoiling and shrinking. (Extracted from Chemical Week, 17 February 1988)

Biotechnical instrumentation forecast

The biotechnical process instrumentation market is expected to reach £12 billion over the next 10 years, according to R. Atkins, UK Parliamentary Under-Secretary of State for Industry. The US market for biotechnical instrumentation will grow from £16 million in 1987 to £200 million in 1991, according to Frost & Sullivan. Enzymes are the primary biosensors, with their ability to catalyze chemical/metabolic reactions with high specificity, but cannot be used above 80°C, making in-line cleaning a problem. Ion-selective field effect transistors can detect H, K and Na ions but are temperature sensitive. Optical sensing provides intrinsically safe circuitry; piezoelectric systems have also been used, but are more costly. Besides 'environmental' applications for the detection or measure of combustion gases, wastewater bacteriological oxygen demand, and crop and livestock diseases, Yellow Springs Instruments (US) has applied immobilized oxidase ions in conjunction with a hydrogen peroxide electrode in a 3 per cent-accurate, 30-second-response flow cell to monitor on-line glucose in fruit juice, wine, food, serum and blood; the system is available in the UK through Clandon Scientific. (Source: Technology Update, 7 March 1988)

Alcohol sensor using acetic acid bacteria enzyme ADH

Asahi Breweries, Ltd. and Professor M. Karube of the Tokyo Institute of Technology have jointly developed an alcohol sensor excelling in selectivity which can be used with stability over a long period of time. It utilizes the membrane bondability of alcohol dehydrogenase (ADH) of enzymes existing in the cell membranes of acetic acid bacteria, which is immobilized by the covalent bonding method.

In the distillation and fermentation industry including beer brewing, the measurement and detection of the alcohol concentration are indispensable in various processes. Normally, samples are extracted from time to time in the respective processes for independent analysis, but these operations require much time, labour and cost.

Against this backdrop, research is in progress to immobilize enzymes and to apply them as sensors, and some of these sensors have already been commercialized, but they are generally usable only for one or two weeks, lack stability and fail to display ample selectivity to various kinds of alcohol.

Asahi Breweries, alert to the fact that the membrane bonding ADH, an enzyme existing in acetic acid bacteria cell membranes, features a high substrate characteristic and is highly stable throughout a wide range of pH values delved into research for its utilization.

In the case of a yeast derivative, an enzyme is normally required to promote ADH activity, but the newly developed alcohol sensor dispenses with this need. This membrane bonding ADH is immobilized by the covalent bonding method, and platinum electrodes are used in the process.

With this new alcohol sensor, its loss of responsiveness is only 20 per cent when used for a month, and it has been confirmed to serve effectively for about a month with stability. Also, it is not adversely affected by methanol, reacting with straight chain alcohols from methanol to C_5 compounds, yet it displays an excellent selectivity of not reacting with alconols with side chains. Further information may be obtained from Asahi Breweries, Ltd., 7-1, Kyobashi 3-chome, Chuo-ku, Tokyo. Tel: 03-567-5111. Telex: 2523591 ABEER (Source: JETRO, January 1988)

E. PATENTS AND INTELLECTUAL PROPERTY ISSUES

Biotechnology patents up 20 per cent in 1987

The US Patent & Trademark Office issued 1,476 biotechnology patents in 1987, 20 per cent more than the year before, according to a survey by the Pharmaceutical Manufacturers Association (PMA). Nearly two thirds of those patents were issued to US-based corporations, universities and government agencies. Of the total number of patents issued, a majority (57 per cent) were for pharmaceutical and health care products. According to William Szkrybalo, PMA's director of biotechnology programmes, 14 per cent of the patents involved recombinant DNA techniques. PMA's definition of biotechnology includes the use of organisms such as bacteria and yeast to produce beneficial products, though not necessarily the use of genetic engineering techniques. (Reprinted with permission from Chemical and Engineering News, 18 January 1988. Copyright (1988) American Chemical Society)

US Patent Office reorganizes biotechnology coverage

The US Patent and Trademark Office (PTO) is isolating biotechnology into a single examining group. The dual goals are to reduce the staggering biotechnology patent backlog and make the most efficient use of PTO's biotechnology expertise.

Currently, most biotechnology-related patents are examined by PTO's Group 120 (biotechnology and organic chemistry), but some of these applications find their way into Group 150 (proteins) or Group 130 (chemical analysis and non-immunological testing). The biotechnology components of these three groups will be extracted and placed into the brand new, 75-member Group 180. (Extracted from Bio/Technology, Vol. 6, April 1988)

BTG forges Japanese licensing connection

The British Technology Group has signed a deal that will allow British inventions to be more widely licensed throughout Japan. It has made the trading house Sumitomo the sole agent for licensing "selected technologies" to other Japanese companies. The BTG exploits technologies, applies for patents and protects those patents on behalf of universities and individual inventors in the UK.

Sumitomo will be allowed to examine the inventions for a period before agreeing to take up the patents.

Giving a large commercial organization access to British inventions may cause concern, but the BTG says that the Japanese firm has signed non-disclosure agreements, and no inventions that they see but do not want will be at risk. The BTG would be ready to sue if confidentiality was broken.

