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Genetic Engineering and Biotechnology Monitor

Issue No. 35 November 1991

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United Nations and other organizations' news

WHO to repeat Kenyan oral-IFN AIDS trial, but this time controlled

One year after a physician in Kenya announced that orally administered alpha-interferon had cleared up all symptoms of AIDS in 99 of 101 patients the World Health Organization (WHO) is about to put his claim to a double-blind test.

David L. Heymann, chief of the Office of Research in WHO's Global Programme on AIDS, announced that three African countries should begin administering the identical interferon-soaked maltose lozenges given by the head of Kenya's Medical Research Institute, Davy K. Koech, to his 101 AIDS sufferers. The three African nations participating in the test are Uganda, Zambia and Zimbabwe.

Principal investigators from these countries completed a rigorous training course for local African physicians, who will treat a total of 600 subjects with the low-dose, once-a-day interferon pellets. Another 600, with matching clinical stage and symptoms of AIDS, will receive placebos.

The six-month study is a direct outcome of two meetings between Dr. Koech and WHO, aimed at setting up a double-blind clinical study that would mimic the Kenyan's open trial, using the same transmucosal, natural, non-recombinant alpha-interferon preparation, provided by Hayashibara Biochemical Laboratories Inc., Okayama, Japan.

Meanwhile, smaller-scale trials are under way in half a dozen countries, coordinated by Amarillo Cell Culture, Inc. (ACC), Amarillo, Texas, which holds the patents to Hayashibara's oral-interferon preparation. Some of these are:

- In Toronto, the Community for Research Initiative, backed by the Canadian Bureau of Biologics, began a double-blind, placebo-controlled study in January 1991. It aims to enrol 150 AIDS patients and expects to break the trial code and evaluate results in eight weeks. So far, 90 patients have signed on.
- In Munich, 30 patients are midway through a cross-over protocol - 15 at a time on interferon, 15 on placebo.
- Poland has an open-label trial in progress, with more than 30 AIDS patients, plus an equal number with chronic, active hepatitis.
- Japan is testing the oral interferon on 20 patients.
- Thailand has more than 40 subjects in a double-blind, placebo-controlled regimen.
- In Manila, a US Naval Research unit is conducting a clinical study of the drug in 37 women who tested positive for HIV.

In the USA, says Samuel H. Ronel, president of Interferon Sciences, Inc. (ISI), New Brunswick, N.J., widespread availability of wildcat, low-dose, trans-mucosal alpha-interferon preparations makes it difficult to recruit

volunteer AIDS victims to take part in properly controlled clinical trials. Two such studies are under way at Mt. Sinai Medical Center, New York City, directed by immunologist Joseph M. Hassett. Instead of Hayashibara's wafers, Mt. Sinai subjects receive daily doses of liquid IFN, formulated by ISI. (Extracted from McGraw Hills' Biotechnology Newswatch, 4 March 1991)

Food and work for the Third World

Unlike the Green Revolution, whose benefits largely bypassed small farm agriculture, biotechnologies are potentially accessible to small-scale cultivators and can be used independently of large enterprises.

Researchers from the International Labour Organisation (ILO) are examining what effects these new technologies could have on small producers and wage labourers in agriculture. Two case studies, from Nigeria and Mexico, point to some promising results.

In Nigeria, a heavily populated country with a relatively underdeveloped agricultural system, the use of biotechnology in the production of animal feed would improve the nutritional level, create jobs and enhance incomes. The so-called SCP technologies (single-cell protein production), which use micro-organisms in combination with natural gases that are abundantly available in the country, would produce animal feed with a particularly high protein content.

Nigeria would no longer need to import expensive feed, which is vital for its widespread poultry production. There would be an increase in production in the subordinate animal husbandry sector, which would also create employment opportunities ranging from wage labour to self-employment.

In Mexico, where existing economic and social structures in agriculture are not easily altered, the introduction of advanced plant biotechnologies (APB) can be successful only if preceded or accompanied by a more progressive labour and social policy. As long as credit and market opportunities are restricted and unequally distributed, there can be no guarantee that everyone will have access to the advantages of APB. (Source: Development Forum, January/February 1991.

Ethics of genetics

More than 4,300 genetic disorders have been identified as depending on a single faulty gene, including cystic fibrosis, haemoglobinopathies, phenylketonuria, haemophilia, and Huntington's disease. It has been calculated that about 1 per cent of all liveborn infants in the developed world have single-gene disorders. Now the possibility can be envisaged for all these genetic disorders to be controlled and perhaps eventually eliminated.

The ethical consequences of these new developments bring into focus potential conflicts between the individual's rights and society's responsibilities. These issues were addressed at the CIOMS (Council for International Organizations of Medical Sciences) Conference on Genetics, Ethics and Human Values, co-sponsored by WHO and UNESCO, which was held in Tokyo in July 1990.

Some 100 delegates from 30 countries, representing such fields as medicine, natural and social sciences, philosophy, theology, law, and health policy-making, focused principally on human genome mapping, genetic screening and genetic therapy. At the final session the Conference participants agreed on the main ethical issues relevant to human genetics and expressed them in the Declaration of Inuyama. A concurrent satellite symposium took place on biotechnology and human genetic diseases.

The CIOMS conferences are intended to create international forums where the scientific and lay communities may exchange views on topics of immediate concern; they do not necessarily arrive at recommendations or decisions if a consensus does not develop on all points. Since 1985, CIOMS has arranged a series of international dialogues under the title of "Health policy, ethics and human values", aimed at bringing about a greater awareness of human values across political and cultural lines and at improving understanding of the concepts inherent in WHO's goal of health for all. (Source: World Health Forum, Vol. 11, 1990)

The ABN in action

Following the International Symposium on the Role of Biology in Resolving the Food Crisis in Africa in 1989, the African Sciences Network (ABN) decided to focus its work on five major areas: plant and animal production, nutrition, agroforestry and biotechnology. Some examples of its work in these fields include:

Against insects that destroy rice-crops. In an effort to limit damage to rice crops before and after harvesting, the ABN launched a study of crop destruction by insects which attack plants or seed in the Tai region of the Côte d'Ivoire. This led to the identification of more resistant varieties of rice, which although yielding less, resulted in better crops because the insects stayed away. The study also concluded that monoculture over large areas often creates conditions favourable for certain destructive insects.

Agroforestry. In Nigeria, an ABN-financed project led to the identification of tree species which, because of their capability to fix and protect soils and improve yields of associated crops, are appropriate for the development of agroforestry.

Biotechnology. In Gabon, a pioneer project on the in vitro cultivation of manioc and banana plantain, and the establishment of healthy genetic stocks based on tissue taken from young plants suffering from viral diseases was financed by the ABN. The Network, through research such as this, hopes to use the knowledge thus gained as a "scientific shortcut" to a solution for Africa's food crisis.

Health. In Rwanda, the ABN financed a study of the transport of stools on filter-paper for analysis, in the case of intestinal illnesses transmitted by water such as dysentery. The advantage of this method is that it provides an extremely simple and cheap way of conserving fragile material for transport to laboratories which, in Africa, are often far from the village where the samples were taken. (Source: UNESCO Sources, No. 23, February 1991)

Monitoring of genetically modified organisms released into the environment

An OECD workshop, hosted by the Danish National Agency for Environmental Protection, was held in Copenhagen, 3-7 December 1990, and attended by more than 70 scientists and regulators from 16 OECD member countries, the Commission of the European Communities and the United Nations Environment Programme.

At this, the first international workshop of its kind, OECD took significant steps towards building an international consensus on sciertific principles and methods for monitoring of genetically modified organisms (GMOs) released into the environment.

Opening the workshop Mr. Ole Plougman, Deputy Director-General of the Danish Environmental Protection Agency, drew attention to the timeliness of such a meeting in view of the increasing number of experimental introductions of GMOs to the environment worldwide. In most OECD countries, frameworks for assuring safety in biotechnology have been established. He said there was now a need for further elaboration of scientific principles and methods for monitoring the fate and environmental interactions of organisms released into the environment.

Previous initiatives on biotechnology safety have led to the development of the widely-used OECD guidelines and principles for assessing potential risks associated with the use of genetically modified organisms in industry, agriculture, and the environment. Commenting on the forward-looking and innovative character of the work achieved, the workshop's overall chairman, Dr. Roger Nourish of the UK said: "The workshop took an important first step in international exchange and cooperation in this rapidly evolving area. I believe it made significant findings and suggestions about general approaches to monitoring; specific design and methods for monitoring of plants and micro-organisms, and for future national and OECD work in this area."

For further information, contact:
Victor Morgenroth, OECD Environment Directorate, 2, rue André-Pascal, 75775 Paris Cedex 16, France. Telephone: (33-1) 45 24 97 75. (Source: News Release, 11 December 1990)

Regulatory issues

How to regulate environmental releases

Gene splicing has been used in agricultural research for at least a decade, and engineered organisms have now been released in many field tests. Yet few governments have decided how to regulate this new technology, if at all. The tensions - in both US and international policy - were on display in February at a symposium on biosafety organized by the US Agency for International Development.

Margaret Mellon, a specialist on biotechnology policy at the National Wildlife Federation, criticized the US Government for what she termed a failure of leadership in controlling the risks posed by the environmental release of genetically engineered organisms. She says that guidelines for research recently issued by the Department of Agriculture (USDA) are inadequate.

Alvin Young, who directs biotechnology policy at USDA, defended the guidelines, which had been drawn up by his office. He says getting other agencies - including the Office of Management and Budget - to reach a consensus and endorse them was very difficult. It was the White House, he said, that insisted that the guidelines be published separately from any plan for implementing them. It is not clear at present when or by whom the plan will be prepared.

European countries do not seem to be much further along. Although the bureaucratic apparatus of the European Community in Brussels has declared its intent to impose special controls on agricultural biotechnology - including case-by-case reviews of possible socioeconomic dislocations - it has issued no rules as yet. However, John Barton, an expert in international law at the Stanford University Law School, pointed out that even developing nations are preparing for action. The Philippines and Mexico have established guidelines to cover bioengineered organisms, and India in 1990 created a full-blown regulatory bureaucracy for this purpose.

Barton and some colleagues at the Stockholm Environment Institute have proposed an alternative to regulation, which he thinks would benefit both the technology-poor developing nations and the industrialized countries where most of the new genetic organisms are being created. His idea is to create an international ad hoc advisory committee, akin to the group of experts that has advised the National Institutes of Health on recombinant DNA activities for the last decade. As Barton envisions it, the group would operate under the aegis of the Stockholm Institute (a private, government-funded organization), serving as an adviser to all comers. It would mainly deal with issues of "hard science", Barton said, although it could also venture into broader questions of intellectual property rights and pest management. A seal of approval from this group presumably would serve as a certificate of safety for genetic engineering tests to be run anywhere in the world. One big advantage of this approach, Barton said, is that it avoids the balkanization of procedural rules and scientific data requirements that could occur if every nation enacts its own system of controls. (Extracted with permission from Science, Vol. 251, pp. 1023-1024, by Eliot Marshall. Copyright AAAS, 1991)

General

AIDS vaccine trials

A February NAS meeting on international trials of AIDS vaccines covered some highly contentious ground. The problems on the meeting's agenda - how to guarantee developing countries access to potential AIDS vaccines, where to hold key upcoming tests of vaccine efficacy, and which of the big institutional players should coordinate such an effort - are touchy.

Perhaps the most sensitive of those issues is the one people in the field call "distributive justice". In more straightforward terms, the issue boils down to who takes the risks and who gets the benefits. Deriving statistically significant data that prove a vaccine's efficacy is difficult: researchers need a large population varied in gender and age that is at high risk for infection. The length of the trial is dependent on all of these

variables. That is why researchers, who want to conduct a sound trial expeditiously, are looking toward developing countries, where HIV infection is spreading rapidly through the general population. However, trial participants must still be educated about infection prevention.

Suppose the international agencies involved choose Zaire as one of the trial countries. If an HIV vaccine proves itself effective there, the first quandary is fairness: how will the people of Zaire be able to afford such a vaccine at free market prices? But if the people of Zaire receive the AIDS vaccine free or at reduced price, due to financial support from the developed world, should not other Third World countries get the same treatment? And if they should, how could such generosity be put into practice: who will foot the bill and who will distribute the vaccine?

Wrestling with such questions at the meeting were 50 representatives of some 20 organizations, including officials and researchers from the World Health Organization (WHO), the National Institutes of Health, the Centers for Disease Control (CDC), the US Public Health Service, the US State Department, the US Army, the Pan American Health Organization, academia, philanthropic foundations, think tanks, and industry.

During the last 12 months, the number of AIDS vaccines to receive the Food and Drug Administration's permission to enter clinical trials jumped from two to six. And after initial failures with a variety of candidate vaccines, several experimental preparations have now demonstrated limited efficacy in monkeys and chimpanzees. Finally, researchers have already initiated small Phase I and Phase II trials of nine experimental AIDS vaccines in the United States and Europe. These are not to be confused with the critical phase of vaccine testing about which meeting attendees wrangled. WHO officials have, since January, been scouting sites for the Phase III efficacy trials.

No one at the meeting was willing to predict on the record when a Phase III trial might begin in a developing country, since getting experimental sites set up is bound to be tricky - both organizationally and politically. The international groups responsible are getting started now. According to Michael Merson, head of WHO's Global Programme on AIDS, this is "the most urgent issue right now".

To that end, WHO representatives have been approaching various ministries of health to learn which countries want to participate in AIDS vaccine trials. WHO plans to conduct site visits in interested countries and, through a newly formed steering committee that met for the first time in April, eventually select six or seven sites. The steering committee also will decide which vaccines to test.

But choosing a group of sites is not the only potential problem in the Phase III AIDS international vaccine trials. Another difficulty that will have to be negotiated is the plethora of big organizations with a vested interest in vaccine work.

Although this overlap suggests the need for some direction from above, several attendees at the meeting said they were uncomfortable with the idea of one organization playing gatekeeper.

But will it be able to handle the price problem and other ethical hurdles? No matter which institution winds up leading the vaccine trials and no matter which countries are chosen as test sites, the final programme will no doubt involve a product developed in a rich country being tested in a poor one. And that problem is at the heart of the many efforts to formulate ethical guidelines for AIDS vaccine testing that is now under way. WHO is developing an ethical checklist for AIDS vaccine trials. WHO's Geneva neighbour, the Council for International Organizations of Medical Sciences (CIOMS), is establishing new ethical guidelines for international human epidemiological research. The US Public Health Service (PHS), parent to both the NIH and CDC, also has a new policy for international HIV research in the works.

Even with all these efforts, the ethics are falling far behind the science in AIDS vaccine trials, says attorney Larry Gostin, head of the Boston-based American Society of Law & Medicine and a professor at the Harvard School of Public Health. "I am terribly afraid that when there a safe and efficacious vaccine it will be too expensive for the Third World", says Gostin, who works for CIOMS, WHO, and PHS. "Should that happen, it would be a tragedy of world proportions ... From an ethical standpoint, to place a research burden on Third World countries and not make plans [to make the final product accessible] is unconscionable".

Gostin is particularly concerned that none of the new ethical guidelines or policies mandates distributive justice.

Almost everyone agrees that access to an AIDS vaccine for the world's poor is an important goal. But even if that goal receives a sympathetic audience, ultimately somebody has to foot the bill for any largesse that might be required - and that is not quite as easy a subject to agree on. Some favour a two-tiered pricing scheme in which developed countries pay more for a vaccine and thereby subsidize others. Jonathan Mann, director of the International AIDS Center at the Harward School of Public Health, has been floating a novel idea he thinks would work better than a tiered setup: patent exchange, in which the developers of an AIDS vaccine donate the patent to an international organization. In return, the developers receive the right to extend the patent on an existing drug, a right they can use for their product or trade as a commodity.

Ronald St. John, deputy director of PHS's National AIDS Program Office, supports a less ingenious but perhaps even more radical solution: take AIDS vaccines out of the private sector altogether. St. John says he would like to see the 14 developed countries sign a treaty to fund and distribute an AIDS vaccine.

International trials may even add to the scientific complications - for example, would a vaccine developed using HIV strains prevalent in the United States and Europe be successful in a Third World country where different strains prevail? But international trials are coming inexorably closer. (Extracted with permission from Science, Vol. 251, pp. 1312-1313, by Jon Cohen. Copyright AAAS, 1991)

Farmers and plant breeders lock horns over royalties

Arable farmers and plant breeders throughout Europe are bracing themselves for a bitter confrontation over changes to an international convention designed to protect the rights of plant breeders. The farmers are resisting moves by the breeders to expand the system of royalty payments on the varieties of plants they sell to farmers.

The countries that have signed the UPOV convention (drafted by the International Union for the Protection of New Varieties of Plants) met in Geneva in March 1991 to discuss updating it. Since the original draft in 1961 developments in biotechnology have made much of it obsolete.

The proposed changes include lifting a ban on the patenting of plant varieties and a requirement that breeders who want to develop and sell hybrid varieties seek consent from the owner of the original stock.

More controversial is an amendment that would enable governments to eliminate the "farmers' exemption". This gives farmers the right to plant seed harvested from a crop without paying anything to the suppliers of the original seed.

Breeders, who now invest heavily in R&D, want this privilege revoked. Currently, farmers pay a one-off royalty, included in the seed price. Plant breeders want royalties from each new crop generated from the original seeds.

The breeders argue that without royalties, they will be forced to abandon important but unprofitable research into new varieties of plants - particularly cereals, which must be continually fortified against new strains of diseases. Breeders may abandon research into traditional cereals and turn to crops such as maize and sunflower, whose seeds cannot be stored.

Whatever the outcome of forthcoming debates on the issues raised by the changes to UPOV, farmers will not have to pay extra royalties until the mid-1990s, the earliest date by which any amendments to UPOV are likely to be enshrined in national or European law. (Source: New Scientist, 2 February 1991)

Biotask Seminars focus on Third World agricultural biotechnology

During 1990, the Task Force on Biotechnology (BIOTASK) sponsored two seminars. The first, Cassava and biotechnology, held in Amsterdam in March, reviewed the priority constraints in cassava production to which biotechnology might be applied. The second, held in Canberra in June, introduced new techniques in genetic mapping to experienced plant breeders from the Third World.

BIOTASK also met in Washington, D.C. in October 1990, at the time of the annual meetings of the Consultative Group on International Agricultural Research (CGIAR). BIOTASK is made up of various elements of the CGIAR system, including bilaterial and multilateral development agencies, the IARCs and national agricultural research systems (NARS).

In 1991, BIOTASK will be concentrating on information activities. These will include an assessment of the needs of scientists at national institutions for access to biotechnology information, and the provision of selected books and journals. (Source: Biotechnology Bulletin, Vol. 9, No. 12, January 1991)

European public opinion on biotechnology

Biotechnology will make life better, according to 63 per cent of people questioned in Britain, France, Germany and Italy, in a survey conducted by the Gallup Organization and financed by Eli Lilly (Indianapolis, IN). Only 13 per cent of respondents feel that life would become worse as a consequence of biotechnology.

Carried out in tandem with a new report, The Case for Biotechnology, the study also shows that only 4 per cent of the population on average in the four European countries want a total ban on biotechnology. Forty-nine per cent believe work should be regulated through standards and practices agreed upon jointly by industry and government; 38 per cent think it should be strictly controlled by government regulation alone. The findings are based on a representative sample of 1,048 adults in Britain, 1,001 in France, 605 in Germany, and 512 in Italy.

The most striking finding was the very low proportion of "do not knows" in the French sample. No French participant gave this reply to the question about perceived benefits (compared with 11 per cent of the German sample). Eugenics emerged as the principal danger thought to be associated with biotechnology. Overall, eugenics was closely followed in the survey by environmental harm as a subject of concern. But 32 per cent of participants feel that biotechnology is "ethical", the same percentage see it as "unethical", and 33 per cent think it is neither. (Extracted from Bio/Technology, Vol. 9, January 1991)

Ethics of gene therapy debated

A press conference at the annual meeting of the American Association for the Advancement of Science in Washington, D.C., in February 1991 turned into an impromptu debate on the ethical and policy implications of human gene therapy. The protagonists were biomedical ethicist LeRoy Walters of Georgetown University, and attorney Andrew Kimbrell of the Foundation on Economic Trends, an activist group that has filed many lawsuits relating to biotechnology.

The first clinical trials of gene therapy - the substitution of a functional gene for a defective one to cure a genetic disease - began last year at the National Institutes of Health. These trials involve somatic-cell gene therapy, in which non-reproductive body cells are modified.