The Sumitomo deal is a first step towards a two-way deal in technology transfer with Japan. The BTG is hoping to be able to licence technology from Japanese companies and universities to companies based in Britain.

The BTG already earns 70 per cent of its money from licensing patents to overseas companies. Japan is its second biggest market, after the USA, and the Sumitomo deal will make it even more lucrative, says the BTG. (Source: New Scientist, 25 February 1988)

Americans bid to freeze out Japanese rival

An American biotechnology company has asked the US Government to block a Japanese rival in a commercial struggle over patent rights to a genetically engineered protein for treating anaemia. The American company, Amgen, claims to have a lead of one year in the manufacture of erythropoietin (EPO).

Several companies around the world have been vying to make EPO by snipping out the human gene that manufactures the hormone and splicing it into bacteria, yeast or mammalian cells that then produce the hormone in large quantities. A Japanese company, Chugai, and its American partner, Genetics Institute, plan to manufacture such a recombinant product and sell it in the US.

Amgen, still awaiting approval of its recombinant version, recently sought intervention by the Government's International Trade Commission (ITC), to bar the Japanese product. Amgen and its own Japanese partner, Kirin, have been manoeuvering since 1984 to corner the market for EPO. The company received an American patent in October 1987.

The patent covers the necessary "starting materials" for the process, such as the modified genes for the hormone and the genetically altered organisms into which the genes are inserted.

In the mean time, Genetics Institute has patented the technique for purifying the hormone from the genetically altered cells or microbes that manufacture it. Both companies are challenging each other's patents in a flurry of law suits. Amgen called in the ITC to deny Chugai an early entry to the American market.

In a narrow vote, the ITC, which can exclude imported products if they are proved to be "unfairly introduced", agreed to investigate. Amgen told the ITC that the Japanese are mounting an "effort to penetrate and ultimately dominate the nascent US biotechnology industry". The company's complaint describes the American biotechnology industry as "young and fragile" and not s that it has poured over $150 million into its effort to deliver the product first.

The appeal is thought to be the first lodged with the Commission that involves a genetically engineered pharmaceutical. (Extracted from New Scientist, 25 February 1988)

Part of AIDS virus patented

Cambridge Bioscience has won world-wide rights to a Harvard University patented protein used in AIDS tests and vaccines. The biotechnology company will pay royalties to Harvard, and will sub-license the protein to other firms that use it in AIDS-related products. Harvard's patent may be a particularly important one, believes one analyst, because the protein has applications in both AIDS diagnostics and AIDS vaccine research. The patent covers a viral protein known as gp120 and related proteins that react with it. The protein is found on the outer coat of the AIDS virus. (Extracted from Wall Street Journal, 18 February 1988)

Lawyers seek patent reforms

Max Planck Institute has, in co-operation with other organizations and agencies, worked out several proposals to make European patent laws more compatible with the needs of industrial biotechnology. Friedrich-Karl Beier and Joseph Straus, legal specialists at the Max-Planck Institut für ausländisches und internationales Patent-, Urheber- und Wettbewerbsrecht, located in Munich, would like to see certain restrictive provisions changed; these shortcomings currently make it difficult or impossible to obtain full protection for many biotechnological inventions.

One of the Institute's reform suggestions has already been implemented. Federal high courts in the FRG recently ruled that a researcher can apply for a patent on a micro-organism simply by depositing a sample and a brief description. This has been the routine procedure in the United States and Japan, but in the FRG one had to submit a report detailed enough to enable specialists to readily recreate the "invention". Genetic engineers often could not comply with this demand because the production of new strains frequently involves biological processes whose results are not totally predictable.

The need for improvements in other aspects of European patent law has also become increasingly apparent in recent years. For one thing, Europeans cannot patent an innovation after details of the research leading to its development have been published. Seminar reports - or even non-confidential oral communications - are often considered equivalent to publication. In the US, by contrast, one can apply for a patent within a year of publishing the details. The Max Planck specialists would like European scientists to have the same option.

Also, newly developed macroscopic plants and animals are largely excluded from patent protection in the nations that signed the 1973 Munich Patent Convention: the Federal Republic of Germany, Austria, Italy, Belgium, France, the United Kingdom, Liechtenstein, Luxembourg, the Netherlands, Sweden, and Switzerland. This has effectively dampened commercial interest in the production of such organisms. (Source: Bio/Technology, Vol. 6, January 1988)

Genentech sues Invitron, Monsanto and Searle

Genentech (South San Francisco) has filed suit against Invitron, Monsanto and Monsanto's G.D. Searle, with charges of misappropriation and improper use of trade secrets by Invitron employees who had previously worked for Genentech. The allegations relate to the development of recombinant tissue plasminogen activator (TPA) and blood protein factor VIII. Genentech's suit asks for an injunction against the alleged use of the trade secrets in question and for undetermined damages. The complaint cites 12 causes of action against the defendants, including misappropriation of trade secrets, breach of contract, unjust enrichment and unfair competition. The suit follows Invitron's announcement that Monsanto, Searle and Invitron had developed novel recombinant forms of the heart drug TPA and that Invitron was working with the Rorer Group to commercialize recombinant factor VIII. Representatives of Invitron, Monsanto and Searle maintain that the litigation is without merit. Genentech has also filed a complaint against Abbott Laboratories, alleging that two Abbott patents on recombinant-DNA plasminogen activators are invalid and unenforceable and seeking a declaratory judgement that Genentech's Activase TPA "does not infringe any valid claim" of the Abbott patents. Genentech also is seeking an injunction that would prevent Abbott from "initiating infringement litigation" against it.

The patents in dispute (US 4,370,417 and 4,558,010), which were awarded to Abbott in 1983 and 1985, cover recombinant-DNA plasminogen activators, as well as the starting materials and recombinant methods that are used to produce them. So far, Abbott does not have on the market any product that uses the technology.

Genentech's only other patent battle that has gone to court was unsuccessful. Genentech had brought suit against the Wellcome Foundation in the UK in February 1986 when Genentech received a patent for TPA in that country. Genentech alleged that Wellcome's TPA infringed Genentech's patent. At the same time, Wellcome had sued to have Genentech's patent declared invalid. Last June, Britain's High Court ruled against Genentech; the company's appeal is scheduled to be heard early this summer. (Source: Chemical Week, 17 February 1988 and 30 March 1988)

Resolution sought on animal patent dispute

Controversy persists over the US Patent & Trademark Office's recently announced policy of granting patents on new forms of animal life produced by genetic engineering or other human intervention.

Several groups are upset over PTO commissioner Donald J. Quigg's judgment that farmers pay royalties on generations of offspring of genetically altered animals. A bill was introduced calling for a two-year moratorium on animal patents until Congress can explore the implications. A similar bill may be offered in the Senate.

What farmers and others fear, notes Jack Doyle, director of the Agricultural Resources Project of the Environmental Policy Institute, is a virtual monopoly on livestock breeds by a few large corporations holding the patents.

A recent poll by the Texas Department of Agriculture finds that 96 per cent of the responding producers oppose animal patenting. Commissioner Jim Hightower of the state agency is urging Texas' Congressional delegation to support a moratorium. In addition, a coalition of 37 farm, animal welfare, environmental, and public interest organizations - as well as individual religious leaders - back a moratorium.

PTO does not expect to issue patents until at least June for any of the 17 applications now pending on new animal forms. So Congress will have time to consider legislation even without a moratorium. (Abstracted with permission from Chemical and Engineering News, 15 February 1988. Copyright (1988) American Chemical Society)

First patented animal is a mouse

The US Patent and Trademark Office said Tuesday that it had approved a patent for a genetically altered mouse to be used in cancer research, the first time a patent has been issued for an animal.

The decision is a milestone in efforts to commercialize biotechnology.

The patent was granted to researchers at Harvard University, who have genetically altered the animal for research purposes.

Man-made life organisms have been patentable under US law since a landmark Supreme Court decision in 1980, but this announcement will mark the first time that patent law will protect a genetic change in a higher life form.

The Harvard patent covers a technique in which laboratory-made cancer genes are introduced into early-stage embryos of mice. The mice and their descendants are born with cancer genes in all their cells and will develop tumours quickly if exposed to even small amounts of cancer-causing chemicals.

Thus, the animals can be used in tests to determine the cancer-causing potential of a chemical, but are expected to be especially useful in breast cancer research because of the type of cancer gene inserted.

The genes inserted into the mouse embryos are combinations of mouse mammary tumour genes and cancer-causing mouse virus.

Licensing rights for the patent, which could have wide commercial possibilities in cancer laboratories, are held by Du Pont Co., which financed the Harvard research. But while the Patent Office decision was greeted warmly by officials of the biotechnology industry and may provide a boon for scientific research, it occurs at a time of mounting ethical questions about the use and ownership of artificially created life forms. (Extracted from International Herald Tribune, 13 April 1988)

Firms to fight ban on animal patents

Biotechnology companies in the US and Britain are preparing to challenge the rule in Europe which states that animals cannot be patented. Last year, the US authorities ruled that researchers could patent animals, but European law still forbids the patenting of higher organisms, such as domestic livestock.

Two companies, one British and one American, have applied for European patents on the technology for inserting human genes into the embryos of mammals. When these "transgenic" animals mature into adult females, they secrete human proteins in their milk. Companies can harvest these proteins for medical or industrial use.

Scientists from the Institute of Animal Physiology and Genetics Research, which has laboratories in Edinburgh and Cambridge, developed the technique involved in creating transgenic animals. The technique has successfully created transgenic mice and sheep, and researchers are working on transgenic goats, cows and pigs. A British company, Pharmaceutical Proteins of Cambridge, has undertaken to patent the technology for the Institute in return for commercial rights to the process.

The company applied for a British patent in June 1986, and last month the World Intellectual Property Organization, which oversees international patent law, published the company's international application. This is the first stage in awarding the European patent.

An American biotechnology company, Integrated Genetics of Massachusetts, has also applied for a European patent on transgenic animals. The company first filed for its patent in the US in April 1986, and a year later filed a similar application in Europe. Integrated Genetics, however, has not yet had its application published.

In April 1987 the US Board of Patent Appeals decided that researchers from the University of Washington, Seattle, could patent a type of oyster that they had developed. The oysters, which the researchers had genetically engineered to given them more than one set of chromosomes, grow larger and more tasty than normal oysters.