According to Walters, the central ethical questions surrounding such procedures are:

- What are the probable risks to the patient, to medical personnel, and to the environment?
- What are the potential benefits?
- How will patients be selected in an equitable manner if there are more patients eligible for the therapy than can be treated?

- How will informed consent transactions be handled?

- How will questions of privacy and confidentiality be dealt with so as to balance the public's right to know and patient rights?

Walters pointed out that 20 out of 20 policy statements on gene therapy by a variety of international groups - including special committees in Sweden and Denmark, the parliamentary assembly of the Council of Europe, the Vatican, and the World Council of Churches - affirm that somatic-cell human gene therapy for the cure of disease is ethically acceptable. "On the question of germ-line intervention", says Walters, "there are mixed positions - some in favour, most opposed. And on enhancement techniques, all statements that take a position ... are opposed".

Nevertheless, Kimbrell calls for wider participation in the approval process for gene therapy trials. He calls for full financial disclosure from members of NIH's Recombinant DNA Advisory Committee, the principal decision-making body for gene therapy. In addition, he asks that Congress hold "extensive hearings in this area" and that a genetic engineering advisory board be set up to provide independent oversight outside NIH. (Abstracted with permission from Chemical and Engineering News, 4 March 1991, p. 19, by Stu Borman. Copyright (1991) American Chemical Society)

Banking cultures

Biotechnology has made cells valuable. Some of the most sought after are cultures of cells taken from people with rare and interesting genetic diseases. Among the other valuable cells are hybridomas, hybrid cultures that produce disease-fighting antibodies according to the genetic programme set for them by their creators. If such things are patented, their owners are compelled by law to deposit 12 ampoules of each in a repository for 30 years.

An overworked laboratory with popular cells can be besieged by requests for samples, from all over the world. The people who need them to help find cures for deadly diseases do not have time to stand in lengthening queues. That is one reason why the European Collection of Animal Cell Cultures (ECACC) is doubling the size of its facilities and taking on more staff. Its huge steel tanks hold about 1,000 different cultures in a general collection that includes cells from insects and fish as well as mammals. A further 400 cultures are patent deposits. And there are 1,500 human cell lines, mostly taken from people with diseases caused by genetic defects. This last category of samples is growing fast.

Housed in the Public Health Laboratory complex at Porton Down in Wiltshire, ECACC was first set up in 1984 as a patent repository. It now does many other jobs too. It stores cultures for drug companies in case anything happens to the ones kept in the companies' own laboratories. And the team tests cultures with DNA probes to make sure that they are what they purport to be. In the 1970s biotechnologists suffered quite a reverse when it emerged that huge numbers of cultures had been taken over by a vigorous cell line derived from a cancer removed from an American woman. Thousands of experiments and hundreds of man-years of research were rendered useless.

Further tests are carried out to see whether cultures sent to ECACC are infected by viruses, bacteria, fungi or, worst of all, mycoplasmas - a sort of mini-bacteria which flourishes undetected in many cultures.

Over the next few years ECACC will do more work on human cell lines for research into genetic diseases, and on cultures of human cells that naturally produce the lymphokines which some people believe will one day play a large part in medicine. There will be less emphasis on hybridomas, because their function is now being taken over by bacterial cell cultures which are quicker, easier and cheaper to grow.

The only other repository of ECACC's kind is the American Type Cultures Collection in Atlanta, Georgia. Now the British repository expects to work in partnership with Soviet and East European scientists. (Source: The Economist, 19 January 1991)

World's rice crop vulnerable to changing atmosphere

Rice, the world's most important food crop, will be especially hard hit by man-made changes to the atmosphere, according to a biologist in the US. Although most plants will grow better as we add more carbon dioxide to the air, these benefits will be more than cancelled out by increased ultraviolet light from the sun, penetrating a depleted ozone layer.

Alan Teramura at the University of Maryland has carried out the first experiments in which the levels of both carbon dioxide and ultraviolet light are raised to those expected by the mid-21st century. He has studied the effect on a number of crops, most notably rice and wheat.

In his latest experiments, Teramura exposed plants to normal sunlight, while nearly doubling the concentration of carbon dioxide, from 355 to 650 microlitres per litre of air. He raised the intensity of UV-B to the level expected if the ozone layer at the equator were thinned by 10 per cent. In "comparison" plots, Teramura increased either carbon dioxide or UV-B alone.

Teramura found that when rice was exposed simply to more carbon dioxide, the yield of its seed and its biomass increased by 20 per cent. Wheat did even better, increasing its biomass by up to 50 per cent. But when he raised UV-B as well as carbon dioxide, the increase seed yield in both was wiped out. He also found that the biomass of rice did not seem to increase at all. Ironically, however, rice paddies emit significant quantities of methane, a gas which contributes to global warming and which also depletes ozone.

Teramura's results are not without some contradictions, however. When he tested soya beans in a similar way to the rice, he found that they actually gained in seed yield and biomass when he increased the level of carbon dioxide and UV-B. Also, Teramura found that when he exposed rice to increased levels of UV-B, without raising the level of carbon dioxide, it had no apparent effect on growth.

Teramura says that different species of plant vary widely in how sensitive they are not only to changes in ultraviolet light but to changes in the ratio of UV-B to visible light. He says it is possible that UV-B may interfere with the process of photosynthesis, making plants unable to respond to enriched carbon dioxide.

Although Teramura has found no clear link between a plant's physiology and its sensitivity, he suggests that geography - specifically, the place where a plant evolved - may count the most. Plants at lower, equatorial latitudes have been receiving 50 per cent more UV-B at midday than plants in higher, temperate latitudes, and they have been receiving this for at least a million years. The reason is that the ozone layer is thinner around the planet's midsection; rays have a shorter path and so are less attenuated.

As a consequence of this, says Teramura, plants from temperate zones have not evolved mechanisms for protecting themselves from UV-B. He and his colleague, Martyn Caldwell of Utah State University, estimate that more than half the crops that originated in the Near East, Northern China and Mesoamerica are sensitive to UV-B. On the other hand, only 18 per cent of those from mid-Africa, Southeast Asia and South America are classified as sensitive.

Global warming can also harm plants by making them too hot. Teramura has reviewed the literature on crops and temperature and found that temperatures near 40°C can seriously stunt the growth of cereals, such as rice, wheat and corn. According to researchers at the Goddard Institute of Space Studies, a doubling of carbon dioxide would raise summer temperatures by almost 5°C, enough to cripple or extinguish rice crops. Such a doubling in concentration could occur by the middle of the 21st century. (Source: New Scientist, 12 January 1991)

Biochemistry offers opportunities in Europe

The rewards of biochemical food production outweighs its risks, and sales in Europe will surpass $2 billion per year by 1995, according to Frost & Sullivan, New York, N.Y. The firm says European biotechnological research in food is focusing on short-term projects that gnerally lower the cost of food production and improve its safety. Genetic engineering of yeast is particularly promising and may yield strains that operate at higher temperatures and produce more enzymes, colours and flavours.

The firm explains that "a one- or two-year programme to develop a specific test could cost in the region of $100,000. For a similar sum it is possible to investigate specific modification of a functional enzyme or protein; that is, protein engineering rather than genetic engineering. There is no guarantee of success, of course, but the sums at risk are considerably less than the millions of dollars needed for totally new ingredients, additives or raw materials." (Source: Chemical Marketing Reporter, 4 February 1991)

Biosensors' bright future

Demand for biosensors will reach $200 million/year by 1995, booming to $1 billion/year by 2000, according to Consulting Resources (Lexington, MA). The largest market will be in clinical diagnostics, with sales reaching $60 million/year by 1995, and in bioprocessing, where sales are expected to reach $50 million by 1995. (Source: Chemical Week, 6 March 1991)

B. COUNTRY NEWS

Australia

The Genetic Manipulation Advisory Committee (GMAC) has recently issued new guidelines for large-scale work with genetically manipulated organisms. These guidelines have been drawn up to bring under GMAC review, large-scale or industrial work involving genetically manipulated organisms, generally applying to cultures of more than 10 litres (although this may be varied in certain circumstances) or the production of plants, animals, fish, insects or other organisms on a commercial scale. Exemptions may apply in certain circumstances and application may be made for projects which are considered not to present a significant risk to occupational and public health or to the environment to be conducted according to a less restrictive containment class known as Good Industrial Large-Scale Practice (GILSP). The guidelines cover the following areas:

1. Roles and responsibilities of GMAC, Chief Executive Officers, Institutional Biosafety Committees, Biological Safety Officers and Project Supervisors.

2. Containment requirements - biological, physical, under GILSP, C1-LS and C3-LS, facilities for large transgenic animals and poultry, large-scale plant houses, aquaria, and insect housing.

3. Transport and import - including transfer of material within and between institutions, transport of micro-organisms by post, and transport of transgenic animals, fish, plants, birds and insects.

The new guidelines replace an earlier version issued in April 1984. Copies of the guidelines may be obtained from GMAC, GPO Box 2183, Canberra, ACT, 2601. (Source: ABA Bulletin, Vol. 6, No. 1, February, 1991)

Foreign investors back gene-snippers

Australia's claim to "gene shears" technology was strengthened when the American multinational Johnson & Johnson decided to invest in Gene Shears, the company set up to develop the technology. Johnson & Johnson's partners in Gene Shears are the Australian national research organization, CSIRO, whose researchers invented the process, and the French seed company Groupe Limagrain.

CSIRO researchers believe they can design and build molecules - gene shears - to target and destroy specific genes and viruses. The molecules could be used against a range of human, animal and plant diseases. The market for gene shears could be worth billions of dollars.

The emergence of Johnson & Johnson as the third partner in Gene Shears has caused a political furore in Australia. The opposition science spokesman, Peter McGauran, claims that it will result in foreign control of the technology, leading to a signficant loss of export earnings.

However, the CSIRO is still looking for another partner, and both foreign partners have agreed that, if the fourth partner is Australian, they will reduce their holdings to allow 50 per cent Australian ownership. (Source: New Scientist, 30 March 1991)

Cooperative research centres

The Federal Government recently announced the first 15 of up to 50 Cooperative Research Centres it will establish under a new $100 million-a-year programme. The first 15 centres will develop and apply Australia's scientific and engineering skills to:

- Improve Australia's industrial base, especially advanced manufacturing and information industries, by drawing on our expertise in the emerging fields of material science and information technologies;
- Capture the benefits of our world-class capability in medical research, both through the development of pharmaceuticals and other commercial products and contributing to public health;
- Strengthen the established resource-based industries both by providing the knowledge that will underpin their continued competitiveness and capacity to value add, and addressing the challenge of the sustainable use and development of our natural resource wealth;
- Contribute to more responsible and effective environmental and waste management and the exploitation of commercial opportunities in this area;
- Take a leading scientific position in the Antarctic, enabling us to continue to strengthen Australia's lead in the international consideration of this unique region.

Commonwealth funding for the 15 centres under the CRC Programme will increase to $30 million a year (in 1990-1991 dollars) by 1992-1993, and total $190 million over the seven years the centres will be initially funded. Participants must at least match this contribution. In most of the first 15 centres, however, their commitment is expected to be well above this level.

Industry support, in cash and kind, is expected to total over $90 million over seven years. Several State Governments have also pledged substantial support for centres located primarily in their States. Most of the 120 applications in the first round were initiated by university or CSIRO groups, and Mr. Crean encouraged private and public sector industry groups to take a more pro-active role in the second and third rounds.

Of the 15 cooperative research centres, the following directly involved biotechnology:

CRC for tissue growth and repair - Adelaide (Contact: Dr. F. John Ballard, Chief Research Scientist, CSIRO Division of Human Nutrition (Tel.: (08) 224-1835, Fax: (08) 224-1841).

CRC for cellular growth factors - Melbourne (Contacts: Dr. Margaret Brumby, The Walter and Eliza Hall Institute of Medical Research, Tel: (03) 345-2555; Fax: (03) 347 0852).

CRC for waste management and pollution control - Sydney (Contact: Professor Chris Fell, University of New South Wales, Tel: (02) 697 2700; Fax: (02) 313 6805).

CRC for plant science - Canberra (Contacts: Professor B. E. S. Gunning, Tel: (06) 249 3841; Fax: (06) 249 0758 or Dr. W. J. Peacock, Tel: (06) 246 5250; Fax: (06) 246 5530).

Brazil

Safe biotechnology enhances soybean crop

In Brazil, soybeans are the stuff of superlatives, replacing coffee as the country's largest agricultural export. Farmers there produced 18 million tons of the crop in 1988 on 10 million hectares of land, accounting for 13 per cent of total exports and earning the country $3.5 billion in foreign exchange.

The country's impressive soybean production - which is double today what is was just 15 years ago - is achieved by employing the most modern technology. At the same time, Brazil has demonstrated that big-time agriculture need not rely solely on massive applications of chemical fertilizers and pesticides, which are costly and environmentally harmful. Instead, researchers have learned to harness the forces of nature to help increase soil fertility and combat pests.

The problem confronting Brazilian researchers was to find a kind of nitrogen-fixing bacteria that would survive in hot and acidic soils and compete successfully with other bacteria on the soybean roots. They have been successful in their search for a substitute for nitrogen fertilizer, which typically accounts for some 75 per cent of a farmer's fertilizer costs.

The research was carried out at the National Soil Biology Research Program, located 50 kilometres west of Rio de Janeiro. The laboratory is part of Brazil's national agricultural research agency, EMBRAPA, which received a $70.8 million loan from the Inter-American Development Bank (IDB) to improve facilities and finance staff training. The EMBRAPA researchers discovered nitrogen-fixing bacteria for a number of crops, but the biggest impact has been on soybeans.

Most Brazilian farmers now inoculate their soybean seeds with nitrogen-fixing bacteria. As such, they avoid the need for nitrogen fertilizer, thus saving some $1 billion annually and making Brazilian soybeans very competitive on the world market.

Researchers have also sought nature's help in combating insect pests. One of the two principal soybean pests is the velvet bean caterpillar.

A natural enemy of the caterpillar was found to be a virus. Researchers at EMBRAPA's National Soybean Research Center, located in Londrina in the southern state of Paraná, developed a method of isolating the virus and mixing it with clay powder. The farmers mix the powder with water and spray it on their crops. A small packet of the powder, costing about $1.00, is sufficient to spray one hectare.

A farmer can also make his own spray by collecting caterpillars killed by the virus. These are frozen and, when the next soybean season comes around, are liquified, diluted with water and sprayed on the crops. The virus contained in 50 dead caterpillars is sufficient to treat one hectare.

The virus pesticide costs up to 75 per cent less than chemical applications - or nothing at all if the farmer produces his own - and it does not add toxic chemicals to the environment.

In 1989, this biological control method was used on 6 per cent of Brazil's soybean crop, saving the country an estimated $43 million. Brazilian scientists are uncovering the subtleties of nature, and in so doing are saving farmers money and protecting the environment. (Source: Development Forum, January/February 1991)

Conquering mountains because plants are there

For more than a decade, researchers at the Royal Botanic Gardens at Kew, with their colleagues in Brazil, have been mapping the plants of the remote mountainous habitats in north-eastern Brazil known as campo rupestre. Each expedition discovers new species found nowhere else on Earth.

The botanists from Kew are working closely with researchers at the Centro de Pesquisas do Cacau (CEPEC) at Itabuna in Bahia, Brazil, and at the University of Sao Paolo. The plan is to survey intensively the plants living in selected mountainous sites in the Serra do Espinhaco of Minas Gerais and Bahia, and to publish inventories.

This approach is the most cost-effective way of discovering the diversity of the plant life, the way various species are distributed and the extent to which plants living in the region are endemic, or unique to that region. These inventories also provide valuable records for researchers in other disciplines such as zoologists and ecologists, as well as a focus for further research and teaching.

So far, the inventories of two such areas have been published - the Serra do Cipó by the University of Sao Paolo and Mucugê by Kew. Both areas are now national parks, partly as a result of this research initiative. The University's researchers are well on the way to completing the Flora of Grao Mogol.

Plans are now afoot to explore an area of campo rupestre further north in the same mountain chain. This project will fall under the umbrella of the Projecto Nordeste, a major Kew/Brazilian initiative which aims to carry out the scientific work essential to the rehabilitation of the degraded ecosystems of north-eastern Brazil. These include the caatinga forest, the Atlantic forest, seasonal semi-deciduous and evergreen forests, as well as the vegetation of the mountainous campo rupestre. (Source: New Scientist, 2 March 1991)

Canada

Rapid growth predicted for Canadian biotechnology

Canadian biotechnology is on the threshold of rapid growth, predicts Canadian Biotech '89: On the Threshold, a survey of 84 of Canada's 220 biotechnology companies. The following are highlights of the report, a collaborative project by Ernst & Young High Technology Group, Winter House Scientific Publications, Industry Science and Technology Canada, and the National Research Council.

As of February 1989, there were 10,600 products at various stages of development in Canada - 62 per cent are in research and development, 15 per cent in testing and 23 per cent in production.

Fifty-six per cent of companies surveyed have in-house manufacturing facilities and 50 per cent expect to build new facilities within the next two years.

Approximately $1.4 billion will be invested in new Canadian manufacturing facilities by 1992. Seventy-six per cent of this investment will be for domestic facilities, with the remainder slated for investment abroad.

1992 revenues from biotechnology industry products are estimated to be $4.6 billion, with 42 per cent of this dedicated to R&D. The net loss for the entire industry in 1988 was $3 million with half of the companies reporting profits.

Companies surveyed rated research expertise, management expertise and products as the top three determinants of their competitive advantage.

Alliances are a common feature among Canadian biotechnology companies: with universities (22 per cent), government laboratories (14 per cent), other biotechnology companies (13 per cent).

Industry will require 5,000 new employees by 1992. This includes approximately 1,500 bioscientists and 400 engineers.

Companies report bioscientists with multidisciplinary capabilities and industry experience are hardest to find.

Canadian companies view other biotechnology firms, government and educational institutions as the chief competitors for qualified personnel.

More than half the companies surveyed report positive net incomes after tax for the past two years.

Sixty-six per cent of small companies earn most of their revenue from contract research, large company revenues stem from sales.

Canadian biotechnology companies spend an average of 42 per cent of their gross revenue on R&D. (Source: Canadian Laboratory, September, 1990)

China

ANBAPH - What is it?

ANBAPH is the abbreviated form of Asian Network on Biotechnology in Animal Production and Health, with its headquarters (regional coordinating centre) located in Beijing, China. Eight countries participating towards the development of this network are China, India, Indonesia, Malaysia, Pakistan, Philippines, South Korea and Thailand.

ANBAPH is funded by the United Nations Development Programme (UNDP) and operated by Food and Agriculture Organization (FAO) of the United Nations.

ANBAPH has eight national coordinating centres. Addresses of these centres and names of national coordinators are given below:

China - Prof. R. X. Wang, Institute of Animal Science, Chinese Academy of Agricultural Sciences, Malianwa, Haidian, 100094 Beijing, China.

India - Prof. B. B. Mallick, Indian Veterinary Research Institute, Izatnagar 243122 U.P., India.

Indonesia - Dr. P. Sitorus, Central Animal Research Institute, Jalan Raya Pajajaran, Bogor, Indonesia.

Malaysia - Prof. Dr. Abd. Latif Ibrahim, Faculty of Veterinary Medicine & Animal Science, University Pertanian Malaysia, 43400 UPM Serdang, Selangor, Malaysia.

Pakistan - Dr. Muhammad Anwar, Animal Sciences Institute, National Agricultural Research Center, Post Office NTH, Park Road, Islamabad, Pakistan.

Philippines - Dr. Patricio S. Faylon, Livestock Agricultural Research Council, PCCARD, Los Banos, Laguana 4030, Philippines.

South Korea - Sr. Sul. Dong - Sup, Livestock Experiment Station, Rural Development Administration, 564, Omodong, Suweon, Korea.

Thailand - Dr. Vanda Sujarit, Faculty of Veterinary Medicine, Kasetsart University, Bangkok, 10903, Thailand.

ANBAPH has one international coordinator:

Prof. T. K. Mukherjee, Department of Genetics and Cell Biology, University of Malay, Kuala Lumpur, Malaysia.

ANBAPH has the following activities:

(a) Creation of databases pertaining to livestock biotechnology research and development, in the regional coordinating centre (RCC) and national coordinating centres (NCCs).

(b) Development of an information exchange system between the countries within the network.

(c) Organization of overseas training for young scientists for a period of six months in one of the following areas:

(i) Embryo culture and transfer;

(ii) Production of monoclonal antibodies;

(iii) Gene mapping and recombinant DNA techniques;

(iv) Manipulation and control of rumen fermentation;

(v) Cloning of specific genes for vaccine production;

(vi) Cloning of specific genes for production-related hormones;

(vii) In vitro treatment of feeds by manipulated micro-organisms;

(d) Conducting eight one-month regional training courses on different aspects of livestock biotechnology for postgraduate or postdoctoral researchers/technicians.

(e) Organization of within-country, on-the-job training programme of laboratory or field technicians.

(f) Conducting training programmes for extension workers and educated farmers.

(g) Publication of a quarterly Animal Biotechnology Bulletin.

(h) Publication of seven manuals on different aspects of livestock biotechnology.

The RCC and NCCs should be contacted for more information.

ANBAPH headquarters in Beijing can be contacted by: Telex: 222720 CAAS CN, Cable: 3668, and Fax: 8316545. (Source: Animal Biotechnology Bulletin, Vol. 1, No. 1, December 1990)

European Community

SAGB 1/ applauds Commission moves on coordination of biotechnology affairs

The Senior Advisory Group on Biotechnology applauds the European Commission's moves of 27 March, to ensure optimal internal coordination in matters involving biotechnology. The future global competitivity of the chemicals, pharmaceutical, food and agricultural sectors will depend heavily on the smooth application of this modern technology.

In 1990, the SAGB delivered several position papers 2/ to the Commission urging the establishment of a coherent Community Policy for Biotechnology. The Group also provided data on the future economic importance of this technology in establishing long-term European competitiveness.

The constitution of the new high-level Biotechnology Coordination Committee (BCC) under the Chairmanship of the Commission's Secretary General, Mr. David Williamson recognizes the need for a well-balanced Community policy for biotechnology. The SAGB hopes that the imminent Commission Communication to Council on biotechnology will be a first step in providing the coherent policy provisions.

Furthermore, the Commission's anrounced intention to encourage dialogue through the creation of round tables as a welcome move. The SAGB has consistently endorsed the principle of active, constructive and transparent dialogue on matters affecting the application of biotechnology within the European Community.

For further informtion, please contact Mr. Brian Ager, Director SAGB, Avenue Louise 250, 1050 Brussels, Tel.: (32-2) 640-20-95. Copies of SAGB position papers are also available from the above. (Source: News Release, 28 March 1991)

1/ The SAGB (Senior Advisory Group on Biotechnology) was established in 1989 under the European Chemical Industry Council (CEFIC).

2/ Community Policy for Biotechnology: Priorities and Actions; SAGB, January, 1990.

Community Policy for Biotechnology: Economic Benefits and European Competitiveness, SAGB, August 1990.

Community Policy for Biotechnology: Creation of a Community Task Force and an Independent Advisory Body; SAGB, September 1990.

SAGB calls for clarity in Community biotechnology policy

The SAGB has reaffirmed its support for efforts to create a coherent European Community policy for biotechnology and called for greater clarity following the European Commission's Communication to Council (adopted on 17 April).

Biotechnologies promise new opportunity for economic growth, new job creation, industrial renewal, environmental management and revitalized strength in the agricultural market-place. Future European competitiveness on a par with the USA and Japan in the many industries which will depend on biotechnology must therefore become the principle objective of Community policy.

The Commission's Communication is an important first step toward a coherent Community policy.

In particular the SAGB welcomes the Commission's commitment to:

- The assessment of biotechnology products based on scientific criteria and the assurance that it is not the intention to add a further regulatory assessment procedure;
- A coherent regulatory approach;
- The setting up of an advisory structure on ethical issues at community level.

The SAGB emphasizes, however, that much work remains to be done to clarify the Commission's thinking on specific policy issues - notably the future European regulatory framework and economic and social policy responses.

An effective regulatory framework must be adaptable, non-discriminatory and avoid unnecessary duplication and overlap. It is unclear how the Commission's ideas will satisfy these objectives.

Where social and economic policy responses are concerned, the Community faces clear political choices. The Community has proven policies for positive social and economic adjustment to new technologies, and must avoid political controls on technology itself.

The SAGB applauds the Commission's call for open procedures and consultative mechanisms for resolving ethical concerns as they arise.

In summary, the SAGB believes that the Commission's Communication provides a good opportunity for bringing clarity and coherence to Community policy for biotechnology, which will in future create the necessary conditions for social, economic and industrial strength. (Source: News Release, 18 April 1991)

Update on EC BioMedicine and Health Programme

Pending resolution of the problems in the European Parliament, the EC R&D programme on BioMedicine and Health (1990-1994) is expected to call for proposals at the end of 1991. The programme's major aim is "better coordination of the member states' R&D activities and application of the results through Community cooperation and a pooling of resources". The programme will therefore mainly provide funding for concerted actions, i.e. for coordination of research already being funded by member states. The topics covered by the programme are:

1. Harmonization of methodologies and protocols in epidemiological, biological and clinical research

This includes testing of drugs, and screening for risk factors. Development of new coherent diagnostic procedures, such as medical imaging techniques; and development of new biomaterials for use in prostheses, tissue replacements and artificial organs.

2. Applications to diseases of great socio-economic impact

The disease groupings which will be emphasized are cancer, AIDS, cardiovascular disease, mental illness and neurological disorders, mental handicap; ageing and related health problems and disabilities.

The cancer research will focus on development and integration of therapeutic methodologies. Cardiovascular R&D will focus on clinical surveys of various forms of heart and circulatory diseases and their relationships to lifestyle etc.; and the effect of therapeutic measures and development of new regimes for drug testing.

3. Human genome analysis

Research on the completion and integration of the human genetic and physical maps. The study of the genetic basis for biological functions will also be pursued, as well as the setting-up of a consortium to sequence a portion of the genome of major biological interest. (Source: Irish Biotech News, Issue No. 28, April 1991)

New European agency for medicinal veterinary products

The EC Commission (DGIII) have made proposals for the establishment of a new European agency for the evaluation of medicinal products. These include the creation of a new centralized Community procedure, compulsory for biotechnology products and veterinary medicines used as performance enhancers.

This agency will be part of a planned system for the free movement of medicinal products (both for human and veterinary use) within the Community. The European Commission claim that consultations with interested parties have shown wide support for the main features of these proposals, which include:

The establishment of a new European Agency for the evaluation of medicinal products;

The creation of a new centralized Community evaluation and authorization procedure, compulsory for biotechnology products and veterinary medicines used as performance enhancers, and available on an optional basis for other innovatory medicinal products;

A decentralized procedure, based on the principle of mutual recognition, which will allow the progressive extension of marketing authorization from one member State to the others.

The new agency will be made up of the existing Committee for Proprietary Medicinal Products and the Committee for Veterinary Medicinal Products. Its task will be to coordinate the evaluation and supervision of medicinal products being conducted in member States.

The existing decentralized procedure will continue to be the most widely used after 1992. The new agency will only be involved if there is a disagreement between member States about the quality, safety or efficacy of a medicinal product. In this case, the agency will provide an independent scientific evaluation of the issues involved. Monitoring will remain the responsibility of the individual member States. Contacts: DGIII/B.6, R. Hankin (Tel.: 32(2) 2359773) for veterinary-medicine; M. Donnelly (Tel.: 32(2) 2360332) for human pharmaceuticals and P. Brunko (Tel.: 32(2) 2362587) for biotechnology aspects. (Source: Irish Biotech News, April 1991)

Europe gives milk hormone seal of approval

Milk and meat from cows treated with an artificial hormone designed to increase milk yields are safe, the European Commission's panel of experts on veterinary products concluded at the end of March 1991. The hormone, Somatech, is a genetically engineered version of bovine somatotrophin (BST), produced by the American chemicals company Monsanto.

Some members of the Committee for Veterinary Medical Products still have reservations. They are worried that BST might not be good for a cow's health and have asked for further studies on the incidence of mastitis and on any reactions at the site where the drug is injected.

The Committee's decision clears the way for countries in the European Community to authorize use of recombinant BST. A European moratorium on the use of the drug ends on 31 December, but regulatory authorities in several countries have expressed reservations about recombinant BST. (Source: New Scientist, 6 April 1991)

France

French mutants

France has now released more genetically modified organisms into the environment than any country apart from the US. The OECD estimates that there are 300 field trials of genetically altered organisms world wide; 175 of these are in the US and 60 in France.

In its annual report, the French biomolecular engineering committee says the number of applications for field trials doubled last year.

The types of trials are also changing. Applications to plant altered crops such as melons and tomatoes now outnumber applications to plant for purely experimental purposes. (Source: New Scientist, 27 April 1991)

New muscular dystrophy laboratory

A "strike force in genetic research," prominent French molecular biologist Daniel Cohen calls the private research laboratory that has just received backing from the French Association for Muscular Dystrophy (AFM). The new laboratory, named Généthon is growing rapidly. Created jointly with the Center for Study of Human Polymorphisms (CEPH), Généthon occupies new space in Evry, near Paris, and has already put together a team of 70 researchers and technicians equipped with automated machinery to tackle "on an industrial scale" the identification of genes involved in the 40 or so known forms of muscular dystrophy.

Lymphocytes of about 800 members of 60 large families are kept frozen in liquid nitrogen in the new Evry facility, ready to be cultured when researchers require DNA for genetic mapping. Généthon also has at its disposal CEPH's gene bank, which has so far mapped about 2,000 polymorphic markers. CEPH, which has been getting significant support from the US National Institutes of Health and the Howard Hughes Foundation, will now be half financed by the Ministry of Research and Technology as part of France's participation in the Human Genome Project. CEPH and Généthon also receive support from the European Eureka-Labimap, which is developing a series of compatible automatic machines for molecular biology research.

The two organizations, however, will remain independent of the major State-run scientific and medical research apparatus and the attendant red tape. (Extracted with permission from Science, Vol. 251, p. 623. Copyright by AAAS, 1991)

Germany

BASF wins approval for TNF unit at Ludwigshafen

Authorities in Ludwigshafen have granted BASF permission to build a plant to produce a target 500g/year of the cancer drug, tumour necrosis factor (TNF).

According to BASF, this quantity of TNF is sufficient to supply annual demand from industrial countries - 110,000 potential patients - for the treatment of tumour-related ascites. Production is due to start within the next two years.

The authorities have ordered immediate implementation of the permit, a practice increasingly being employed in Germany to assure that construction is not blocked by public opposition.

The permit, issued on 9 January, places several restrictions on the plant, which authorities said were aimed at protecting the environment from the bacteria - Escherichia coli - used in the process, eliminating or safely disposing of production residues and protecting workers.

BASF's drugs subsidiary Knoll has submitted applications for registration of the drug to the German Federal Health Authority, the BGA, which will then pass on data to the European Committee for Proprietary Medicinal Products (CPMP) in Brussels, under the so-called "high-tech" drug registration procedure.

BASF is also continuing trials using TNF in conjunction with alpha-interferon for the treatment of renal cell carcinoma. These have already shown success in a number of patients. (Source: European Chemical News, 21 January 1991)

India

Biotechnology to help improve productivity

Biotechnology can be used to improve the productivity of several essential oils and medicines at both the whole-plant and single cell culture levels, according to Dr. P.S. Ahuja of the Central Institute of Medicinal and Aromatic Plants (CIMAP), Lucknow.

He said this, at the international symposium on "Genetic research and education" in New Delhi.

Essential oils and medicinal compounds form an important sector of the industry, with a potential trade volume of over Rs. 3,500 crore by 2000 A.D.

They are usually referred to as secondary metabolites as they are not essential for the growth and development of plants but help them in developing resistance to pests and diseases and in pollination. The primary metabolites are very useful to man as they form important ingredients of perfumery, flavouring, cosmetic and pharmaceutical industries.

The Himalayas are a vast storehouse of such useful plants, including cinchona which yields quinine, artemisia which yields artemslin, ephedra which gives ephedrin used in nasal drops and for bronchial coughs, poppy the source of the pain killer opium, rauwolfia, the source of rauwolfin used for hypertension and digitalis which gives digitalin used for heart ailments.

They can regenerate entire plants from single cells grown in a special medium provided with optimum light, temperature and nutrition. (Source: Chemical Business, 5-19 March 1991)

Japan

MHW to set guidelines for biotechnology foods

In mid-1991, Japan's Ministry of Health and Welfare will publish safety guidelines for foods manufactured with genetically engineered microbes. They will be based on its two-year study, conducted in expectation of a major influx of biotechnology-based foods during the '90s. The guidelines will spell out restrictions on manufacturing methods and prescribe the use of specific tests for toxic by-products. Initially they will target cheese and other dairy products. Manufacturers will be required to use a prescribed marking system to inform consumers that the products were manufacturerd using biotechnology. (Source: McGraw Hill's Biotechnology Newswatch, 4 March 1991)

US-Japan collaboration to develop oil-eating bacteria

US and Japanese researchers recently announced an unprecedented joint effort to genetically engineer micro-organisms that can mop up oil spills and degrade other man-made chemical pollutants.

The five-year $15-million project, which will be funded equally by the US National Science Foundation (NSF) and the Research and Development Cooperation of Japan (JRDC), is the first major project to come under the umbrella of the 1988 US-Japan Science and Technology Agreement and is indicative of a new cooperative spirit in basic research between the two economic giants.

The microbe project will be led by James Tiedje, director of Michigan State University (MSU) Center for Microbial Ecology, and Kieji Yano, professor of biology at Nagaoka University, a leading authority on the molecular biology of genes involved in biodegradation. The research will be carried out by 20 researchers, half of whom (five Americans and five Japanese) will be based at MSU. The other half will work at Nagaoka University of Technology and the Institute of Physical and Chemical Research (RIKEN) in Japan.

The project is the first US-Japanese collaborative effort under a new programme for joint international research introduced by JRDC, an affiliate of Japan's Science and Technology Agency.

The research is based on the fact that microbes ultimately consume or degrade all natural organic products, from leaves that fall in a stream to garbage in landfills. Genetic engineering and an understanding of microbial evolution can be used to produce microbes that can degrade oil spills and other man-made pollutants such as PCBs. (Source: Nature, Vol. 350, 28 March 1991)

New research institute

Toyota Motor Corp. (Toyota) has budgeted 500 million yen for a new biotechnology research institute, to be headquartered at its technical centre. In addition to the ongoing biotechnology research activities at Toyota Central Research and Development Laboratories, the new "Bio Lab" further strengthens the company's research potential in fundamental biotechnologies.

Research at Bio Lab will be focused on protein engineering and plant biotechnology. Researchers will use protein engineering to develop new biomaterials such as decomposible plastic; in-plant biotechnology, the focus will be on developing plants with greater abilities to fix CO_2. In 1991, research areas will expand to include biomonitoring and information processing. (Source: Bio/Technology, Vol. 9, February 1991)

Tomatoes approved

Japan's Ministry of Agriculture, Forestry and Fisheries (MAFF) has approved Japan's first release of a genetically engineered organism into the open environment.

The Ministry's National Institute of Agro-Environmental Sciences in Tsukuba will begin field experiments with tomato plants that have been genetically engineered to resist tobacco mosaic virus. The tomato plants will be grown alongside unaltered plants in open fields surrounded by only a fence and trees to investigate natural pollination and growth of the plants, and their effects on soil bacteria and flora.

Approval was given only after closed experiments had been carried out in the laboratory and greenhouses for over two years under two sets of regulations for the handling of genetically engineered organisms laid down by MAFF and the Science and Technology Agency. (Source: Nature, Vol. 349, 31 January 1991)

Human genome project stalls

Plans by Japan's scientists to launch a human genome project have foundered in the cash-starved

Ministry of Education, Science and Culture (MESC). MESC will set aside a small amount of money this fiscal year to establish the first division of a new human genome analysis centre at Tokyo University's Institute of Medical Science and grants for genome research will be increased. But the sums of money involved are considerably less than the modest amount scientists were hoping for. Failure to launch a large-scale project is likely to lead to renewed US criticism of Japan's failure to contribute sufficiently to the international effort to map and sequence the human genome.

Money is not the only problem for the new centre. The Institute of Medical Science has no biologists with expertise on computing and heated discussions are now underway to decide whom to appoint as professor of the new division.

MESC scientists originally hoped that the new centre would be established at the National Genetics Institute in Mishima where the small DNA Data Bank of Japan (DDBJ) is located. But some researchers at Mishima opposed the idea because they did not want to get involved in providing DNA analysis services for all of Japan.

MESC is not the only government organization supporting genome research. There are small genome-related research projects supported by the Science and Technology Agency, the Ministry of Health and Welfare and the Ministry of Agriculture, Forestry and Fisheries.

Discussions are now under way between the various ministries and agencies on how to "cut the pie" of genome research, but Japan's only hope for a substantial human genome project now seems to lie with the Ministry of International Trade and Industry (MITI) and private companies. (Source: Nature, Vol. 349, 31 January 1991)

United Kingdom

Research efforts face national scrutiny

The United Kingdom will soon have its first national bioethics committee. The Nuffield Foundation plans to launch a Council on Bioethics in May, to run initially for three years, with funds of about £150,000 a year. The council will be purely advisory. Its task will be to identify and define ethical questions raised by research, and to set up specialist working parties to tackle particular topics.

The council will deal with the whole field of bioethics. This marks a radical change from the traditional British approach of ad hoc committees on particular topics, such as embryo research or gene therapy. The new council will focus on all "ethical issues arising from biological and medical research and its initial applications", says David Shapiro of the Nuffield Foundation, who is in charge of the bioethics initiative. Ethical dilemmas relating to "practice and established techniques" will be left to the British Medical Association and the General Medical Council.

One of the prime motives for the new British venture is concern about the public's reaction to biomedical research. The national body will also enable Britain to play a greater part in European bioethics discussions. The Foundation spent almost two years consulting scientists, lawyers, theologians and philosophers.

The size and composition of the committee are still undecided, but the Nuffield Foundation proposes to appoint a dozen or so people "chosen for their individual expertise, experience and public standing". A majority should be "lay" in the sense of being neither scientists nor clinicians. An eminent lawyer is favoured for the chair.

Nuffield acknowledges that there are "reservations in some quarters" and stresses that the new national body must have enough authority to influence the Government and Parliament. But support for the project seems widespread among biomedical researchers in Britain, beleaguered as they are by antivivisectionists, environmental activists and "right-to-lifers" who oppose embryo research. (Source: New Scientist, 2 March 1991)

Statements on food packages

UK food packaging could soon carry the statement "Contains products of gene technology", according to a new set of guidelines drawn up by the Food Advisory Committee. But the guidelines, which cover all foods produced using genetic engineering, say that such labelling will be required only in limited circumstances.

Under the Ministry of Agriculture's voluntary approval procedures, the FAC will "consider each case on its merits", the guidelines say. As a general principle, labelling will only be required for products which differ from those traditionally consumed in western Europe, or for foods containing trans-species genetically modified organisms.

The guidelines argue that foods containing trans-species GMOs are "the greatest potential source of public concern", because incorporating genes from one species into a host organism of a different species "represents a departure from that which can be achieved by conventional breeding practices."

Thus, no labelling is required on bread made with the genetically modified yeast approved in Britain last year. Apart from some synthetic linker sequences, the new strain of yeast was produced by inserting genetic material obtained only from the normal yeast species. (Source: Chemistry and Industry, 4 February 1991)

Additional funding for bioprocessing expansion

Protein Separations Limited has raised £1.35 million from a group of European venture capital investors. This second round investment will be used by the company to fund a significant expansion programme for its PROSEP™ range of affinity chromatography systems used in the downstream processing of monoclonal antibodies and other genetically engineered proteins.

Until now, the company has focused its resources on satisfying the requirement of a small number of targeted customers but this investment will allow them to expand market awareness to a wider audience and to fund further research and development programmes. (Source: News Release, 21 March 1991)

United States of America

Council recommends streamlining biotechnology regulations

Regulations on biotechnology ought to be streamlined and simplified, according to the White House Council on Competitiveness. Regulators should assess new products made via biotechnology in the same way they assess any other products made by traditional methods. The proposal would affect a wide range of possible geneti engineering products: drugs, crops, pesticides and even animals. In effect, the report says that the fact that a product is created via genetic engineering is irrelevant. Federal funding for biotechnology research should be shifted to increase support for agricultural and environmental uses. Congressional initiatives to force closer regulation on biotechnology activities should be defeated.

The Council also recommends that the Orphan Drug Act be retained, despite criticisms that drug companies are profiting handsomely from the law.

The US patent regulations need to be revised so that foreign firms cannot use patented organisms to make a protein and then import the protein into the US without violating the patent.