This was the first patent to be awarded on multicellular animals. In 1980, the patent authorities in the US ruled that it was possible to patent single-celled organisms, such as bacteria. (Extracted from New Scientist, 11 February 1988)

F. BIO-INFORMATICS

Agricultural biotechnology markets

Virtually every major agricultural chemical company is investing in new technologies to compete in an expanding world of alternative products, which include biological insecticides, pheromones, fungicides, nematocides, bacteriocides, herbicides, plant growth regulators, fertilizers and genetically manipulated seeds. A number of products have already been launched, reports the Technology Management Group, and several others currently under development are due out within three years. The United States continues to dominate this field.

TMG's latest report, The Impact of Biotechnology on Agricultural Chemicals: An Assessment of Worldwide Markets for New Products Related to Fertilizers, Pesticides and Seeds, is the third in a series. Earlier reports covered the impacts on the animal care, and the food and feed industries. Next in line: a report on plant-derived pharmaceuticals and fine chemicals. Details of the agricultural biotechnology report, priced at $2,990 ($3,490 from 30 April) from: Technology Management Group, 25 Science Park, New Haven, Connecticut 06511, USA or on (203) 786-5445.

The Biotechnology Directory 1988, by J. Coombs and Y. R. Alston.

The expanded and updated edition of this reference work brings:

- 1,585 new organization listings;
- 1,174 other updated and/or revised entries;
- Information on more than 5,350 commercial and non-commercial organizations;
- A greatly expanded Buyer-' Guide of products, research and services;
- Alphabetical and classification indexes for quick access to all information.

November 1987, 500 pp., 0-333-437268, price £75.00. Available from Globe Book Services, FREEPOST, Brunel road, Houndmills, Basingstoke, RG21 2BR, England.

From Genes to Clones, an introduction to gene technology, by Ernst-L. Winnacker.

From Genes to Clones offers an integrative view of the concepts and strategies behind the art of gene cloning. This textbook is a comprehensive treatise of the techniques employed in the isolation, manipulation, and chemical synthesis of nucleic acids and the identification and characterization of recombinant DNA molecules. The development and practical applications of plasmids, bacteriophages, cosmids, phasmids, and eukaryotic viruses as cloning vehicles are discussed in great detail together with the respective hosts, i.e., prokaryotes, streptomyces, yeasts, plant cells, and eukaryotes. This book, written by a single author, leads to the frontiers of current knowledge and will help advanced readers in planning and designing their own experiments. At the same time it may be read as an introductory text by undergraduate and graduate students trying to become familiar with the unit operations of gene manipulation. The controversial issue of safety regulations for such manipulations is addressed in a separate chapter, and the 1986 NIH Guidelines for Research Involving Recombinant DNA Molecules are included. An extensive list of references, appendices on useful host strains, restriction enzymes, restriction maps, and sequence data, as well as a very detailed index, allow this textbook to be used as a reference manual. 1987, XIII, 634 pages with 438 figures and 54 tables. Softcover: DM 60.00/$US 34.50. ISBN 3-527-26644-5. Hardcover: DM 120.00/$US 68.00. ISBN 3-527-26199-0.

Gnomic - A Dictionary of Genetic Codes by E. N. Trifonov and V. Brendel.

Hereditary information carried by the DNA molecules of a cell and coded in the sequence of nucleotides can be written as a text in a language

with a four-character alphabet (A, C, G, T). This book is the first compilation of the words of this language. For the molecular biologist, the systematic comparative study of nucleotide sequences has become an invaluable research tool which has led to insights into phenomena of genetic control, the nature of genetic defects, molecular structure, and molecular and general evolution. 1987, 272 pages. DM 160.00/$US 98.95. ISBN 3-527-26723-9.

New service for readers

A new product from BioCommerce Data and The British Library will be on show at Life Science Technologies. Launched in January 1988, Biotech Knowledge Sources (BKS) is a unique service which alerts readers to new market surveys, books, and forthcoming conferences relevant to the biotechnology industry.

BKS will provide a comprehensive monitor of new publications as well as a full international listing of meetings, seminars and exhibitions, useful to librarians, researchers and executives. Covering both scientific and business information sources it will supplement, in periodical form, the book, Information Sources in Biotechnology by Commerce Data's Managing Director, Dr. A. Crafts-Lighty. Produced monthly, BKS will be edited by the British Library Biotechnology Information Service, a specialist group formed to continue and develop the work of the EEC-funded European Biotechnology Information Project.

Publications on environment and development

Conservation of species and genetic resources

This action guide enables NGOs to take urgent and positive action to prevent disappearing crop varieties and less known tropical plants with promising economic potential. The guide covers a wide variety of subjects i.e., values, threats and politics of genetic resources; examples of endangered plants and animals; an agenda for action and the role of NGOs. It also contains names and addresses of NGOs and other institutions actively involved in conservation. Available in English, French and Spanish; A5 size, 76 pp., price $US 3.50 plus postage $US 2.00 (surface) $US 4.00 (air). Free to third world NGOs. Available from: Publications Officer, Environment Liaison Centre, P.O. Box 72461, Nairobi, Kenya.