Some Congressmen and environmentalists are expected to criticize the new report as being too lenient, but industry officials say the recommendations in the report are sound. (Extracted from New York Times News, 19 February 1991)

WRI report shows major expansion of US efforts to slow down extinction of plants and animals in developing world

US funding for projects to preserve biological diversity in developing countries increased dramatically from 1987 to 1989. For the first time, funding from US charitable foundations nearly matched that provided by the US Government.

According to Investing in Biological Diversity: U.S. Research and Conservation Efforts in Developing Countries, a new World Resources Institute report by associate Janet N. Abramovitz, US public and private institutions invested $62.9 million in 1989, two-thirds more than a previous WRI study two years ago showed. Some 1,100 projects in 127 developing countries were funded in 1989.

Contributions from private foundations jumped 750 per cent over the two year period to a total of $21.4 million. The John D. and Catherine T. MacArthur Foundation provided more than half of all foundation funding in 1989. Other foundations that substantially increased their contributions since 1987 were the Pew Charitable Trusts and the W. Alton Jones, Jessie Smith Noyes, and A.K. Mellon Foundations.

The US Government, primarily through the National Science Foundation and the US Agency for International Development, continued to be the leading source of funds, investing $23.1 million, a 16 per cent increase over 1987.

Thirty-eight per cent of the funding in 1989 went for research programmes on "biodiversity" - and other resources. Species and site management projects received 25 per cent, with most of the funds targeted for regions rather than for individual species. Debt-for nature swaps accounted for about 5 per cent.

Direct assistance to strengthen local organizations in developing countries nearly doubled, largely because of the contributions by US foundations. Funds were also targeted to priority areas identified as biodiversity "hotspots", major tropical forest wilderness areas, and threatened tropical areas requiring special attention.

The largest share of investment was in Central and South America and the Caribbean, reflecting the mounting concern about widespread tropical deforestation as well as the degradation of coral reefs and other fragile marine ecosystems. Together, Lacin American countries received $42.5 million, or 67 per cent of total 1989 funds, compared to $22.9 million or 61 per cent in 1987.

Costa Rica, which has acknowledged competence in conservation programmes and a firm commitment to conservation goals, received $6.2 million, more than any other individual country. Most of the funding went for programmes of the respected Organization for Tropical Studies, two large US AID projects, and two debt-for-nature swaps.

Even with the large increase in overall funding, many threatened and high priority conservation areas, particularly in Asia and Africa, did not fare well. For example, Indonesia, the most biologically diverse country in Asia and the site of serious deforestation, received $1.4 million, 2 per cent of total funds. Asia, as a whole, received only $6.5 million or 10 per cent of the global total.

Africa, despite its vast size and pressing biodiversity problems, received only 17 per cent of the total funds or $10.4 million. The majority of funding for Africa went to Madagascar ($2.8 million), Kenya ($2.1 million), and Uganda ($1 million).

Of the 127 countries receiving US funding, 111 countries received less than one cent per acre. Copies of Investing in Biological Diversity: US Research and Conservation Efforts in Developing Countries can be purchased for $12.50 plus $3.00 for shipping and handling from WRI Publications, P.O. Box 4852, Hampden Station, Baltimore, MD, 21211. Complimentary copies are available for journalists. (Source: News Release, 19 March 1991)

Calgene asks for FDA review

In an effort to head off potential concerns over biotechnology crops, Calgene (Davis, CA) has voluntarily requested the US Food and Drug Administration to issue an opinion on the use of a marker gene in genetically engineered tomato, cotton, and rapeseed plants that are under development by the firm. Calgene says it is the first FDA submission asking for an evaluation of a component of a plant intended as a food. The company hopes FDA's OK of the marker gene will expedite and simplify future regulatory approvals of genetically engineered crops. (Source: Chemical Week, 5 December 1991)

Biotechnology research faculty to be catalogued

Cataloguing all academic faculty in the US working on research in biotechnology is the aim of a new project undertaken by the North Carolina Biotechnology Center, Research Triangle Park. The center's information division, which has collected information on commercial biotechnology world wide for the past five years, will work with project partner Synergistic Technologies Inc. to contact full-time faculty at research institutions early in 1991. Those engaged in biotechnology research will be asked to fill in a questionnaire about their research activities and interests. The center is using a broad definition of biotechnology to include all research involving new techniques related to cell biology, molecular biology, and genetics. The end product will be a data base called the Biotechnology Research Faculty Profile. Plans call for a directory of faculty to be published later in the year. (Reprinted with permission from Chemical Engineering News, 21 January 1991, p. 17. Copyright (1991) American Chemical Society)

USSR

Biotechnology windfall from the Soviets

Soviet biotechnologists have licenced three potential treatments for AIDS to Oxford Virology, a small London-based biotechnology research company, for development in the West. The British company believes it has chanced upon a windfall of worthwhile bio-innovations, from novel insecticides to heart drugs.

According to Derek Lennon, managing director of Oxford Virology, the Soviet AIDS compounds show similar efficacy to zidovudine (AZT), the Wellcome drug, on the basis of laboratory testing, but they are all non-toxic. The compounds are chemically modified forms of a plant extract. One the Soviets call niglizini has just begun clinical trials in the Soviet Union.

Oxford Virology is planning tests with Britain's Medical Research Council, which manages the national AIDS research programme, to confirm the Soviet laboratory data. It hopes to find a pharmaceutical company to undertake clinical trials.

Oxford Virology has contracts that cover patenting of Soviet biotechnologies, marketing of biotechnology products and processes, and introductions of Soviet organizations to joint ventures with western companies.

Under these contracts, signed in the "science city" of Novosibirsk in January, Oxford Virology has 50 per cent of the rights to innovations from the Institute of Molecular Biology, where the AIDS compounds were discovered. Soviet biotechnologists would like Oxford Virology to undertake a more ambitious programme of technology transfer on their behalf. One proposal is that the company should have rights to the discoveries of the entire chain of 36 Biopreparat companies engaged in pharmaceuticals, biological preparations and animal feedstuffs. The big attraction of viral insecticides is that they are not toxic to animals.

Soviet scientists have cultivated seven viral insecticides on a substantial scale. Among them are agents for controlling gypsy moth, cabbage moth and cotton worm moth, all used in the Soviet Union.

The Soviet connection is Naucho-proizvodstvennoe Objedinenie Vector (NPO Vector), an organization devoted to biotechnology and bioengineering. NPO Vector, set up in 1985, has its own laboratories, pilot plant and experimental farms. Its director, L.S. Sandakhchiev, a member of the Soviet Academy of Sciences, signed the contracts on behalf of the Soviet Union.

NPO Vector employs about 4,500 staff, including more than 600 scientists. The innovations it claims range from a powerful but non-toxic thrombolytic ("clot-busting") drug, to computer software for molecular modelling.

It is one of many NPO's set up when the Soviet Government freed Soviet innovators from the bureaucracy of the big Moscow trading houses that preceded perestroika, and allowed them to negotiate entrepreneurial contracts. (Source: Financial Times, 3 January 1991)

C. RESEARCH

Research on human genes

Location of Type II diabetes gene found

The Type II diabetes gene may be located near a specific gene on chromosome 20's long arm, according to Dr. Graeme Bell, professor of medicine at the University of Chicago and other researchers from the University of Pennsylvania and the University of Michigan. The gene itself has not been isolated, but the general location has been determined. Type II diabetes, non-insulin-dependent, usually affects people after the age of 40. Some 12 million people in the US alone are affected with this form that is usually controlled by exercise and diet or oral medication, according to the American Diabetes Association. (Extracted from The New York Times News. 15 February 1991)

New method to synthesize heart muscle protein

An efficient method of synthesizing human heart muscle protein by manipulation of E. coli has been developed by researchers at the Institute of Applied Microbiology (Japan), the University of Tokyo, and Yamasa Shoyu. The technique yields 17-mg of myocardial protein/g of proteins produced. It involves siting a virus-controlling gene next in sequence to the targeted protein via gene recombination. Invasion by the virus T4phage activates the control gene and suppresses the normal protein decomposition enzyme. Under proper conditions, E. coli will produce the protein for 6-7 hours without lysis. The method is seen as permitting synthesis of previously unavailable protcins. (Extracted from New Technology Japan, January 1991)

Single defect links heart disease and diabetes

The University of Texas Health Science Center at San Antonio (UTHSCSA) has uncovered new evidence linking a genetic defect to the development of hypertension, atherosclerosis, obesity, high cholesterol, and non-insulin-dependent diabetes. The defect - insulin resistance syndrome - occurs when body tissues become resistant to the effect of insulin, and glucose is not properly converted into energy or into its stored form of glycogen. After a period of time, the high insulin levels that result

can raise blood pressure and cholesterol levels, and cause hardening of the arteries. Research is now being conducted at UTHSCSA to compare drugs that resensitize the body tissues to insulin. Researchers theorize that a cure for insulin resistance syndrome could decrease about 80 per cent of a typical physician's caseload. (Source: BioBytes, San Antonio Biotechnology News and Information, Dublin-McCarter & Associates Inc., March 1991)

Gene therapy trial on melanoma patients

Genes intended to generate cancer-fighting agents have been implanted in two patients in what is described as an historic cancer trial. Begun at the end of January 1991, the trial comes in the wake of several years of experiments and months-long scrutiny by regulators. The trial is being undertaken by the National Institutes of Health and is the first effort by US researchers to fight cancer with gene therapy. Heading the experiment is Dr. Steven A. Rosenberg, chief of surgery at the institute. The therapy's goal is to eradicate cancer by strengthening a patient's own cells that fight tumours with a powerful toxin that occurs naturally. The patients are a 29-year-old woman and a 42-year-old man who have malignant melanoma, a fast-growing and lethal skin tumour. Other therapies were unsuccessful in thwarting the maligancies' growth. (Extracted from Wall Street Journal, 30 January 1991)

Cancer culprit

Scientists have found a gene whose mutant form may trigger cancer of the colon. The gene, which is known as MCC, is on chromosome 5 in a region of DNA that researchers have long suspected is linked with the disease.

Bert Vogelstein and his colleagues at Johns Hopkins University, Baltimore, and others in Britain and Japan, believe that MCC may be a "tumour suppressor" gene. In their healthy form, such genes prevent cells from growing out of control; when they are mutated, cells may turn cancerous.

Vogelstein and his colleagues have previously identified two other tumour suppressor genes, p53 and DCC, which seem to play a role later in the cells' progress towards cancer.

The researchers found that tumour cells from patients with colon cancer contained altered sequences of DNA in the MCC region. "The MCC gene is therefore a candidate for the suppressor gene", they say.

Although the team says there is more work to be done, they hope that the finding could lead to a test to detect cancer of the colon at an early stage. (Source: New Scientist, 23 March 1991)

Gene deletions linked to cancer metastasis

Japan's National Cancer Center Research Institute has found a correlation between deletion of cancer-inhibitor genes and cancer metastases. Researchers found that two colon-cancer inhibitor genes were deleted in 67 per cent of 15 colon cancer patients, and in 100 per cent of the patient population that exhibited metastases to the liver. They also found that three lung cancer inhibitor genes were deleted in about 60 per cent of such patients, and were absent in 90 per cent of the victims with metastasis to the brain. (Source: McGraw Hill's Biotechnology Newswatch, 4 March 1991)

Seragen IL-2 fusion protein acts like Trojan horse to ferry toxins into tumours

Instead of using interleukin-2 (IL-2) as a cancer therapeutic itself, Seragen Inc. has hitched IL-2 to a toxin, and then used it like a Trojan horse to trick tumour cells into admitting deadly fusion proteins into their interior. In Phase I trials against B- and T-cell lymphomas, Hodgkin's disease and several leukemias, IL-2-linked diptheria toxin "had a significant antitumour effect in 12 of 24 patients, with two in complete remission," according to Seragen vice-president of development, Jean C. Nichols. Phase IIa dose-level trials are now under way at three US centres in 15 patients with a wide range of cancers; efficacy studies are expected to begin in the summer of 1991.

To make the fusion toxin researchers take the diptheria-toxin gene - including the membrane-translocating region - and replace just the diphtheria binding-domain DNA with the IL-2 gene. After insertion in E. coli, what results is a 68kd diphtheria toxin with an IL-2 molecule sticking out of one end. When the IL-2 of the hybrid protein binds to the high-affinity IL-2 receptors of tumour cells, the next segment of the diptheria molecule sends a signal to admit the toxin, which in theory kills the cell. Seragen claims that these small molecules - half the size of monoclonal antibodies - are more effective than immunotoxins, which are not readily admitted inside cells. The company also has a Phase I study of this molecule to test its ability to destory the activated lymphocytes found in arthritis and juvenile diabetes patients. The company is also linking other immune modulators to diptheria toxin, in the theory that other malignant cells display receptors. It has animal trials under way with fusion proteins containing epidermal growth factor and melanocyte stimulating hormone. Others in the works include human G-CSF, IL-2 and mouse IL-4. (Source: McGraw Hill's Biotechnology Newswatch, 17 December 1990)

Human cells make antibodies

Human cells that make antibodies have been cultured by researchers at Schering-Plough laboratories in Lyon, France. The feat could allow scientists to study how the cells are controlled and might allow industrial production of antibodies. The technique merges B-lymphocytes with cancer cells to "immortalize" them. Previous efforts at making human antibodies have infected B-cells with Epstein-Barr virus to stimulate reproduction of the cells, but this technique is inefficient and generally works only with B-cells that make antibodies of little therapeutic interest. The new technique uses a fibroblast cell with several CD40 antibodies on the surface to simultaneously stimulate several CD40 molecules on the B-cell surface. The research might also aid studies of some types of autoimmune disease, in which the body loses control of antibody production. (Extracted from New Scientist, 19 January 1991)

Hepatitis B gene implicated in liver cancer

The University of Tokyo's Faculty of Medicine and the Japanese National Institute of Health (NIH) have found a gene from the hepatitis B virus (HBV)

that induces liver cancer in mice. Researchers have suspected for some time that an HBV gene segment, named X, induces carcinogenesis, but evidence of its oncogenicity has not been found until now. The team cleaved the X segment from the gene, then cloned it in fertilized mouse ova. The ova developed into adult mice, which were crossbred with normal mice to produce an X-segment-bearing line. Liver cancers developed in 80 per cent of 84 of these mice within 21 months of birth. Cells of the liver cancer tissue contained roughly 5 to 10 times more X-segment protein than cells of normal tissue. (Source: McGraw Hill's Biotechnology Newswatch, 17 December 1990)

Mitsubishi clones cholesterol-reducing protein

Mitsubishi Kasei Corp., Tokyo, and the National Cardiovascular Disease Center, have produced a recombinant version of apolipoprotein E, which reduces intracellular levels of cholesterol. The genetically engineered form of the protein is bound to a phospholipid to improve adhesiveness. When 5 micrograms of apolipoprotein E-phospholipid complex was added to cultured mouse cells they expelled excess cholesterol and restored the concentrations to normal levels. Mitsubishi plans to run animal trials to test the compound's potential as a therapeutic for arteriosclerosis and hyperlipidaemia. (Source: McGraw Hill's Biotechnology Newswatch, 4 March 1991)

Battling hepatitis with man-made cells

Southwest Foundation for Biomedical Research (SFBR) in San Antonio has developed a serum-free medium that can culture hepatocytes (liver cells) for much longer than has been possible in the past. The ability to grow liver cells in culture is expected to help in the effort to develop a vaccine for the blood-borne hepatitis C virus, which is a major cause of acute and chronic hepatitis, cirrhosis of the liver, and liver cancer. The SFBR laboratory is the only one in the nation where any type of viral hepatitis can be studied in tissue culture. Researchers will be able to screen a wide variety of drugs against a virus in a test-tube setup by studying viral replication in hepatocytes in the serum-free medium. (Source: BioBytes, San Antonio Biotechnology News & Information, produced by Dublin-McCarter & Associates, March 1991)

University of Tokyo isolates asthma-protein gene

Takao Shimizu of the Faculty of Medicine at the University of Tokyo (Japan) has isolated a gene that encodes a protein implicated in the bronchial spasm of asthma. Platelet activating factor (PAF) is an asthma-inducing substance that acts after binding to a protein on the plasma membrane of cells in the lungs and bronchi. Shimizu's team isolated the gene that encodes from guinea pigs. The resultant protein has 342 amino acids. Shimizu has expressed the gene in cultured monkey cells. (Source: McGraw Hill's Biotechnology Newswatch, 4 February 1991)

Mitochondria implicated in several disorders

Researchers have linked human mitochondria DNA defects to several human disorders, and they may be implicated in Parkinson's disease. Mitochondria are cell components that process oxygen and nutrients into energy, using enzymes in a complicated multistage process. They contain DNA received only from the mother, that resembles bacterial DNA in form and exists in small units compared to DNA from the cell's nucleus. When the mitochondrial DNA reproduces itself, defects can occur which may, but do not always, result in degenerative vision problems or muscle disorders. (Extracted from Discover, February 1991)

Researchers clone natural killer cell gene

Massimo Trucco and colleagues at the Pittsburgh Cancer Institute (Pittsburgh, PA) have cloned a gene that characterizes natural killer (NK) cells. The gene describes a cellular protein that may solve the mystery of how these cells work. To isolate the gene, the scientists generated cDNA from mRNA isolated from the NK cells. All the pieces constituting the cDNA library were inserted into expression vectors and placed into fibroblasts, which expressed the NK cell protein encoded by each piece of cDNA.

The researchers generated antibodies specific to the antigen by injecting mice with NK cells from rats. The antibodies were then isolated from the mice, labelled with a fluorescent marker for tracking, and mixed with the fibroblasts in test-tubes. Only the fibroblasts containing DNA that produces the surface protein of the NK cells is recognized by the NK cell-specific antibody. The researchers extracted the fragment of cDNA from this fibroblast and sequenced it. (Source: Genetic Engineering News, February 1991)

Muscular dystrophy gene cloned

In a development that could represent an early step toward gene therapy, researchers have cloned the coding portion of the mouse gene responsible for Duchenne muscular dystrophy. The researchers - Cheng Chi Lee, C. Thomas Caskey, and colleagues at the Institute for Molecular Genetics and Howard Hughes Medical Institute at Baylor College of Medicine, Houston - inserted the cloned gene into cell culture, where it produced dystrophin, a protein essential to normal muscle function. Duchenne muscular dystrophy is an incurable, inherited disease that causes voluntary muscles to weaken progressively and waste away. Most patients are crippled before they reach their teens and die in their early 20s. The dystrophin gene was first identified in 1986 by Louis Kunkel and colleagues at Children's Hospital in Boston. Mutation of the gene can shut off dystrophin production, leading to Duchenne muscular dystrophy. The cloning and expression of the gene, says Caskey, "opens opportunities for the study of structure and function of dystrophin and provides an opportunity to initiate gene therapy studies". (Reprinted with permission from Chemical and Engineering News, 28 January 1991, p. 18. Copyright (1991) American Chemical Society)

Phospholipid receptor gene cloned

The cloning of the gene encoding the cell-surface receptor for platelet-activating factor (PAF) - has been accomplished by Zen-ichiro Honda of the University of Tokyo and colleagues. PAF is a phospholipid that plays an important role in the development of bronchial asthma, toxic shock syndrome and anaphylactic shock. The work represents the first cloning of a receptor for a lipid mediator, a class of chemical messengers that includes prostaglandins and leukotrienes in addition

to PAF. Lipid mediators are believed to play an important role in inflammatory diseases. Honda found that the PAF receptor is a G protein-coupled receptor, a type of cell-surface receptor that transmits signals to the cell interior by a complex process that begins with the binding of guanosine triphosphate. The findings "provide a clue to the complicated signal-transduction system following PAF receptor activation and may help in the rational design of therapeutic antagonists for bronchial asthma and [toxic] shock". (Reprinted with permission from Chemical and Engineering News, 28 January 1991, p. 18. Copyright (1991), American Chemical Society)

The genes that protect against malaria

Scientists in the UK and The Gambia have discovered two genes that seem to protect people against severe malaria. Both are members of the complex family of HLA genes on chromosome 6, which are involved in the body's immune response to infection.

The findings are exciting because they offer clues to the body's defence mechanism against the Plasmodium parasites that cause the disease. Also, they provide part of the answer to a riddle that has long puzzled geneticists: why have we evolved with so many different forms of HLA genes?

The HLA, or human leucocyte antigen, genes are the most variable in the genome - that is, there are more alleles, or alternative forms, of them than any other group. Each one codes for an antigen on the surface of cells, and no two people's antigens are the same.

The HLA antigens enable cells of the immune system to "recognize" foreign proteins invading the body. T cells will recognize such proteins only when they are bound to HLA antigens. Class I HLA genes govern the "killer" T cells, and Class II genes govern the "helper" T cells, making them organize other cells of the immune system to produce specific antibodies.

In theory, scientists argue, different HLA genes must protect people against different infectious diseases, so natural selection has resulted in the large variety of genes. However, strong evidence for this theory has been hard to find.

But now the picture has changed. Adrian Hill, from the Institute of Molecular Medicine in Oxford, led the team from Oxford, London and the laboratories of the Medical Research Council near Banjul in The Gambia, who analysed the HLA "signatures" of 1,800 children in The Gambia, where a quarter of all child deaths are from malaria. They classified the children into four groups: those with severe malaria that had affected the brain; those with severe malaria causing anaemia; those with mild malaria - that is, symptoms but no physiological damage; the healthy children who acted as controls. The control children were matched with the cases for age and district.

The team took blood samples from each individual and studied the sequences of DNA encoding their HLA genes, using gene probes and the polymerase chain reaction. In the Class II genes, they found that a particular unit of several linked alleles, which is usually inherited together, was much rarer in the group with severe malarial anaemia than in the healthy controls. This unit of alleles, known as a haplotype, was also rarer, but less markedly so, in the group with cerebral malaria.

For the Class I genes, children with severe malaria - both cerebral and anaemic - were much less likely than controls to have a particular allele of the HLA-B series which is much commoner in Africans than in other populations.

The researchers calculate that the alleles offer between 40 and 50 per cent protection against severe malaria: that is, if someone who does not carry them has a 100 per cent chance of suffering severe malaria, a carrier's risk is only about half of that risk. Given that 7 per cent of all Gambian children die of malaria, geneticists can then work out how much the alleles increase an individual's chance of surviving to have children.

Like the gene for sickle cell, whose protective effect against malaria is well known, the protective HLA genes are commonest in parts of Africa where malaria is endemic. They are very rare in Europeans and others. About 4 in 10 Nigerians and 1 in 4 Gambians carry the genes.

The research should help to identify the important part of the immune response to malaria. (Source: New Scientist, 23 February 1991)

Team finds malaria parasite's Achilles' heel

The gene that makes the malaria parasite resistant to the principal malaria drug, chloroquine, has been mapped to a single region of DNA on the parasite's seventh chromosome. The discovery, soon to be published by an American team, dramatically improves chances of outwitting the parasite.

Chloroquine-resistant strains of the main malaria parasite, Plasmodium falciparum, are spreading rapidly in many parts of the world, including the Amazon basin, Thailand and areas of Africa. The drug, once considered the best available because it is relatively non-toxic, is increasingly failing to protect people against the disease, which kills up to 2 million people a year.

Resistant strains of P. falciparum, which can pump chloroquine out of themselves, have spread since the late 1950s. Some researchers thought that the genes governing the resistance mechanism must be multiple and spread around the parasite's genome. Now, that theory appears wrong. Experiments show that the gene governing resistance lies within a specific region of DNA, about 400,000 base-paris long, on chromosome 7.

The elegant way in which the team from the National Institute of Allergy and Infectious Diseases in Bethesda, Maryland made their discovery is as interesting as the finding itself. In the tradition of Mendel, they crossed chloroquine-resistant parasites with chloroquine-sensitive ones and observed the offspring. However, unlike Mendel, they were able to analyse the DNA of the offspring.

The team made the genetic cross by mixing the parasites in the laboratory during the sexual phase of their life cycle, then feeding them into mosquitoes to breed as normal. In order to produce large quantities of of offspring, the researchers

used the mosquitoes to infect a chimpanzee with the parasites. They then recovered individual offspring by cloning infected red blood cells from the chimp. In all, they recovered 16 unique offspring, each with a different "mixing" of their parents' genetic material.

Next, they determined which offspring were resistant and which sensitive to the drug. Eight turned out be resistant and eight sensitive. None was intermediate, suggesting that a single genetic locus was responsible for resistance. The team then analysed the inheritance of the parasite's 14 chromosomes using 85 genetic markers.

They found that one particular pattern of inheritance on chromosome 7 was always linked to chloroquine resistance. With the aid of three adjacent markers, they were then able to narrow down the locus to within a segment of DNA 400,000 base-pairs long. The probability that this pattern of inheritance and resistance to chloroquine would be perfectly linked by chance is less than 1 in 1000. The research will appear shortly in the Proceedings of the National Academy of Sciences.

The next step is to find the gene within this region.

There is already a drug that partially stops P. falciparum from pumping chloroquine out of itself. But that drug, verapamil, is too toxic to give in a dose sufficiently large to do any good. The new discovery may enable scientists to discover how verapamil works; this could enable them to design a non-toxic analogue of it. If that were possible, then doctors could prescribe chloroquine with the verapamil analogue. (Source: New Scientist, 6 April 1991)

Altered gene that can lead to Alzheimer's disease

Researchers at St. Mary's Hospital in London have discovered a genetic mutation that can lead to a form of Alzheimer's disease. Alzheimer's is the major cause of mental deterioration or dementia. The finding marks an important step in understanding the molecular basis of a form of the disease that runs in families, known as FAD.

The mutation occurs in a gene that codes for what is termed the amyloid precursor protein, or APP. APP is a long protein chain, which is eventually cleaved by nerve cells into a number of smaller fragments. The new results strengthen the suspicion that abnormal cleavage of APP, resulting in the release of hazardous amounts of APP fragments, may be the root cause of some forms of Alzheimer's disease.

Scientists first studied APP because one of its fragments, known as A4, is often seen deposited in "plaques" outside the nerve cells in the brains of Alzheimer's patients. Plaques are a characteristic feature of the disease. The question that has plagued researchers is whether this deposition of A4 is a cause or an effect of Alzheimer's disease. Until now, direct evidence has been lacking.

To tackle this question, geneticists have been studying hereditary cases of Alzheimer's disease. Between 1 and 5 per cent of cases of Alzheimer's disease run in families. These are notable because the disease strikes at an earlier age than usual - sometimes as early as 35. The majority of Alzheimer cases have an unknown origin, although scientists think that genetic and environmental factors may be involved. Much attention has been focused on the role of aluminium in the disease, for example. In Alzheimer's sufferers, this may not be kept out of the brain efficiently.

Last year, a new piece in the puzzle fell into place. People with a rare genetic disorder common in the Netherlands, called hereditary cerebral haemorrhage with amyloidosis, have similar brain deposits to those found in Alzheimer's sufferers, but without dementia. Belgian researchers mapped the defective gene to the same chromosome as FAD, and shortly afterwards Efrat Levy and colleagues at the New York University Medical Center discovered a subtle defect in the APP gene, very close to the site where A4 is released from APP.

Encouraged by the news, John Hardy, who is leader of the St. Mary's group, and his team decided to sequence the APP gene from FAD patients. They chose one FAD family that they suspected had a defect in the APP gene. In an affected member of the family, there was indeed a mutation in the APP gene close to the change seen in the similar Dutch families - only 30 amino acid residues away.

The FAD mutation creates a new site for a restriction enzyme called BclI which cuts DNA at a particular sequence.

The APP gene is very large and complex, so it is too early to know if all of the early-onset cases of FAD are due to mutations within it. Hardy's group is currently sequencing larger stretches of the gene from patients in order to identify other possible mutations.

What still remains unclear is how a single change in the APP leads to the release and deposition of A4.

The discovery also suggests why patients with Down's syndrome, who have an extra copy of chromosome 21 containing the APP gene, usually suffer from dementia as they grow older. The extra copy of the APP gene probably results in increased amounts of the A4 fragment being released.

Understanding one cause of FAD still leaves unanswered the question of what provokes the thousands of sporadic cases diagnosed each year. But the latest findings suggest that the amyloid protein is a good place to look. (Source: New Scientist, 23 February 1991)

Water-borne parasite succumbs to allergy antibody

The body's reaction to a tropical parasite has thrown new light on allergic reactions such as hay fever. Researchers in The Gambia have confirmed that the "allergy antibody" immunoglobulin E (IgE) plays a major role in combating water-borne parasites known as schistosomes, which cause schistosomiasis, also known as bilharzia. Unexpectedly, they have found that a second antibody, IgG4, appears to hamper IgE.

Paul Hagan of the National Institute for Medical Research in London and a British research team monitored how Schistosoma haematobium reinfected Gambian villagers who had been cleared of

infection by drugs. The risk of reinfection is high whenever people bathe or paddle in rivers polluted by sewage.

Hagan and his colleagues looked at how the antibody IgE affected the flukes. All antibodies are specific to a particular target molecule, or antigen. The researchers compared individuals with large and small amounts of IgE in the blood. They found that people with little IgE were 10 times as likely to become reinfected. Children were at the greatest risk. In children between 2 and 4 years old, the level of IgE was very low. It rose rapidly, reaching a peak in 15-year-olds, an age group that was reinfected the least.

The results confirm the importance of IgE in fighting parasites. They also tie in with laboratory studies that have shown that IgE can combat schistosomes in various ways. IgE binds to two different groups of blood cells, the platelets and the eosinophils, rousing them to kill the flukes.

In addition, IgE is the detonator for mast cells and basophils, the "ultimate weapons" of the immune system, which can release a devastating barrage of defensive chemicals. Mast cells and basophils unleash their weaponry when the IgE carried on the cell surface binds to its antigen. This antigen can be a molecule on a parasite; in allergies it may be a molecule on a pollen grain.

Having confirmed the role of IgE in attacking schistosomes, Hagan and his colleagues turned their attention to IgG4. They found the opposite effect: people with a high level of IgG4 are 10 times as likely to suffer reinfection with schistosomes, regardless of the level of IgE in their body. The researchers also made the intriguing discovery that IgG4 was high on average in childhood but low in teenagers.

The role of this enigmatic antibody has long puzzled immunologists. It is known to bind to mast cells and basophils without detonating them. By doing this, it may keep IgE molecules away, and this might inactivate the cells. Because of this behaviour, a few immunologists have suggested that IgG5 may protect against allergy.

Allergies are rare in the rural tropics, for reasons that are not yet understood. But these results suggest that IgE is an excessively powerful weapon which the body must keep in check at least during childhood. Despite strong selective pressure from parasitic infections, the immune defence of Gambians has not evolved to provide children with maximum protection from flukes.

Instead, there is a control system which keeps IgE at low levels in the under-15s, and further damps its fire with high levels of IgG4. No one knows exactly how it does this or why. Finding out could help to combat both schistosomiasis and the condition of hay fever. (Source: New Scientist, 2 February 1991)

Ancient DNA gives up its secrets

Two American biologists have pinpointed a gene sequence from DNA in human brain tissue about 8,000 years old. The remains came from an ancient burial ground in Florida. Identifying the gene sequence is the first step in establishing what links there may be between modern American Indians and past inhabitants.

Peter Parham of Stanford University and Bill Hauswirth of Florida University College of Medicine used the polymerase chain reaction (PCR) to amplify the gene sequence in a minute sample of tissue. The sample came from one of 165 humans preserved in wet peat at Windover, Florida. He believes that by analysing a number of these samples, it will be possible to tell if any of them are from the same family, and how they relate to modern people.

Hauswirth and his colleagues extracted the DNA from a small sample of preserved brain tissue, then used PCR to amplify segments of it. Parham and his team analysed the gene sequences, and found that most of the segments belonged to a family of genes called HLA (human leucocyte antigen).

Parham was interested in this gene because he knew its probable sequence from his studies on modern HLA. The HLA family includes about 20 related genes, three of which code for the proteins that mark cells in the body so that the immune system does not mistake them for a foreign antigen.

Parham says that PCR analysis opens up the possibility of identifying specific gene sequences in the tiny amounts of DNA preserved in body tissue in museums all over the world. With PCR, researchers need only a small amount - perhaps 1 gram - of tissue, depending on how well it is preserved. Also, the DNA does not need to be intact for the PCR to work. This is important because DNA from ancient remains is often severely damaged.

So far, most researchers have concentrated on the DNA found in mitochondria, which is much more abundant than the DNA in cell nuclei. However, it provides less genetic information than nuclear DNA.

Parham acknowledges that a single molecule of modern DNA from the end of someone's finger could ruin their results, because it, too, would be amplified. His team took extraordinary care to avoid this.

The pattern of gene combinations he found indicates that the genes came from ancient DNA: because ancient DNA is damaged, it is only possible to amplify a continuous sequence of about 125 base pairs, whereas PCR allows amplification of much larger segments from modern DNA. Parham thinks that in time the problems of contamination will be overcome. (Source: New Scientist, 9 March 1991)

"Interpreter enzymes"

The molecular units of genetic information contained within DNA are arranged in an extremely complex code. On their own, these individual cyphers do not make life possible. Life is only created when they are decoded - one by one - and translated into amino acids, the building blocks of which protein molecules are made. This translation process is carried out by special enzymes known as "interpreter enzymes". For a long time it was a mystery how they were able to transfer the genetic code so precisely. Now a Göttingen-based team led by Professor Friedrich Cramer has discovered how these special enzymes function. The researchers found out that the enzymes not only simply translate the molecular code, but also check each "word" twice and correct errors in the process. They even appear to continue functioning perfectly during the biological aging process. The causes of aging, an

area on which biochemists are currently carrying out intensive study, thus have to be sought elsewhere. For Friedrich Cramer interpreter enzymes represent an impressive example of the "complexity of life". (Source: Scala, December 1990)

Hopes grow for "perfect" contraceptive

The ideal contraceptive - one that never fails, lasts as long as a woman wants and has no side effects - could be ready for testing among women within a decade. A vaccine against pregnancy, based on proteins from the human egg or sperm, could eventually consign the contraceptive pill to the scrap heap.

Trials of a potential birth control vaccine are already under way in Australia and India. This vaccine stimulates the production of antibodies against human chorionic gonadotrophin - a hormone produced during pregnancy. Blocking its action causes a failure of the embryo. "This could be considered a form of early abortion" says John Herr, a biologist at the University of Virginia.

Herr is in the early stages of testing a vaccine based on a molecule called SP-10, found in the head of all sperm at a crucial stage in the maturation process. A woman immunised with SP-10 should produce antibodies to the protein. The antibodies would then bind with sperm and prevent it from penetrating the egg membrane. The effect should last several years, or as long as there are enough antibodies circulating in the woman's body.

Herr and his colleagues in Virginia have isolated the protein in pigs and primates, and have identified the gene for the protein. With this information, the researchers can refine their vaccine by selecting the part of the protein molecule that will work best. Large-scale trials on baboons this year will show if the vaccine makes the animals infertile and whether the effect wears off.

Paul Primakoff and Diana Myles of the University of Connecticut Health Center are also working on a vaccine based on sperm. They have three candidate proteins, taken from the surface of the sperm. One of these, called PH20, produces 100 per cent infertility in both sexes of guinea pigs. The protein normally plays a part in the binding of the sperm to the zona pellucida. Unfortunately, injection of PH20 causes inflammation of the testes.

At the Laboratory of Cellular and Developmental Biology at the National Institutes of Health in Bethesda, Maryland, researchers are investigating vaccines based on proteins from the egg. Jurrien Dean at the NIH is concentrating on proteins from the zona pellucida, the transparent "envelope" that surrounds the oocyte. Any of the three glycoproteins the zona is made of might make a good vaccine.

Like the sperm proteins, these zona proteins are highly specific, in this case occuring only in the zona pellucida. The genes which code for them are present only in growing oocytes. An immune response to these proteins should not have unwanted side effects in other parts of the body.

All three proteins play some part in fertilization. Antibodies raised to zona proteins bind to the zona and effectively keep out sperm. Unfortunately, while tests have shown that animals do make the antibodies, they sometimes suffer from an inflamation of the ovaries. The challenge is to separate the two responses: to find the part of the protein that triggers infertility without causing the disease.

Tests of a vaccine based on the protein ZP3 have been very successful in mice. Three-quarters of the mice immunised with the ZP3 protein became infertile for many months, after which the mice were able to conceive and give birth. But the problem of inflammation of the ovaries remains.

Ken Tung, at the University of Washington, analysed fragments of ZP3 and found that a tiny piece, made of eight amino acids, caused the inflammation. The challenge now is to design a vaccine that uses the part of the molecule causing infertility while excluding the part causing disease. (Source: New Scientist, 2 March 1991)

Humans will benefit from a little less mouse

Scotgen, a company based in Aberdeen, claims to have broken new ground in third-generation antibody technology. Researchers there have built a "humanised antibody" and used it to treat a mouse suffering from respiratory syncytial virus (RSV). The techniques they used to make the antibody were pioneered by Greg Winter at the MRC Laboratory of Molecular Biology in Cambridge.

Frank Carr, director of research at Scotgen, explained that their "humanised" or "reshaped" antibody is almost entirely human. The only parts of it to come from a mouse are the complementarity determining regions (CDRs) of what was once a complete mouse antibody.

The researchers harvest the complete antibodies from mice previously inoculated with RSV, selecting those that bind most tightly to the virus.

Humanised antibodies retain all the properties of ordinary human antibodies but have the added bonus of being able to recognize a new invader. To make them, researchers begin with the variable regions of a complete mouse antibody. First, they identify, copy and sequence the DNA in these regions. They then "fish out" the particular DNA sequences that code for CDRs (CDRs are the precise sites of an antibody that bind to binding regions called epitopes on an antigen). Then they synthesise these regions of DNA in the laboratory.

Next, they take the genes that code for human variable regions and graft the synthetic mouse DNA on to these genes. The grafting process is called site-directed mutagenesis, and leaves the researchers with a human variable region "interdigitated" with the CDRs of a mouse.

The last step in rebuilding the antibody is to splice these reshaped variable regions on to human constant regions. The result is an antibody in the shape of the familiar "Y" that is almost entirely human.

Such third-generation antibodies represent a considerable advance on second generation "chimaeric" antibodies. Researchers made these by copying entire variable regions of the mouse antibody, then joining these to human constant regions. For therapy, such antibodies still contained too much mouse. (Source: New Scientist, 9 February 1991)

Research on plant genes

Transgenic crops get a test in the wild

A novel British research programme called PROSAMO - Planned Release of Selected and Modified Organisms - has just produced its first batch of results on the ecological behaviour of a genetically manipulated variety of rape. As expected, the preliminary data indicate that these plants do not outgrow their competitors in the wild, nor is there any evidence that they pass on their foreign genes to other species. PROSAMO is moving on to test other crops with other foreign genes. If these results are as reassuring, scientists around the world will have solid evidence with which to soothe fears.

PROSAMO started life about three years ago in Britain's Department of Trade and Industry (DTI), which is responsible for encouraging biotechnology. It is designed to provide scientific data on the fate of both engineered plants and microbes released into the environment. The microbial work is still firmly in the laboratory, but the plant programme has just completed its first full growing season.

The basic plant experiment is being run by Michael Crawley, a plant ecologist at Imperial College in London. It pits Westar, a standard agricultural variety of oil seed rape (Brassica napus ssp oleifera), against identical plants engineered for resistance to Basta, a herbicide, or kanamycin, an antibiotic. There are three sites: one in Scotland, one in Cornwall and one at Imperial College's country station in Berkshire, west of London. At each site, transgenic seeds have been sown alongside control seeds in four habitats: wet and dry, sunny and shady. And at each habitat seeds were given full protection - spraying to eliminate insect pests and fungal diseases, a fence to keep out larger herbivores, and cultivation to remove plant competitors - or no protection, and all combinations in between.

This apparently complex experiment throws up an extremely simple conclusion: "Where you have got no cultivation and no fence, not a single seed sown, in a single site, in a single harbitat, reproduced." Cosseted in a field, rape reproduces beautifully. But outside those special circumstances it is a lousy competitor in any climate, and being transgenic is apparently no help.

If the plant itself is safe, what about the foreign genes it carries? Could they be transferred to other species? Charlock (Sinapis arvensis) is a close relative of rape, as black nightshade (Solanum nigrum) is of potato; both are common agricultural weeds that would pose an even greater problem if they picked up genes for herbicide resistance from their engineered relatives. Philip Dale, a plant geneticist and deputy head of brassica and oil seeds research at the Cambridge Laboratory of the AFRC's John Innes Centre for Plant Science Research in Norwich, is responsible for PROSAMO's pollen programme. He said that after many thousands of laboratory crosses between engineered potatoes and their relatives "we have no evidence of any hybrid being produced". With brassicas, such as oil seed rape, the story is slightly different: "If you try very hard and use sophisticated techniques of culturing embryos and culturing ovaries, then you can make hybrids," Dale said. Mimic nature more closely, putting oil seed rape plants and charlock plants next to each other and giving them the opportunity to cross pollinate, and they refuse. Hi-tech hybridization, although highly artificial, allows Dale to assess the consequences of a cross in the unlikely event that one occurs. Hybrids "tend to be sterile", said Dale, "which is another barrier to genetic spread".