Safe pest control: an NGO action guide

This booklet challenges the conventional approach of most pesticide how-to books which implicitly assume that by giving the pesticide user a set of safety rules, the problems associated with pesticide use will be ameliorated.

It provides both practical information and an analytical framework by which NGOs can examine the use of pesticides in their region. Divided into two sections it examines the health and welfare requirements of pesticide users in the third world and the implications for the medical, educational and health institutions and the pesticide industry serving this group.

The second section gives practical information and starts off with a set of safety rules for pesticide use, written from the users' point of view. Available in English, French and Spanish, A5, pp. 70, price $US 3.50 plus postage $2.00 (surface) $4.00 (air). Free to third world NGOs. Available from: Publications Officer, Environment Liaison Centre, P.O. Box 72461, Nairobi, Kenya.

Institute to focus on third world biotechnology

The Panos Institute is planning an information programme on biotechnology and its effects on people and countries in the developing regions of the world. Panos, an international organization specializing in objective information on sustainable development has attracted start-up funding from the Rockefeller Foundation. Details from: Dr. Robert Walgate, Director, Biotechnology Programme, Panos Institute, 8 Alfred Place, London WC1E 7EB.

ATCC Directory of Biotechnology Information Resources

A National Library of Medicine contract to develop and manage an on-line database for a directory of biotechnology information resources has been awarded to the American Type Culture Collection (ATCC). Organizations with resources which are available to the public should contact the ATCC. Details from: BioInformatics Department, American Type Culture Collection, 12301 Parklawn Drive, Rockville, MD 20852-1776, USA.

Biotechnology software

Until recently, only a few large companies enjoyed the benefits of the expensive hardware and custom-tailored program needed for computerized analysis of biological data. Now virtually any laboratory can utilize the computer's speed and power, thanks to inexpensive personal computers (PCs) and moderately priced software for restriction mapping, gel fragment analysis, molecular modeling, protein and DNA sequencing, and several other tasks. Unlike previous systems that required large mainframes or sophisticated workstations, current offerings run on the IBM PC, XT, or compatibles with 640K RAM. Most applications also require a 35 Mb hard disk (usually around $500 or less) for enhanced data storage, retrieval and comparison.

Obviously no computer can do anything that cannot be done manually, but they do offer extreme speed and accuracy, while relieving workers of tiring, mundane tasks. In molecular design, for example, several program allow the researcher to "assemble" new structures on a computer display terminal instead of in the laboratory.

One such program is Polygen's PC-based ChemNote, which is used to create two-dimensional molecular diagrams, then display them in three dimensions for further study and manipulation. The operator can also set precise bond lengths and angles, assign atomic charges and connect additional groups or atoms. According to the company, ChemNote even alerts the operator to inaccurate or incomplete structures.

The structure may then be transmitted to Polygen's CHARMm, a more complex program that uses empirical data (NMR data and the effects of solvent and temperature, for example) to construct and illustrate intra- and intermolecular forces and energy relationships. (Unlike ChemNote, CHARMm requires VAX-type hardware or a similar workstation.) Polygen's CENTRUM - described as a "technical information management system" - integrates written, graphical, and analytical data from several files or program into a single document for publication or electronic mail transmission. CENTRUM is priced at $4,4000 (which includes all software plus updates through 1989), and is now being used by about 20 customers in the US and Europe.

Other programs are simplifying such time-consuming chores as restriction mapping, pattern-matching and

database searches. One such program, called R-Map and offered by DNASTAR (Madison, WI), derives restriction maps directly from restriction fragments.

Most biotechnology program can also be used to search various popular databases. DNASTAR software, for example, provides access to both GenBank and PIR (the Protein Identification Resource). The National Library of Medicine's Medline will be added shortly, with the entire database collection contained on a single CD-ROM (compact disk, read only memory); the CD should provide sufficient data storage for about five years. As with many of the company's other program, databases are updated quarterly.

Other examples of biotechnology software include GENEPRO from Riverside Scientific (Seattle, WA) and DNASIS from Hitachi (San Bruno, CA). Both use colour graphics to generate restriction maps, translate DNA sequences into amino acid sequences (and vice versa), define and check levels of homology between sequences, and other tasks; derived sequences may then be compared against one or more databases. DNASIS permits the user to search both GenBank and NBRF (the National Biomedical Research Foundation); GENEPRO provides access to GenBank, EMBL (the European Molecular Biology Laboratory), and PIR. (Source: Bio/Technology, Vol. 6, March 1988)

High-level graphics software. Dynamic Object-Rendering Environment (DORÉ) software from Ardent Computer Corp. (Sunnyvale, CA) allows interactive visualization of complex data generated by supercomputer-class applications. It is the first package to integrate the computation and analysis of complex data with advanced graphics. The software library lets users describe a scene, produce highly complex images from the scene data, and manipulate the data interactively and dynamically. The company is offering source-code licences to universities and research laboratories for a nominal charge ($250), prior to the package's release in July 1988; licences are also available to commercial users for a $15,000 fee.