Although these first e periments proved benign, much still needs to be done before releases become widely permitted and acceptable. What happens, for example, if you give plants resistance to insect predators, as many companies are trying to do? Based on experiments to date, Crawley does not anticipate much effect, because competition with other plants is by far the most important factor. Resistance to insect pests is unlikely to give engineered plants much of an edge, but the experiment is high on the list for next season.

Other crops are bound to differ from oil seed rape, perhaps in important ways. He hopes to examine maize (Zea mays) this year and sugar beet next, but at some stage the individual experiments on particular crops with particular foreign genes are going to have to give way to general principles governing the safety of environmental releases. Although the current PROSAMO programme is due to end in 1992, some would be happy to see it extended, but only after a review of the effect PROSAMO data has on regulators. (Extracted with permission from Science, Vol. 251, p. 878, by Jeremy Cherfas. Copyright by AAAS, 1991)

Transgenic rice resists dwarf virus

Sumitomo Chemical Co., Ltd., Osaka, and Kaoru Furuzawa of Kyoto University have developed a transgenic rice strain that is resistant to the rice dwarf virus (RDV). The team isolated the gene encoding the viral-integument protein from an RDV strain, then introduced it into protoplasts of Japonica rice. Regenerated plantlets exhibited resistance to a virus challenge. Sumitomo Chemical hopes to develop a commercial strain of RDV-resistant rice for marketing in Taiwan, South-east Asia, and Okinawa and Kyushu where RDV is prevalent. (Source: McGraw Hill's Biotechnology Newswatch, 4 February 1991)

Protein protects bacterial DNA from UV light

Scott C. Mohr, a chemist at Boston University, has solved the mystery of how bacterial spores can sit in dry soil for over 60 years and then come to life when conditions are conducive to growth. Previous work showed that bacteria in the early stages of sporulation produce large quantities of proteins called small acid-soluble spore proteins (SASPs), which seem to help protect DNA from ultraviolet light.

Mohr's research team showed that SASPs bind to DNA, unwinding it slightly. This changes the geometry of the DNA's thymine pairs, leaving them relatively nonreactive to ultraviolet light. (Source: Genetic Engineering News, February 1991)

Frozen plant tissue can be made to grow again

This technology was developed by researchers at the National Institute of Agrobiological Resources (Ministry of Agriculture, Forestry, and Fisheries), of Japan in a collaboration with scientists at Iwate University.

They excised a five millimetre piece of apple tree tissue called winter bud - which is formed at the tree's base in cold weather - and froze it in liquid nitrogen to -40°C. When defrosted, 45-100 per cent of the winter buds regenerated.

There are well over 1,000 varieties of apple; preserving the entire gene pool would require a vast number of orchards. The freezing technology will greatly reduce efforts for managing this gene pool. Further, raspberries and blueberries could be preserved using similar methods. The researchers are now working on improving regeneration rates and developing easier freezing methods. (Source: Bio/Technology, Vol. 9, February 1991)

Free genes for sweet potatoes

One of the most important food crops in developing countries, the sweet potato, may soon come in an insect-resistant variety - and at a reasonable cost. A team of researchers from Britain and Peru are attempting to transfer a gene from cowpeas into sweet potatoes. For this biotechnology project - one of the minority that may truly benefit poorer countries - one of the collaborators, the Agricultural Genetics Company (AGC) of Cambridge, has agreed to waive its patent rights to the cowpea gene for use in sweet potatoes. AGC waiving its rights means that anyone will be able to use the sweet potato technology.

The sweet potato's susceptibility to insect damage can slash yields by up to 80 per cent. With 98 per cent of the world's sweet potato crop grown in the developing regions and consumed locally, the key beneficiaries of the modified potatoes will be the farmers and consumers of the developing world. The growers will benefit from increased yields, lower input costs (in terms of labour, insecticides and equipment) and increased productivity and profitability.

With funds from the Overseas Development Administration, scientists at AGC, the University of Durham, and the International Potato Centre (CIP) in Lima, will attempt to incorporate AGC's insect resistance gene, the cowpea trypsin inhibitor (CpTI) into the sweet potato. The gene prevents the breakdown of certain proteins in the digestive system of insects so that insect larvae are deprived of essential nutrients and die.

Chemical control of sweet potato pests has had varying degrees of success, with many chemicals being too expensive, and conventional plant breeding has not been successful in producing high-yielding insect-resistant crops.

Champions of the rights of developing nations welcomed AGC's offer with the caveat that the patent system still favours the rights of richer nations and penalises poor nations. David Cooper of Genetic Resources Action International, based in Barcelona, pointed out that it was farmers in West Africa who first noted the resistance of some varieties of cowpea to insects and who nutured superior varieties that carried this characteristic. (Source: New Scientist, 16 February 1991)

Gene protects plants from tobacco mosaic virus

Research in viral diseases may lead to genetic alterations to fight fatal diseases. It now appears within the realm of reality that genes can be added to people that would make them resistant to lethal viral illnesses. Progress has already been made with regard to plant genetics. In a serendipitous discovery, a Cornell University researcher and a UK researcher found that a gene from tobacco mosaic virus guards tobacco plants from the disease when the gene is placed into tobacco cells. Research is under way to protect cucumbers and peas with similar methods. In time, viral diseases may be avoided in other crops, livestock and pets, as well as humans. (Extracted from The Economist, 25 January 1991)

Microbial mergers and the single-celled organism

A team of Canadian researchers has produced the first molecular evidence that the world of single-celled algae is just about as complex as it can be. By analysing sequences of certain ribosomal genes, the researchers have demonstrated that the single-celled alga Cryptomonas is the product of a union of two eukaryotic cells - that is, cells in which the genetic material is packaged within nuclei.

The demonstration by Susan Douglas and her colleagues at the Institute of Marine Sciences in Halifax, Nova Scotia, that Cryptomonas is built from two eukaryotic cells makes unicellular life look yet more complicated.

Cryptomonas is an oddball of the unicellular world. Its cell not only contains chloroplasts with two different photosynthetic pigments, but something called a nucleomorph as well. First discovered a quarter of a century ago, the nucleomorph looks like a slimmed-down nucleus, and has been shown to contain both RNA and DNA.

Not surprisingly, biologists have speculated that the nucleomorph is the vestigial nucleus of a eukaryotic cell that became incorporated within Cryptomonas early in evolutionary history. Until now, however, proof of the speculation has been lacking.

Exploiting the power of the polymerase chain reaction (PCR) to pull out and amplify minuscule pieces of specific DNA from Cryptomonas cells, Douglas and her colleagues were able to sequence a ribosomal gene, the so-called nuclear-type 18S sub-unit. They discovered that, unlike most organisms, which have only one such gene, Cryptomonas has two. Not only that, but the genes are distinctly different from each other.

One is of the kind normally found in the nuclei of a photosynthetic group that includes certain green algae and land plants. The other is similar to the ribosomal gene of red algae, a more primitive group.

The first of the two genes comes from the nucleus of Cryptomonas, while the second is almost certainly from the nucleomorph, say Douglas and her colleagues. In which case, the early history of Cryptomonas involved two evolutionary events. First, a eukaryotic host incorporated a photosynthetic prokaryotic cell, forming a primitive red alga. Then this red alga was incorporated into a different eukaryotic host, resulting in Cryptomonas as it is known today. (Source: New Scientist, 30 March 1991)

Immunity gene transferred between plants

Not only human beings and animals but also plants cope with viruses and bacteria by means of a

special immune system. Immune genes release substances which counteract a variety of disease-causing pathogens and in doing so often resort to some amazing tricks. For example, if a leaf is infested by a fungus, some plants immediately let all the cells surrounding it die, resulting in a brown circular stain. The pathogen can no longer spread and so literally starves to death. Sometimes a proliferation of growth occurs in diseased areas, which in the course of time, regenerates to form a "second plant". It must also be admitted, however, that in many cases the plant's immune system fails, so that often only chemical pest control can help. However Bayer AG of Leverkusen have now succeeded in transferring an immune gene from one plant to another - from a peanut to a tobacco plant. This feat has already been crowned with success: the tobacco plant, which had been previously infected with grey scale, recovered from the fungus. This opens up new vistas for the scientists. In future, resistance genes, which form part of the immune genes, could be transferred to non-resistant plants. This would give the plants long-lasting protection against a particular pathogen. In addition to this cultivated plants could be given a kind of "chemical early warning system". To achieve this, the natural substances which activate the immune systems of cultivated plants, the elicitors, are being emulated in the chemistry laboratory. For the first time, one of these elicitors has now been isolated. This means that there is a chance that this substance could also be chemically reproduced. The scientists hope that it would then be possible to give plants "an environmentally harmless, life-saving advantage over the destructive germ". (Source: Scala 1991/March/April)

Investigation of apomixis in higher plants: Are extrachromosomal factors associated with apomixis in the crucifer Arabis holboellii HORNEM?

Apomixis gives rise to mother-like offspring, i.e. exact genetic copies of the mother plant. In contrast to hybrids they can be propagated and used in developing countries as well with stable yield. Being protected by breeders' rights, even in industrial countries they offer economic advantages. At present, the most important aspect of apomixis research is the attempt to introduce apomixis into sexual crop plants, especially those which cannot be multiplicated vegetatively in large scales, e.g. cereals and other crop plants. This publication is the first of its kind to offer fundamental results for the hypothesis of cytoplasmatic genetics of apomixis.

Model plant for our experiments is Arabis holboellii, which is a member of the North-American-Greenland crucifere. The feature apomixis of A. holboellii is characterized by diplospory, pseudogamy and parthenogenesis.

Regeneration of A. holboellii in tissue cultures leads to isogenic lines, which differ only in their capability to form apomictic seeds. The use of intercalating substances is not necessary to induce this kind of somaclonal variation.

The transfer of a hypothetical apomixis factor by grafting fern-leaved Brassica napus, bearing a heterozygous marker, on A. holboellii did not succeed.

Electrophoretical separated undigested mtDNA (mitochondrial DNA) of S-plants (seed-borne plants) shows three extra bands of 3,0, 3,4 and 5,3 kb. G-plants (in tissue cultures regenerated plants) have no extra bands. The chemical nature of these bands and their connection between apomictic seed-formation has to be investigated.

First SOUTHERN hybridizations with the mtDNA probes COXII, COXIII and atpA indicate no differences between S- and G-plants.

The size of the mitochondrial genome of A. holboellii is about 249 kb.

Restriction fragment analysis of mtDNA from single plants shows differences between S- and G-plants whose connection between apomictic seed formation has to be examined.

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New shuttle vector developed

A collaboration between the National Institute of Agrobiological Resources of the Ministry of Agriculture, Fisheries and Forestry and Joachim Messing's group at Waksman Institute, Rutgers University has resulted in the development of a shuttle vector for use in plants, as announced at the annual meeting of the Japan Molecular Biology Society.

The new vector is derived from a wheat virus, WDV. Genes responsible for the virus's replication have been isolated and connected with both a marker gene and genes needed for replication in Escherichia coli. This is the first shuttle vector for plants which can be manipulated in E. coli to insert foreign genes and then transfer them into plant cells. The vector multiplies in the plant cell, producing higher foreign-gene expression than conventional methods. (Source: Bio/Technology, Vol. 9, 1991)

Viral genes

Mab acts against VZV

Tejin (Osaka, Japan) has isolated a human monoclonal antibody that acts against the chicken pox and herpes zoster (shingles) virus (VZV). The firm plans to proceed with safety and clinical tests as rapidly as possible. The antibody was produced by stimulating human lymphatic tissue with gpIII antigen and polyethylene glycol to crossbreed with mouse myeloma cells P3U-1, to obtain a hybridoma strain (V3). The antibody has shown effectiveness of 127 times that of the VI antigen and 14,000 times that of human polyclonal antibody, and totally stopped infection spread in cultures. (Extracted from New Technology Japan, January 1991)

Virus activation enzyme

Shionogi (Osaka, Japan) is investigating a virus activation enzyme implicated in A-type influenza infection, with Professor Y. Nagai of Nagoya University. The activation enzyme appears to be identical to the chicken blood coagulation factor Xa, and acts on a viral part common to

several virus strains. Similarities of Factor Xa with human and cow gene structures lead researchers to believe the blood coagulation factor is involved in human influenza infections, and presents an opportunity to develop therapeutic measures. (Extracted from New Technology Japan, January 1991)

Herpes virus linked to AIDS

Infection with human herpes virus-6 (HHV-6) appears to induce a class of T lymphocytes to begin production of the cell surface antigen CD4, thus rendering the cells susceptible to infection with human immunodeficiency virus. A key element in the process by which HIV infects a cell is interaction between the viral envelope glycoprotein and the CD4 molecule. T-cells that express CD4 but not the related antigen CD8 ($CD4^+CD8^-$T-cells) are a principal target of HIV. Two years ago, Robert C. Gallo, head of the laboratory of tumour cell biology of the National Cancer Institute, and colleagues proposed that HHV-6 was a co-factor in development of AIDS in people infected with HIV. The researchers have now shown that when T-cells that carry CD8 but not CD4 ($CD4^-CD8^+$T-cells) are infected with HHV-6, they begin to express CD4. Presumably, the herpes virus activates transcription of DNA that encodes CD4. This DNA is inactivated during maturation of $CD4^-CD8^+$T-cells. The research suggests yet another mechanism by which HIV disrupts immune function: infection with HHV-6 makes vulnerable a new subset of immune system cells, the $CD4^-CD8^+$ T-cells, to attack by HIV. The researchers say that other human herpes viruses appear not to exert this effect. (Reprinted with permission from Chemical and Engineering News, 11 February 1991, p. 16. Copyright (1991) American Chemical Society)

HIV-1-infected cells secrete neurotoxins

Human immunodeficiency virus-1 causes neurologic damage even though it does not directly infect neurons. Rather, the virus invades cells of the central nervous system known as mononuclear phagocytes. Once these cells are infected, they begin releasing one or more toxins that disrupt neurons and can even destroy them if the toxins are secreted in sufficient amounts, according to an *in vitro* study conducted at Baylor College of Medicine in Houston. Although researchers Dana Giulian, Ken Vaca and Christine A. Noonan have not yet been able to identify the neurotoxins, several possibilities have been eliminated, including gp120, the neurotoxic envelope glycoprotein of HIV-1. Experiments indicate the toxic agents are small (under 2000 daltons), heat-stable, protease-resistant molecules that act by way of N-methyl-D-aspartate receptors. (Reprinted with permission from Chemical and Engineering News, 17 December 1990, p. 15. Copyright (1990) American Chemical Society)

Broad-spectrum HIV antibodies elicited

In research that boosts hopes for a successful AIDS vaccine, scientists at Repligen Corp. and Duke University have shown that antibodies produced against one strain of human immunodeficiency virus can neutralize the infectivity of divergent HIV strains. Repligen's Kashi Javaherian and colleagues immunized guinea pigs with synthetic peptides consisting of sequences from what is known as the V_3 loop of the HIV envelope glycoprotein. Previous research had shown that this highly variable segment of the HIV envelope glycoprotein contains the region most commonly recognized by neutralizing antibodies. However, because it is so variable, most neutralizing antibodies are HIV-strain specific, which complicates efforts to develop a broadly protective subunit AIDS vaccine. The current work shows that two peptides from divergent HIV strains, which share a common six amino acid sequence in the centre of the V_3 loop, elicit antibodies that are cross-neutralizing. The group reports that 60 per cent of 245 HIV isolates recently characterized contain the six amino acid sequence, suggesting that a large percentage of HIV strains will be neutralized by antibodies that recognize this sequence. (Reprinted with permission from Chemical and Engineering News, 17 December 1990, p. 15. Copyright (1991) American Chemical Society)

Suspect virus

Scientists believe they have new evidence to strengthen a suspected link between Epstein-Barr virus and Hodgkin's disease, a cancer of the lymph nodes. Researchers in Birmingham and Aarhus in Denmark have found a protein called LMP, produced by the virus and thought to be involved in the cancer, in cells from about half of a sample of 84 tumours from patients with Hodgkin's disease.

The finding suggests that vaccination against the virus might prevent at least some cases of Hodgkin's disease. (Source: New Scientist, 16 February 1991)

Warfare in the body

Researchers at the Albert Einstein College of Medicine in New York and the Max Planck Institute for Biology in Tübingen, Germany, have shown exactly how cells infected by virus particles signal to the immune system that they are in trouble. The immune system responds to viruses in two waves. In the early stages of infection, while virus particles float free in the bloodstream, they are latched onto by antibodies. The antibodies fasten onto specific proteins (called antigens) on the surfaces of virus particles. If the immune system has seen the virus before, then with a bit of luck there will be antibodies specific to its particular antigens around already, and the virus particles will be caught before they can get into cells. Once the virus gets into the cells, it is hidden from antibodies. The genes in the virus subvert the invaded cells and use them to manufacture proteins which can be put together to make more virus particles.

Still, the invaded cells may manage to signal news of the incursion to the outside world and thus summon the immune system's second wave of defences. They do this by chopping up some of the viral protein that they have been ordered to make. Then they smuggle the little snippets of protein, called peptides, onto their outside surfaces. There the peptides are displayed in a groove on the surface of the cell, among the proteins of the major histocompatibility complex (MHC). These MHC proteins signal to the immune cells which patrol the body - the T-cells - that the MHC-bearing cell is on their side. The appearance of a foreign peptide in among friendly MHC proteins rouses the ire of the ever-vigilant T-cells; they kill the cell, thus destroying the virus inside it.

The researchers in New York and Tübingen, who published their results in Nature, have now shown exactly how infected cells chop up viral proteins into peptides of a specific size (eight or nine amino-acid subunits long) and smuggle them to the surface. In the case of one of the viruses they studied, the influenza virus, they also showed that the peptide the cells chose to display provokes a strong response from the T-cells, and is common to all strains of influenza.

Dr. Grada van Bleek, one of the researchers in New York, suggests that this peptide, selected by the body itself to stimulate immunity, might form the basis for a vaccine against all forms of influenza. But she warns that it will not be easy to make the vaccine. The peptide will need to be engineered into MHC proteins, or the T-cells will ignore it. There are some 150 different MHC proteins, and no one knows how many of them would be required. Other peptides or proteins will be needed in order to goad the antibody army into action in support of the T-cell regiments.

Nonetheless, such "cocktail" vaccines are worth striving for. Because each constituent protein would be genetically engineered, such vaccines would not have the occasional side-effects of vaccines made from insufficiently weakened whole viruses. The challenge of making genetically engineered vaccines has proved far more formidable than was hoped in the early days, when all that seemed to be necessary was to reproduce one antigen from each virus's surface. But bioengineers are learning fast how to mix the cocktails of peptides that the immune system craves. (Source: The Economist, 1 December 1990)

Luring immunity with a decoy

California researchers are developing a method for making decoy viruses, exact replicas of viruses that look real on the outside but are lifeless inside.

When the decoys are injected as vaccines, researchers say, the human body might be tricked into building particularly strong immunity against viral diseases, without running the risk of infection.

The decoy technology is being tested in animals, said Dr. Nir Kossovsky, an assistant professor of medicine at the University of California in Los Angeles who heads the research team. The concept is described in the December 1990 issue of The Journal of Applied Biomaterials.

The research pays close attention to the fact that the shape of a molecule determines its biological function and may also lead to blood substitutes and novel drug delivery systems.

The decoy research is just one example of an expanding effort to apply biotechnology to vaccine development. Current vaccines have many drawbacks and some viruses have been resistant to vaccine development.

The idea for the decoy originated two years ago, Dr. Kossovsky said, when a colleague returned from Japan with samples of ultra-fine ceramic particles and asked what might be done with them biologically.

Dr. Kossovsky and his colleagues set about the problem of developing a viral decoy. A Toronto company, Diasyn Technolgies, provided venture capital for the project.

For a delivery system or carrier, Dr. Kossovsky chose ultrafine particles made of a ceramic, tin oxide. For his first protein, Dr. Kossovsky chose a common component of blood, serum transferrin, instead of a viral coat protein. He later placed coat proteins from the Epstein-Barr virus on decoys. Both proteins naturally assemble around the decoy, retaining the correct shape.