Protein sequence analysis is facilitated with HIBIO PROSIS from Hitachi (San Bruno, CA). Key features in the progra include secondary structure predictions; amino acid maximum homology between two sequences; amino acid conversion, composition/ molecular weight, and homology search; hydrophobicity analysis; homology plot; and keyword search and database access functions. The AMIEDIT phase of the program creates or edits amino acid sequence files; data may be keyed in or entered by digitizer and voice feedback. The PROTES phase performs analyses on sequences and displays the results graphically. DBREF searches the NBRF-PIR database for a target sequence, and can perform homology searches. The company's DNASIS program, for DNA sequence analysis has been improved to achieve faster homology searches.

Image-processing software. Media Cybernetics (Silver Spring, MD) announces the release of Image-Pro II, a new version of its powerful image-processing software. A new interface allows the user to select a single monitor configuration with pull-down menus on the display monitor or a dual-monitor configuration in which the menus appear on the system monitor. A free-form feature allows processing on "n vertex polygonal areas" which users specify by tracing the area desired; an automatic preference feature provides for maintenance of global environmental settings from one session to the next. The accompanying manual includes diagrams, illustrations, a tutorial, and a chapter on image-processing theory and terms. A variety of input and output devices allow camera-, film recorder-, and printer-interchangeability. Versions are compatible with products offered by major hardware vendors including Data Translation, Imagraph, AT&T, and more.

Software for publishing scientists. Reference Manager™ is a microcomputer-based software package designed specifically for publishing scientists. A specialized database management program combined with a text-reformatting module, the package stores bibliographic references that may later be incorporated into manuscripts and used to create bibliographies. The recently updated Version 4.0 is compatible with IBM/PCs, ATs, XTs, and PS/2s, and may be used with most word processing systems; a version for use with Macintosh computers is newly available as well.

Data acquisition hardware/software package. The CODAS (Computer-based Oscillograph and Data Acquisition System) from Dataq (Akron, OH) features a graphics accelerator card and disk streaming software routine; together they provide unparalleled real-time display and storage performance. Using CODAS with an IBM PC/AT host computer cuts the total time necessary to acquire, display, and store a single A/D value from 329,030 μ to 250 μ, while increasing attainable sample rates from 3 Hz to 4,000 Hz. Included is waveform analysis software with scroll speed of over 4,000 points per second - large data files may be reviewed from beginning to end in seconds, then copied-and-pasted to other files for further analysis and hard copy using such packages as Lotus 1-2-3, ASYST, RS/1, and ASYSTANT.

LC system controller. ChromNet™ from Spectra-Physics (San José, CA) sets up and monitors methods and analyses for multiple systems operating on LABNET®, and is designed to run on an IBM XT or AT, or compatible. The program is menu-driven through screens, set up by the user with a series of prompts for parameter entries, system configuration, analysis description and method information. Methods development is simplified, and both methods and analyses can be stored in memory for later use. The system performs checks on operations and updates analysis information to provide an ongoing status report. Hard copy may be generated as well.

A fermentation monitoring package developed by Biotechnology Computer Systems and marketed by LH Fermentation Ltd. (Stoke Poges, UK), the BIO-pc is designed for use with up to four bioreactors and associated online ancillary equipment. BIO-pc is configured for an IBM-AT® or compatible; it uses MS-DOS 3.1 to perform data monitoring, logging, and feedback control in background mode. The SMART applications package, incorporated into the system, is accessible at any time during operation.

Software to examine the effects of drugs

A computer model to determine adverse effects of drugs has been developed by researchers at the University of Surrey. The software may be able to screen out some molecules before they are tested on animals. Cytochromes P450 are generally responsible for breaking down organic substances in the body. P448 activate compounds so that they can interact with DNA and possibly cause cancer. The new software examines the shape of the molecules and examines which cytochrome family it will interact with. (Extracted from New Scient: 3 March 1988)

New molecular modeling software

ChemStat, a new molecular modeling software module, has been added to the Chem-X family by Chemical Design Inc., Mahwah, NJ. It is designed to

help chemists identify structure-activity relationships - a particularly important factor in drug design, Chemical Design notes. ChemStat, given a list of molecular structures of interest, calculates a range of user-specified parameters for each, not only geometrical variables such as distances or angles between atoms, but the results of complex energy and quantum mechanical calculations. A typical study, Chemical Design says, may consider a hundred parameters for any number of molecules up to several thousand. Having calculated the parameters, ChemStat then automatically carries out an extensive search for correlations between observed activity data and calculated structural parameters and generates a linear regression equation linking structure with activity. More elaborate data analysis techniques can then be employed through interfaces to standard statistics packages. (Reprinted with permission from Chemical and Engineering News, 8 February 1988. Copyright (1988) American Chemical Society)

Database on environmental impact of pesticides

The Overseas Development Natural Resources Institute in London has compiled a bibliographic computer database of books and scientific articles about the environmental side-effects of pesticides (including herbicides and fungicides) in the tropics.

This database called ENVIRON, has been designed to provide a rapid and comprehensive information service freely to scientists, farmers and agricultural administrators living in developing countries. Topics covered in ENVIRON include:

- Pesticide toxicity to non-targets;
- Pesticide persistence and residues;
- Environmental fate of pesticides;
- Ecological impact of pesticides on non-target organisms.