A series of tests showed the decoy was biologically active, Dr. Kossovsky said. Results were described in the December article.

A second phase of experiments has been completed with Epstein-Barr viral proteins on a tin oxide carrier. The virus causes mononucleosis and two types of cancer.

The results of the experiment, which Dr. Kossovsky said were "extremely encouraging," are being reviewed for publication in a scientific journal. (Extracted from International Herald Tribune, 25 April 1991)

Research Instrumentation

New membrane liposome

A synthetic two-layer membrane liposome with transfection ability three times conventional liposomes has been developed by researchers at the Fukuoka Industrial Research Centre and Kyushu University in Japan. The new liposome has a structure permitting temperature range of 0°C-50°C, as well as more efficient gene transfection to eukaryotic cells. The liposome method of DNA transfer into cultures is seen as the most convenient of the techniques available, requiring less instrumentation than others. (Extracted from New Technology Japan, January 1991)

Optics and antibodies

Chemical sensors based on the highly specific bonding that occurs between antibodies and antigents are an emgerging technology that has yet to achieve widespread use in continuous monitoring. One problem is the bonding itself - highly specific but also effectively irreversible. This means sensors based on immunoassays are not very good for long-term, continuous measurements of chemicals.

However, Steven Barnard and David Walt at Tufts University in Boston think they have found an answer: controlled-release polymers. They incorporated immunochemical reagents into ethylenevinyl acetate polymer in a tiny reaction chamber on the end of an optical fibre. In this way, the immunoassay was replenished continuously with new antibodies relased slowly from the polymer matrix. The reagents were labelled with fluorescent markers and optically excited via the fibre, through which their emission spectra were also measured to determine the level of analyte.

The Tufts team says a typical sensor can be designed to last 30 days. Although not all the problems have been worked out, the two scientists believe existing immunoassays can be coupled to optical fibres in this way. "The most immediate

applications are likely to be in the monitoring of pollutants at toxic waste sites, groundwater aquifers, and agricultural areas where there is pesticide runoff, since antibodies to these analytes are becoming available commercially." (Source: Chemistry and Industry, 18 March 1991)

Out of thin air

Scientists who study aeroponics, the growth of plant tissue or seeds in a nutrient-rich mist without soil or water, can now get help from a device called the Mistifier system.

Developed by Bio Rational Technologies in Stow, Mass., but marketed by Manostat Corp. in New York City, the system employs a horizontal growth chamber about the size of a household ultrasonic humidifier. A tube inside the chamber evenly disperses nutrient mist from an ultrasonic mist generator over a perforated stainless steel tray.

An electronic controller regulates the system's various settings. These include a control that determines fluid level in the mist generator by regulating a peristaltic pump (which pumps fluid by waves of mechanical contractions along the tubing), a flowmeter that determines the rate of gas flow through the system, and a control for intermittent mist generation. (Source: IEEE Spectrum, January 1991)

A new BIOTIN phosphoramidite

Cambridge Research Biochemicals announce the launch of a unique DNA Chemistry reagent for the 5' biotinylation of oligonucleotides.

The phosphoramidite DMT-biotin-Cs-PA permits the synthesis of biotinylated oligonucleotides on the column, giving much higher yields than the conventional off-column procedure and with less hands on time.

Soluble in acetonitrile the reagent can be used with normal synthesis protocols. Coupling yields are greater than 95 per cent, which in many applications allows the biotinylated oligonucleotide to be used without purification.

A key feature of the reagent is the dimethoxytrityl (DMT) protecting group on the biotin, which accounts for its high solubility in acetonitrile. Removal of the DMT group, by the standard on-column detritylation procedure, provides a ready method of assessing the coupling yield.

The biotinylated oligonucleotide can be used in many applications, including dot blots, Southern blots, in-situ hybridisation and PCR. Reader Enquiry Service cards etc. should be addressed to: Simon Douglas, Senior Product Manager, Bioscience, Cambridge Research Biochemicals Ltd., Gadbrook Park, Northwich, Cheshire, CW9 7RA - Tel.: (0606) 41100, Fax: (0606) 49366. (Source: Cambridge Research Biochemicals Press Release)

New bioreactor system for protein mass-production

Kirin Brewery (Tokyo) has developed a new radial-flow bioreactor system for protein mass-production. In experiments with an erythropoietin (EPO) production system using Chinese hamster ovary cells, the new bioreactor has proven stable up to 100 days, with 1,000-fold higher production efficiency than conventional methods.

The radial-flow bioreactor utilizes multi-pore glass beads as a substrate for cell fixation. The beads - carrying cells at a density of 1.3 X 10^8 cells per ml - are packed in the core of the cylindrical tube. Culture medium flows from the outer side of the cylinder into the core (thus the medium flows in the reverse-radial direction). This system attains the highest known cell density with stable oxygen and nutrient supplies, resulting in high efficiency and stability. The company aims to use this system to mass-produce EPO and other substances with important physiological activities. (Source: Bio Technology, Vol. 9, January 1991)

General

Collaborative pact on DNA sequencing

Los Alamos National Laboratory and Life Technologies Inc., Gaithersburg, Md., have signed a collaborative agreement to develop a DNA sequencing technique patented by LANL scientists. The technique involves use of an enzyme to mark DNA with four different fluorescent, base-specific tags. A second enzyme cleaves the labelled nucleic acid base pairs, which are then identified by fluorescence detection. According to LANL and Life Technologies, commercial DNA sequencing methods can handle only short fragments of about 500 base pairs. If the LANL technique proves successful, they say, it will be possible to sequence fragments at least 100 times longer, and at faster rates. (Reprinted with permission from Chemical and Engineering News, 25 March 1991, p. 17. Copyright (1991) American Chemical Society)

Neural network identifies oligosaccharides

Neural network-based pattern recognition techniques can be used to identify ^{1}H-NMR spectra of complex oligosaccharides, say Bernd Meyer and colleagues at the University of Georgia. The oligosaccharide structures can be identified, in an average computer time of less than 0.1 second, even if their spectra differ by only one glycosyl residue in 20. The work is especially impressive because NMR spectra of oligosaccharides contain overlapping signals from repetitive residues, making pattern recognition difficult. This type of partially overlapping NMR spectrum is also typical of DNA, RNA, proteins, and other biomolecules, suggesting the potential applicability of neural networks to spectral identification of such structures. The advantages of neural networks over conventional spectroscopic library searchers, they say, are that they are faster and that they extract characteristic spectral difference information in an automatic fashion, instead of requiring prior definition of rules by scientists. (Reprinted with permission from Chemical Engineering News, 4 February 1991, p. 24. Copyright (1991) American Chemical Society)

Shooting up

A simpler kind of gene therapy may be elbowing its way forward. Its proponents call it "gene therapeutics" to distinguish it from conventional gene thereany. It is now being touted as the coming way to treat Parkinsonism and coronary heart disease, as well as genetic diseases like muscular dystrophy and cystic fibrosis. Its biggest potential could be in vaccination.

Gene therapeutics was born when John Wolff of the Department of Medical Biochemistry at Wisconsin University reported the discovery of something which at first he could not believe. What he found was that when he injected a simple solution of genes and water into muscle tissue, at least some of the genes were soaked up by the muscle cells and affected them. The genes did not need to be built into anything like a genetically engineered virus. Tests on mice showed that genes injected into muscle in this way went on working for most of a mouse's lifetime. And the level of expression could, it turned out, be improved with practice.

The unexpected success of this technique (which was originally intended merely to help evaluate a more elaborate one) quickly led to the idea of using injections of genes like an injection of an ordinary medicine. This is the direction being following by a Californian biotechnology company called Vical, which is working with Dr. Wolff.

According to Philip Felgner, director of the gene therapeutics division of Vical, the company has shown that reasonable levels of proteins will be produced by direct injections of genes into muscles; other laboratories have shown that other tissues are accessible to direct gene delivery too, including the brain and the endothelial cells that line blood vessels. The first human tests of gene therapeutics will probably be for muscular dystrophy, now that the gene for dystrophine, the protein which is absent or defective in those affected by the disease, has been isolated.

Several other conditions caused by defects that do not affect muscle itself might be treated by genes injected into muscle - for example, growth-hormone deficiency or haemophilia.

Vaccines made from genes, instead of in the usual way from whole virus particles or from engineered viral proteins with no DNA, could have significant advantages. Vical's experiments have shown that when genes from foreign organisms are injected into muscle, they strongly stimulate an immune response on the part of T-cells. These are the cells that directly attack and kill micro-organisms infecting cells. They also stimulate the immune system's other weapon, known as the antibody-mediated immune response. Vaccines that can provoke a T-cell attack as strongly as they can stimulate an antibody-mediated response should have several uses. They could be more effective in immunizing against parasitic diseases such as malaria and against some virus diseases.

For now, the genes used in gene thereapeutics will have to be taken in injections, but some doctors think that the means will eventually be found to prepare genetic material so that it can withstand digestion and find its way from the gut to the right part of the body. (Source: The Economist, 16 February 1991)

D. APPLICATIONS

Medical and pharmaceutical applications

Hope for quick leprosy cure

A new antibiotic promises to help cut the time it takes to treat leprosy from several years to just one month. The World Health Organization (WHO) will test the drug this year in combination with existing drugs at several leprosy centres in Asia and Africa. If the trials prove successful the cost of treating leprosy will fall, reducing the burden on poor, developing countries.

The antibiotic, called ofloxacin, has been prescribed for a wide range of bacterial infections since the mid-1980s. Now animal experiments have shown that it is also a potent killer of Mycobacterium leprae, the organism that causes leprosy.

Leprosy was incurable until the discovery of the drug dapsone in the 1940s. Dapsone is effective, safe and cheap, and when taken daily kills 99 per cent of M. leprae. The drawback is that dapsone is weak and acts slowly; it can take years to cure the disease.

But by the mid-1970s, the shortcomings of dapsone were becoming even more serious. Studies began to show that 30 per cent of people with leprosy - in some areas, up to 70 per cent - were infected with strains of M. leprae that were resistant to dapsone. Fortunately, researchers had by this time found other drugs that kill M. leprae, notably rifampicin and clofazimine.

In 1981, a WHO study group recommended that people with leprosy be given rifampicin and clofazimine to kill those bacterial cells that are resistant to dapsone. The strategy is called multi-drug therapy (MDT). The three drugs kill bacteria in different ways, and no single bacterial strain is likely to be resistant to all three drugs.

Of the three, rifampicin is the most potent. The difference in potency is reflected in the time it takes for MDT to work. People infected with rifampicin-susceptible bacteria can be cured in six months. Those infected with rifampicin-resistant strains respond to clofazimine and dapsone but, because those drugs act more slowly, their treatment can stretch to two or three years.

Ofloxacin is almost as effective as rifampicin in killing the leprosy bacterium, according to Jacques Grosset and his colleagues at the Pitie-Salpetriere Hospital in Paris, who carried out clinical trials. The drug works by disrupting the activity of an enzyme in the bacterium called gyrase. Gyrase cuts DNA at particular points so that it is able to uncoil to be replicated or transcribed.

The WHO now wants to test a combination of dapsone, rifampicin and ofloxacin in MDT in several countries. (Source: New Scientist, 16 March 1991)

Reports of mosquitos and coconuts

In Lima, Peru, a research team headed by microbiologist Palmira Ventosilla, has developed an innovative approach to malaria control that is cheap, safe, and grows virtually beside the larvae's breeding ground.

In a study supported by IDRC, researchers at the Alexander von Humboldt Tropical Medicine Institute discovered that coconuts are the perfect incubator for a bacteria that kills mosquito larvae.

The bacteria Ventosilla used in the projert - Bacillus thuringiensis var israelensis H-14 - known

as Bti, has been around for a long time. It was discovered almost 20 years ago by Israeli scientists who noticed a large number of mosquito larvae dead in certain ponds. On analysis of the pond water, they isolated the Bti spore.

It is a perfect insecticide because it is deadly to mosquitos and blackflies, but harmless to livestock and humans. During the first three of the larvaes' four stages of development, they eat the bacteria along with algae. The Bti then eats away the larvae's stomach lining, killing them.

But, up until now, developing countries have been slow to use the bacteria because of its commercial cost.

Hoping to overcome the financial barrier, the Peruvian research team in 1988 began trying to multiply the Bti spore by fermenting it with various locally grown produce. Because fermentation is a common practice in Peru, the researchers thought it would be relatively easy to teach the technology to villagers, if it worked.

Their research soon showed that coconuts were the best option. At room temperature, Bti spores added to coconut water in petri dishes multiplied from 100 spores per ml to a maximum 100,000,000 spores per ml in 3 days. Doing the same experiment, but injecting the bacteria by pipette into whole coconuts, 100 spores multiplied to a respectable 1,000,000 spores.

Just as Ventosilla was reaching these conclusions, a colleague sent her a research paper from New Zealand that reinforced her results. Written by C.N. Chilcott, the paper discussed the effectiveness of coconut water as a medium for growing Bti spore.

With IDRC support, Ventosilla and Peruvian entomologist Enrique Perez took the new technology out to two northern communities for field studies - Yurimaguas, in the jungle region, and Huan in the coastal area.

In field tests around Yurimaguas, Ventosilla's team found that after a single application of Bti-filled coconuts, the bacteria lived up to 18 days. It killed virtually all the mosquito larvae and stopped further larval growth for up to 45 days.

Having proven its effectiveness, Ventosilla now wants to take the technology into a village to see how effectively villagers would use it independently.

The research team has developed a Bti kit that villagers with only minimal instruction can use. It contains a plastic bag full of swabs doused in Bti and cotton plugs. The villager inserts one swab into each coconut through a hole drilled at the top and plugs it with cotton. After the coconuts have fermented 2-3 days, depending on their size and the local temperature, the villager would take the coconuts to a nearby pond, break open the fruit over the water and throw it all in.

A typically sized pond needs 2-3 coconuts for one treatment, said Ventosilla.

Although the technology sounds simple, the biologist said she knows that technology transferred to the village level can fail very easily. She recently applied to IDRC for a second grant to support a 30-month village project to help in the study of the village's socioeconomic dynamics.

But the project will only work if they train villagers who are interested in participating and take on the responsibility to complete the work, she said. Ventosilla would eventually like to teach the technology to community health workers who could train a wider audience.

The magic of the project, is that any country that has coconuts can use it, said Ventosilla.

Innovative malaria research is happening in other Latin American countries. In Brazil, researchers are testing different snails as possible larval predators and, in Colombia, fish are being introduced into ponds for the same purpose.

The researchers also took the first steps toward creating an information-exchange network within Latin America on malaria research. Further information from: Blga. Palmira Ventosilla L., Investigadora Asociada, Instituto de Medicina Tropical, Alexander von Humboldt, Universidad Peruana, Cayetano, Heredia, A.P. 5045, Lima 100, Peru Telf: 823401; Fax: 5114-823404.

Dragonflies help to defeat dengue fever

Researchers in Myanmar (formerly Burma) and Britain have devised an ingenious and highly effective method of dealing with the mosquito that carries the serious viral disease dengue haemorrhagic fever. The method relies on dragonfly larvae, which consume larval mosquitoes.

Dengue haemorrhagic fever is characterized by prostration, shock and, in some cases, death. The carrier of the virus is the mosquito Aedes aegypti, whose larvae, like those of other mosquitoes, are water dwellers. A. aegypti likes small receptacles of water, and it has been quick to exploit opportunities offered by humans.

People in Myanmar store water intended for washing or cooking in "pegu jars". In an urban area, such as Yangon (Rangoon), about 98 per cent of all the larvae live in such domestic water containers.

People are understandably reluctant to treat their water supply with insecticides, so any other method of suppressing the mosquitoes has considerable appeal. Observations made by chance during the course of other work suggested that dragonfly larvae were ideally suited for this most important of tasks.

With this in mind, Anthony Sebastian, Myint Myint Sein and Myat Myat Thu of the Ministry of Health, Myanmar, decided to put the dragonflies through their paces in a field trial in Yangon. With the cooperation of 2,200 local residents, the team added four larvae of the dragonfly Crocothemis servilia to all the major water containers within a study area of 0.02 square kilometres. Over a period of several months, the team made regular checks on the number of mosquito larvae and adults. An untreated area two kilometres away provided a baseline for comparison.

Within a month, the number of larvae fell by as much as 96 per cent. In general, people preferred

the amiable predator to the ill-smelling pesticide they would otherwise have been obliged to use. Their cooperation, say the scientists, played a central part in the success of the test.

The team's result augurs well for control of dengue haemorrhagic fever in particular and for biological control in general.

A number of circumstances combined to create this favourable outcome, notably the specialized breeding habits of A. aegypti, the participation of the local people and the ready availability of a suitable predator. Applying the technique on a wide scale - where suitable conditions exist - should not present insuperable problems.

A. aegypti is a major scourge of mankind - it carries yellow fever as well as dengue - so the new technique could have much to offer across the world. (Source: New Scientist, 27 April 1991)

Use of defensins in new antibiotics

Defensins, antibiotics produced by immune cells called neutrophils, could be imitated for a new family of antibiotics. Dr. Robert I. Lehrer of the University of California (Los Angeles) says that it is amazing that researchers are just now starting to study defensins, which have a critical role in the body's immune system. Purified samples of defensins can destroy pathogens including bacteria, fungi and viruses almost instantly. Dr. Michael E. Selsted of the University of California (Irvine) says the defensins may be effective against the Cryptococcus neoformans fungus that is a major cause of death in AIDS patients.

Bone marrow produces some 100 billion neutrophils each day. They congregate quickly around an infection, and neutrophils are the basic ingredient of pus that forms around wounds. Neutrophils can kill in two ways: with hydrogen peroxide and chloride bleach or by piercing the bacterial membrane. Researchers must now determine how to mass produce defensins. (Extracted from New York Times News, 26 February 1991)

Botulism toxin in neuromuscular treatment

The botulism toxin can be used to treat neuromuscular disorders. Botulinum, produced by Clostridium botulinum, has now been used to treat muscular spasms in the eyes, face, throat, limbs and torso. The toxin is produced for medicinal use by the University of Wisconsin-Madison Food Research Institute. The bacterium produces seven neurotoxins, but Type A has been most used and researched. The protein has three regions: one targets a muscle nerve ending, one helps the toxin enter the cell, and another blocks the release of acetylcholine from nerve cells. Type A toxin (in minute quantities) can effectively treat excessive muscle contractions characteristics of dystonias. Doses are generally 0.1-0.5 nanograms. (16 nanograms are needed to produce mild botulism poisoning).

Allergan is the only firm marketing Type A botulinum toxin in the US. It is seeking FDA approval for new indications for the compound, but it will not specify what they are. An NIH panel has agreed that the toxin is safe and effective for treating spasmodic torticollis, oromandibular dystonia, and adductor spasmodic dysphonia. Many conditions that could be treated with botulinum have no other effective treatment. Tinkering with the molecule may further improve its effectiveness as a medicine. (Extracted from Science News, 19 January 1991)

Mabs in future medical applications

Although monoclonal antibodies have not found medical applications in the 1980s, their usefulness could greatly increase in the 1990s. Antibodies produced by B lymphocytes attach to antigens and mark them so that other cells can attack the invader. When monoclonal techniques were discovered in the mid-1970s, it was thought that they would hold the key to treating all sorts of diseases, including cancer. In practice, monoclonals have not yet been very useful, since they are generally made as hybrids of mouse and human proteins, and are attacked by the immune system. Making purely human monoclonals has been very difficult. Scotgen, an offshoot of the Medical Research Council (MRC), has created a humanized antibody effective against respiratory syncytial virus (RSV), a major respiratory illness in children. Cetus (US) has now patented another innovation pioneered by Greg Winter at MRC, in which polymerase chain reaction (PCR) is used to reproduce the DNA for an antibody so that it can be inserted into bacteria for mass production. The light chain of antibodies can also bind to target antigens without the presence of the heavy chain, and this finding might allow the preparation of mini antibodies that could penetrate tumours. Another technique being tested is that of inserting antibody-producing genes into the embryos of animals such as sheep, so that the fully-grown animals will secrete the antibodies in their milk.