Dr. H.Q.P. Crick, in charge of ENVIRON, writes that he can handle inquiries about the effect of pesticides on non-target organisms (including soils), after first specifying the pesticide, the target pest or non-target organism, or a combination of these. The output will consist of a list of references, each of which is followed by an indication of the contents of each paper and in some cases a relevant abstract. There are no plans to provide an on-line facility for external users at present so you can write to: Pesticide Impact Section, Tropical Development and Research Institute, College House, Wrights Lane, London W8 5SJ, UK. (Source: Ecoforum, Vol. 12, Nos. 3 and 4, 1987)

G. MEETINGS

May 1988

23-27 May. Hamburg-Blankenese, FRG. 10th Conference on Macromolecular Synthesis. Details: Dr. D. Richter, Institut für Zell-biochemie und klinische Neurobiologie, UKE, Martinistr. 52, Hamburg, FRG.

25-27 May. Rockville, Maryland, USA. Freezing and Freeze-drying of Micro-organisms. Details: Doug Drabowski, Workshop co-ordinator, American Type Culture Collection, 12301 Parklawn Drive, Rockville, MD 20852, USA.

25-27 May. London, UK. Advances in the Applications of Monoclonal Antibodies in Clinical Oncology. Details: Dr. A. Epenetos, Royal Postgraduate Medical School, Hammersmith Hospital, London W12 0HS, UK.

27-29 May. Vienna, Austria. Inaugural Conference on "Genes in Control of Growth, Differentiation and Disease". Details: Prof. Max L. Birnstiel, Research Institute of Molecular Pathology, Biozentrum, Dr. Bohr-Gasse 7, Vienna A-1030, Austria.

31 May - 4 June. Les Embiez, France. Third European Network of Immunology Institutes Conference. Details: Dr. A. McMichael, ENI Conference, Nuffield Department of Medicine, John Radcliffe Hospital, Oxford, UK.

June 1988

2-5 June. Arlington, Virginia, USA. Third Annual ASM Conference on Biotechnology. Details: Karen Johnson, American Society for Microbiology, Meetings Dept., 1913 I Street, NW, Washington, DC 20006, USA.

5-11 June. Frankfurt-am-Main, FRG. ACHEMA '88. Details: DECHEMA Conference Secretariat, P.O. Box 970146, D-6000 Frankfurt-am-Main, FRG.

6-8 June. Szeged, Hungary. International Conference: From Biotechnics to Biotechnology. Details: MTESZ Biotechnology Conference, H-6701 Szeged, Kigyó u.4., Hungary.

12-16 June. Stockholm, Sweden. Fourth International Conference on AIDS. Details: Prof. Stephan Rossner, King Gustav V Research Institute, P.O. Box 60004, S-104 01, Stockholm, Sweden.

20-24 June. Cambridge, Mass., USA. American Solar Energy Society Annual Meeting (contains sessions on biotechnology and biomass conversion). Details: John Hull, Argonne National Laboratory, MCT-308, 9700 South Cass Ave., Argonne, IL 60439-4815, USA.

28 June. New York, NY, USA. The Coming Profit Opportunities in Biotechnology: A New Assessment. Details: Ray Goodwin, Consulting Resources Corp., 6 Northbrook Park, Lexington, MA 02173, USA.

July 1988

5-9 July. Frederick, MD, USA. Fourth Annual Meeting on Oncogenes. Details: Margaret Fanning, Conference Co-ordinator, PRI, NCI-Frederick Cancer Research Facility, Frederick, MD 21701-1013, USA.

6-8 July. Prague, Czechoslovakia. 21st Century Prospects for Biotechnology in Agriculture and the Environment (immediately preceding the meeting of the International Union for Biochemistry). Details: Karel Zeleny, Agrogen, JSD Slusovice, CS-753 15 Czechoslovakia.

17-22 July. Paris, France. 8th International Biotechnology Symposium. Details: Secretariat, VIIIe Symposium de Biotechnologie, 14 rue Mandar, 75002 Paris, France.

18-21 July. New York, NY, USA. Interphex USA. Details: Cahners Exposition Group, Cahners Plaza, 1350 E. Touhy Avenue, P.O. Box 5060, Des Plaines, IL 60017-5060, USA.

18-31 July. Denver, Colorado, USA. Somatic Cell and Molecular Genetics Workshop. Details: Dr. Sherry Leonard, Programme Director, Somatic Cell and Molecular Genetics Workshop, Eleanor Roosevelt Institute for Cancer Research, 1899 Gaylord Street, Box N, Denver, Colorado 80206, USA. (Restricted to US citizens)

25-30 July. Leuven, Belgium. Third International Human Genetics Summer Course: DNA Diagnosis in Constitutional and Malignant Genetic Diseases. Details: J.J. Cassiman, Centre for Human Genetics, Campus Gasthuisberg, O. and N., Herestraat, B-3000, Leuven, Belgium.

31 July - 4 August. Davis, CA, USA. Risk Assessment in Agricultural Biotechnology. Details: Donna Hyatt, Dean's Office, College of A. and E.S., University of California, Davis, CA 95616, USA.

August 1988

1-5 August. Hong Kong. 8th International Conference on Global Impacts of Applied Microbiology. Details: S.T. Chang, Dept. of Biology, The Chinese University of Hong Kong, Shatin, New Territories, Hong Kong.

7-12 August. Chicago, IL, USA. 1988 Annual Meeting of the Society for Industrial Microbiology. Details: Ann Kulback, SIM, P.O. Box 12534, Arlington, VA 22209-8534, USA.

7-13 August. Espoo, Finland. 14th International Conference on Yeast Genetics and Molecular Biology. Details: Tarja Koistinen, Research Laboratories, Alko Ltd., P.O. Box 250, SR 00101, Helsinki 10, Finland.

9-11 August. Port Angeles, WA, USA. North American Tannin Conference. Details: College of Forestry, Oregon State University, Corvallis, OR 97331, USA.

11-13 August. Davis, CA, USA. International Symposium on Population Genetics and Germplasm Resources in Crop Improvement. Details: Donna Hyatt, Dean's Office, College of A. and E.S., University of California, Davis, CA 95616, USA.

14-18 August. Davis, CA, USA. American Institute of Biological Sciences Annual Meeting. Details: Louise Salmon, Meetings Manager, AIBS, 730 11th Street, NW, Washington, DC 20001, USA.

14-19 August. Montreal, Canada. Fourth International Congress of Cell Biology. Details: Congress Secretariat, 4th International Congress of Cell Biology, National Research Council of Canada, Ottawa, Ontario, Canada K1A 0R6.

20-27 August. Toronto, Canada. 16th International Congress of Genetics. Details: Congress Manager, 16th International Congress of Genetics, National Research Council of Canada, Ottawa, Ontario, Canada K1A 0R6.

23-26 August. Ghent, Belgium. 7th International Symposium on Mass Spectrometry in Life Sciences. Details: A. de Leenheer, Laboratoria voor Medische Biochemie en voor Klinische Analyse, Harelbekestraat 72, B-9000 Ghent, Belgium.

31 August - 3 September. Gargnano del Garda, Italy. Fourth Separation Science and Biotechnology Symposium. Details: Prof. P.G. Righetti, Symposium Chairman, Euro Business Centre, P.O. Box 10552, 1001 EN Amsterdam, The Netherlands.

September 1988

4-8 September. London, UK. Course on Biochemical Engineering. Details: Lynne Mason, Dept. of Chemical and Biochemical Engineering, University College London, Torrington Place, London WC1E 7JE, UK.

18-22 September. Domaine de Seillac (Blois), France. Micro-environments for T-Lymphocyte Differentiation. Details: INSERM Conferences, 101, rue de Tolbiac, 75654 Paris, France.

25-29 September. Florence, Italy. Fifth International Symposium on Bioluminescence and Chemiluminescence. Details: OIC, Via G. Modena 19, 50121 Florence, Italy.

25-29 September. Cambridge, UK. Fourth International Congress on Computer Applications in Fermentation Technology. Details: Conference Secretariat, Society of Chemical Industry, 14-15 Belgrave Square, London SW1X 8PS, UK.

28 September - 1 October. Orlando, Florida, USA. North American Cystic Fibrosis Conference. Details: Cystic Fibrosis Foundation, 6931 Arlington Road, Bethesda, MD 20814, USA.

October 1988

2-6 October. Domaine de Seillac (Blois), France. Adhesive Reactions and Cellular Functions. Details: INSERM Conferences, 101, rue de Tolbiac, 75654 Paris, France.

6-8 October. La Vieille Citadelle, Villefranche-sûr-mer, Côte d'Azur, France. EMBO Workshop on Mechanisms of Immunoglobulin Gene Diversification, Rearrangement and Expression. Details: Kenneth B. Marcu, Biochemistry Department, Life Sciences Building, State University of New York at Stony Brook, Stony Brook, NY 11794-5215, USA.

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08	Other governmental department	19	Consultant		
09	Non-governmental aid agency	20	University		
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11	Manufacturers' association	22	Industrial training or productivity centre		

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003	Tobacco	019	Precision instruments	032	Transfer of technology (licensing)
004	Textile and garment	020	Agricultural machinery	033	Industrial research and development
005	Leather	NON-MANUFACTURING INDUSTRIES AND PROJECTS		034	Standardization
006	Wood processing	021	Mining and quarrying	035	Industrial organization and administration
007	Pulp and paper	022	Utilities (including power plants)	036	Industrial co-operatives
008	Petrochemical and plastics	023	Public services (transport, communications, tourism)	037	Industrial information and documentation
009	Industrial chemicals and fertilizers	024	Construction (civil engineering) projects	038	Industrial promotion
010	Pharmaceuticals and other chemical products	SUPPORTING INDUSTRIAL ACTIVITIES		039	Industrial training
011	Rubber	025	Industrial planning and programming	040	Industrial management
012	Non-metallic mineral products and building materials	026	Industrial policies	041	Industrial consulting services
013	Iron and steel	027	Industrial financing and investment promotion	042	Development of small-scale industries
014	Non-ferrous metal	028	Promotion of export oriented industries	043	Industrial estates
015	Fabricated metal products	029	Industrial development surveys	044	Appropriate technology
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