The top seven US biotechnology companies in 1985 spent $443 million on monoclonals research. Centocor focuses entirely on monoclonals, and has 18 in clinical trials. The only monoclonal antibody-based drug on the market, however, is Ortho Biotech's OKT3 to prevent organ transplant rejection. Monoclonals to treat septic shock are being developed, as are monoclonals to treat AIDS. John Savin of the Centre for Exploitation of Science and Technology points out that monoclonals will not be able to compete against antibiotics, which cost far less, but that monoclonals will be valuable for combating viruses, for which no other drugs are effective. Some monoclonal anticancer drugs might also be available in the mid-1990s. (Extracted from New Scientist, 9 February 1991)

Follow-up therapy antibody test

An antibody test is being developed that could determine when breast cancer patients need follow-up therapy. Researchers at the Imperial Cancer Research Fund Laboratory at Hammersmith Hospital say there is a protein that is present in high levels in women likely to relapse even after a cancer is surgically removed. The protein is produced by the gene c-erbB-2. It probably is a receptor for a growth factor. Malignant cells have twenty times as much of the protein as benign cells. Normal cells that are made to produce the protein are able to induce cancer in mice. The protein may help surgeons decide which patients will need follow-up chemotherapy. (Extracted from New Scientist, 19 January 1991)

Mab trial indicates reduction in deaths from bacterial infections

Centocor's Centoxin human monoclonal antibody is said to reduce deaths from a type of bacterial infection. An important clinical trial indicates

the antibody lowered death rates from what is referred to as gram-negative bacteria, a virulent kind of bacterial infection. The death rate reductions vary from 30 to 49 per cent. The antibody, still in its experimental stage, is intended to forestall shock and death from bacteremia, commonly known as "blood poisoning". The Centoxin obliterates bacterial toxin that is released in the blood stream by gram-negative bacteria. Analysts say the antibody is a major achievement for Centocor. Around 100,000-300,000 people are thought to be victims of gram-negative bacteremia annually, leading to deaths ranging from 30,000 to 100,000. (Extracted from Wall Street Journal, 14 February 1991)

Plastic "dipstick" cuts cost of HIV testing

A piece of plastic the shape of a comb and the size of a credit card could cut the spread of AIDS by blood transfusion in developing countries. It is a reliable "dipstick" test for antibodies to HIV and costs one-eighth the price of the most widely used existing test and takes just a fraction of the time to perform.

The test has been developed by Milton Tam of the Programme for Appropriate Technology in Health in Seattle, Washington, with funding from the International Development Research Centre in Ottawa, Canada. The other major sponsor was the Rockefeller Foundation based in the US.

The widely used ELISA tests for HIV antibodies, common in the developed world, can be used only at the highest level of health care in developing countries, says Don de Savigny of the IDRC.

The new test is for HIV-1, the virus that causes most of the world's cases of AIDS. HIV-2, a related virus that causes immune deficiencies, is found mainly in West Africa with a few small pockets occurring in Europe and the US.

Unlike the ELISA test, the HIV dipstick test does not need a laboratory, refrigeration or even a specially trained technician. At the bottom of each tooth of the comb-shaped plastic strip there are spots of a synthetic peptide that mimics part of a protein from HIV-1 known as gp41. Analysts dip the strip into a blood sample for 10 minutes. If antibodies to HIV are present, they will bind to the peptide.

The strip is washed briefly then put into a solution known as a signal reagent. Particles in the solution stick to any antibodies to HIV, and turn the dots red. The health-care worker just needs to look for the red dot. If the dot appears, the blood is not considered safe for transfusion.

The dipstick test takes about 20 minutes, and is expected to cost less than 25 cents a test. The ELISA test takes from 2 to 4 hours, and costs at least $2, but the two tests are claimed to be equally reliable.

The World Health Organization Global Programme on AIDS carried out a laboratory assessment of the dipstick test. The WHO tested 449 blood samples from Africa, South America and Europe, of which 200 were positive. The dipstick test results were comparable to the ELISA tests on the same specimens. The test recognizes different strains of HIV-1 from different parts of the world because the peptide is taken from an outer protein of the virus that is common to all known strains.

Tam is currently attempting to expand the capacity of the dipstick test to pick up HIV-2 and hepatitis B. Meanwhile de Savigny and the IDRC are trying to develop the technology so that developing countries can produce the test themselves. (Source: New Scientist, 9 March 1991)

Iron "scavenger" could help thalassaemia sufferers

Chemists may soon have a way to help children with the fatal genetic disorder thalassaemia. They have synthesized a compound which effectively "mops up" excess iron in the body. A side effect of the treatment for thalassaemia - frequent blood transfusions - is that iron builds up to dangerous levels in the body.

Arthur Martell and Ramunas Motekaitis of the Texas A&M University and M.J. Welch of Washington University in St. Louis, Missouri, have made a compound that binds tightly to iron, and iron alone. They say it could be used as prototype for a new and effective drug.

Each year, almost 100,000 babies are born with thalassaemia, also known as Cooley's anaemia. The disease occurs mainly in the Middle East, India and South-East Asia. World-wide, 100 million people may carry the faulty gene.

Until scientists find a genetic cure for the disease, the toxic effects of transfusion therapy must be counteracted with drugs that can soak up iron. For the past 20 years, most of these drugs have been based on siderophores, compounds that are produced by certain kinds of bacteria and fungi.

Micro-organisms use siderophores to help them "scavenge" iron from their surroundings. These natural compounds are part of a larger class of compounds, called "metal chelators", which trap the metal ions between chemical groups by acting like a crab's pincers.

So far, the only drug that efficiently counteracts iron overload in thalassaemics undergoing transfusion therapy has been the siderophore, desferrioxamine. But to work properly, it must be injected over a 10-hour period up to six times a week, making it a very impractical drug.

And this is not the only disadvantage of the siderophore-based drugs. Because some scavenge other essential metal ions, such as copper and zinc, from the body's fluids, they are highly toxic.

Martell and Motekaitis's compound binds to iron far more tightly than even the strongest siderophore, a compound called enterobactin. And it does it at the levels of acidity found in the body. The compound, called N,N',N"-tris-(3-hydroxy-6-methyl-2-methyl-pyridyl)-1,4,7-triazacyclononane, also has the advantage of being soluble in water.

Iron chelators might even save people who are exposed to dangerous levels of radioactive plutonium. Metal chelators discriminate between metal ions on the basis of a property of the ion known as its charge to size ratio. Because iron (3+) and plutonium (4+) ions have very similar ratios, metal chelators cannot tell the difference. A chelator that can scavenge iron could just as easily be used to scavenge plutonium in the body. (Source: New Scientist, 2 February 1991)

Amgen to launch second biotechnology product

Amgen has received FDA approval for the manufacture and marketing of its recombinant granulocyte colony-stimulating factor (G-CSF), which promotes the production of infection-fighting white blood cells called neutrophils. G-CSF has been approved for use in treating low white blood cell count, or neutropenia, associated with cancer therapy - a US market expected to be worth nearly $400 million by 1994. This will be the second product for the Thousand Oaks, California-based biopharmaceutical company, which currently markets erythropoietin, a red blood cell stimulant. In 1990, Amgen had product sales of more than $280 million. (Reprinted with permission from Chemical and Engineering News, 25 February 1991, p. 9. Copyright (1991). American Chemical Society)

Genentech halts study

Discouraged by initial clinical studies, Genentech has halted trials of CD4-IgG as a stand-alone therapy for HIV-infected adults. The company now plans to test the drug's ability to prevent transmission of the AIDS virus from infected mothers to the foetus.

Recombinant CD4-IgG is based on a synthetic copy of the human cell target site for HIV. Genentech scientists then added on a human antibody, in hopes of boosting the active immune response.

After the establishment of a special fund for CD4 research, Genentech launched initial clinical studies in 1989. However, the company reports that AIDS patients "have not shown consistent clinical improvements" during phase I trials of soluble CD4 and CD4-IgG.

Genentech says that animal studies confirm placental transfer of CD4-IgG, and initial human safety tests in newborns are already under way. (Source: Chemistry and Industry, 4 February 1991)

Immunex gets FDA's approval on CSF

Immunex (Seattle) and Hoechst-Roussel Pharmaceutical (Somerville, NJ) - the drug unit of Hoechst Celanese - have received US Food and Drug Administration approval to market granulocyte macrophage colony-stimulating factor (GM-CSF) for use in bone marrow transplant patients. The drug speeds growth of white blood cells, reducing risk of serious infections. Hoechst-Roussel and Immunex, which collaborated on the GM-CSF development, will market the product separately in the US. Less than a month ago, FDA approved a related compound - granulocyte colony-stimulating factor (G-CSF) - developed by Amgen (Thousand Oaks, CA) for reducing infection risk in patients undergoing chemotherapy. Schering-Plough (Madison, NJ) and Sandoz Pharmaceuticals (East Hanover, NJ) are also working on a GM-CSF product. (Source: Chemical Week, 13 March 1991)

Biocine plans US trials for two AIDS vaccines

Biocine, The Ciba-Geigy/Chiron vaccine joint venture, is planning two trials for potential AIDS vaccines this year. The first involves a potential therapeutic, while the second, planned for later in the year, will use a more conventional vaccine approach.

The US/Swiss joint venture is developing a range of recombinant vaccines that use a novel adjuvant developed by Ciba-Geigy scientists in Basel. This adjuvant is believed to be capable of helping stimulate immune responses in sufferers of herpes, hepatitis C and cytomegalovirus.

The two AIDS vaccines to undergo trials this year both use adjuvants. The first vaccine uses the non-glycosylated form of the HIV surface protein, gp120 combined with the Ciba-Geigy adjuvant MTP. Biocine scientists believe the vaccine will stimulate the cell-mediated response.

Trials with a less potent form of the adjuvant two years ago demonstrated that the vaccine can stimulate the cell-mediated response. In the new trial, healthy patients will be tested with the new version.

"Once the safety and efficacy t· stimulate the immune response has been established we will test in AIDS patients", according to a Biocine spokesman. Such a trial could be started as early as mid-1991.

A more conventional preventative vaccine is to be tested at the end of the year. Biocine will use a vaccine composed of the MTP adjuvant plus a natural form of the HIV surface protein gp120. This version should stimulate the antibody response. (Source: European Chemical News, 31 December 1990/ 7 January 1991)

AIDS inhibitor

Boehringer Ingelheim, in conjunction with scientists at the University of Massachusetts Medical School, has synthesised an inhibitor of the AIDS virus.

The drug, BI-RG-587, blocks the HIV-1 reverse transcriptase enzyme and is claimed to have a very high therapeutic index with no cytotoxic effects on human bone marrow.

Boehringer intends filing a treatment Investigational New Drug (IND) application with the FDA in the USA soon. (Source: Manufacturing Chemist, February 1991)

Another source for DHA found

Researchers at the Sagami Chemical Research Centre in Japan have found relatively high levels of docasahexaenoic acid (DHA) stored behind the eyes of tuna and bonito fish. DHA, a fatty acid, is thought to inhibit the coagulation of platelets and prevent thrombosis. It was previously only found in sardine oil, and the research group says the discovery could lead to a supply of less costly, high-purity DHA. (Source: European Chemical News, 14 January 1991)

Recombinant clotting protein passes trials

An international clinical study of recombinant blood clotting factor VIII in 107 haemophiliacs indicates that the genetically engineered material is at least as effective as protein isolated from blood plasma. This result will help pave the way for approval by the Food and Drug Administration of a haemophilia therapy free of risk of contamination by AIDS or hepatitis viruses.

Factor VIII is one of 17 components of the cascade of reactions that forms the insoluble,

crosslinked fibrin of a blood clot. More than 10,000 Americans have such a severe inborn deficiency of factor VIII (called haemophilia A) as to need injections of it to control bleeding. A few thousand others have severe deficiency of factor IX (haemophilia B).

The study was done by the Recombinant Factor VIII Study Group, a consortium of 40 investigators at 19 medical centres in the US, Canada, UK, Germany, Italy, and Japan. They found that recombinant protein had a half-life at least as long as plasma-derived protein. Patients also treated themselves successfully at home. Recombinant factor VIII effectively controlled bleeding during surgical procedures, and very few patients developed antibodies against factor VIII. (Extracted with permission from Chemical and Engineering News, 7 January 1991, p. 8, by Stephen Stinson. Copyright 1991 American Chemical Society)

Blood clot drug approved by FDA

The US Food and Drug Administration has given its approval to a new purified blood clotting agent for people who suffer from haemophilia B.

The newly approved product is called Coagulation Factor IX (Human), and is an extract of human plasma. It was developed and will be marketed by Alpha Therapeutics Corporation.

The product will be marketed as a dry concentrate, to be reconstituted with sterile water and administered intravenously. It can be used in treatment and prevention of bleeding episodes, which can be caused by accidental cuts, abrasions and bruising.

It can also be administered prophylactically to prevent uncontrolled haemorrhage in haemophilia patients undergoing surgery.

Haemophilia B, also known as Christmas Disease, is incurable and affects approximately 2,800 Americans, FDA says.

In clinical trials of the new product, a total of 11 patients received 115 infusions of the new Factor IX, and no adverse reactions were reported. (Extracted from Chemical Marketing Reporter, 7 January 1991)

Blood substitute undergoing tests

Biopure's purified cattle haemoglobin will be tested as a blood substitute in humans. The US Food and Drug Administration recently gave the firm approval to conduct human trials, which has begun. Volunteers will be injected with small quantities of the purified cattle haemoglobin, known as Hemopure. Upjohn will supervize the clinical studies. If no major adverse reactions are reported, the trials will be expanded to determine the product's efficacy. One advantage of the blood substitute is the absence of the AIDS virus and various impurities that cannot be eliminated from human blood. Some 12 million pints/year of blood are used in transfusions in the US. Hemopure could be especially useful in less developed countries that do not always test for the AIDS virus.

Cattle haemoglobin is similar to human haemoglobin, and Hemopure has about the same capacity to transport oxygen as human haemoglobin. Hemopure would be effective for about 7 days in humans. When administered in sufficient amounts, it could provide enough oxygen to cells while the bone marrow replenishes its red blood cell supplies. A study by researchers at Massachusetts General Hospital showed that all of the blood can be removed from sheep and replaced with Hemopure with no adverse effect. Similar studies have been performed on rats, dogs and primates. Some 40 pints of blood can be recovered from a cow that is slaughtered, but a human can only donate about 1 pint at a time. Hemopure can be stored for one year at a lower cost than freezing human red blood cells. Blood typing would be unnecessary, because the cattle haemoglobin used does not contain the outer portion of the red blood cells that gives blood its particular type. (Extracted from New York Times News, 25 February 1991)

Yeast brews up artificial blood

A subsidiary of the brewing company Bass is putting its excess brewer's yeast to good use. Using genetic engineering, the company Delta Biotechnology, has inserted the human gene for the manufacture of haemoglobin into yeast, which then produces haemoglobin that could be used, in a suitable formulation, to treat people seriously injured in accidents and assist in the treatment of heart disease and tumours.

Peter Senior, the technical director of Delta Biotechnology, stresses that haemoglobin can never do the same job as donated blood transfused into patients, but formulations, which may survive in the body for up to 24 hours, could be invaluable for people whose tissue needs urgent replenishment with oxygen because of serious blood loss.

The company says that the haemoglobin it harvests from the yeast is cheap, safe and identical to natural haemoglobins. Senior expects Delta's haemoglobin to cost around 50 pence per gram, ten times less than the cost of purifying it from red blood cells, the main existing source. Moreover, he says Delta's haemoglobin is guaranteed to be free of the viruses that could contaminate the blood-derived product and of any residual matter from the blood cells that might trigger allergic reactions in patients.

The oxygen-carrying formulations could also be invaluable for the treatment of tumours and cardivascular disease. The small size of the formulations compared to red blood cells means they could penetrate solid tumours, making them more susceptible to chemotherapy and radiotherapy and reaching inaccessible parts of the heart during surgery. (Source: New Scientist, 16 February 1991)

Ultrasound puts the heat on cancer

Using highly focused ultrasound to destory tumours with a blast of heat may soon bring relief to some cancer sufferers and avoid the use of invasive surgery. So far the technique has only been tested in rats and on tissue in test tubes, but its inventors say it could be regularly used in people in as little as one year from now.

Gail ter Haar, head of Therapeutic Ultrasound at the Royal Marsden Hospital in London and her colleagues are currently investigating the technique's use for treating liver cancer, but it

also has potential for curing tumours of the prostate, bladder, kidney and breast.

Their system works by directing ultrasound from a transducer outside the body through a lens to a localized target point inside the body. The lens, which is a biconcave piece of perspex, bends the sound waves to a focus in the same way as light waves. The team has also experimented with using a transducer, made of a piezoelectric ceramic, in the shape of a hemisphere so that the ultrasound is already focused and a lens is not required.

The concentrated ultrasound agitates the tumour tissue and very rapidly generates a temperature of 80°C. This produces a volume of destroyed tissue which is shaped like a cigar, about 1.5 centimetres long and 1.5 millimetres in diameter.

Because each shot takes only a couple of seconds, the process can be repeated as often as necessary until the required amount of tissue is destroyed. And since it is such a clearly defined area of damage, the tumour can be selectively destroyed without harming other tissues. The equipment can be linked up to an ultrasound imaging device at the same time so that users can see and direct the process.

Ter Haar and her colleagues proved the precision of the technique when they used it on rats which had tumours implanted in the liver. The technique proved so precise that the layer of cells between those that were completely destroyed and those which were unharmed was only six cells wide.

The new method should be particularly useful for treating metastases in the liver since these tumours arise from other major cancers elsewhere in the body and such patients are therefore very ill already. They might not survive the major operation that is currently required to remove the metastases, said ter Haar.

Almost any cancer that can be shown up on the imaging device will be suitable for the technique. This excludes tumours in the lung because the ultrasound cannot penetrate air or bone, but it could be used in muscle and even in the brain.

Another likely use for the technique is in the treatment of a swollen prostate gland according to John Wickham, director of the Institute of Urology at London University. (Source: New Scientist, 19 January 1991)

Cancer test singles out radiation-resistant cells

A new test could help to explain why some tumours are more resistant to therapy than others. The probe, developed in Britain, could one day help cancer patients by enabling doctors to tailor treatment to fit the composition of a particular tumour.

The test detects cells that lack oxygen, known as hypoxic cells. Scientists have long reasoned that a shortage of oxygen within a malignant cell enables it to survive radiation and drugs. Even if most of the cells in a tumour have an oxygen supply and are killed by therapy, the survival of just a few hypoxic cells may allow the cancer to survive.

When a cell is irradiated, much of the damage is caused when water molecules split. Highly reactive hydroxyl radicals form, and these damage the cell's DNA. This damage becomes permanent when oxygen is present. Without it, there is less permanent damage and more cells survive.

Doctors do not know what proportion of tumours recur because of hypoxic tumour cells that survive irradiation, but they do know that it takes almost three times as much radiation to inflict lasting damage on a hypoxic cell as on a fully oxygenated cell. If they could identify the hypoxic part of a tumour, they could supply more oxygen, increasing the chances of destroying the cells. They could also find out how wide-spread the problem is.

The new test, developed by Richard Hodgkiss and his team at the Mount Vernon Hospital in Northwood, Middlesex, and John Parrick and colleagues at Brunnel University uses specific antibodies that bind to a compound that forms only on hypoxic cells.

The probe is based on a compound known as NITP, which is formed from theophylline and the aromatic molecule nitroimidazole.

In the absence of oxygen, the NITP is reduced and binds to molecules within the cell. A specific antibody to theophylline then binds to the newly formed compound and the resulting complex is identified by a second, fluorescent antibody that makes the cells visible. Using flow cytometry, the team can count and locate the hypoxic cells.

The main advantages of the technique, says Hodgkiss, are its avoidance of radioisotopes and its precision. He doubts that NITP itself will be given to patients because, as a new pharmaceutical compound, it would have to be tested for years. Instead, the team hopes to develop related probes. (Source: New Scientist, 19 January 1991)

AIDS vaccine found safe in humans

The first AIDS vaccine to be tested on healthy volunteers has been found to be safe, although its effectiveness has not yet been established. The vaccine, called VaxSyn, stimulated the release of antibodies against human immunodeficiency virus-1 in 30 of the 33 people receiving it, indicating it triggered an immune response. However, the neutralizing activity of these antibodies was quite modest: Only five of 24 people tested produced antibodies that were able to block one strain of the virus from infecting cells in vitro. The neutralizing activity of these antibodies against other strains of HIV-1 has not yet been determined. Conducting such a study will be critical because a successful HIV-1 vaccine must be able to protect against several HIV-1 strains. VaxSyn was developed by MicroGeneSys Inc. of Meriden, Conn. It is based on a recombinant form of gp160, the precursor envelope protein of HIV-1. The trials, which are continuing, were conducted by Raphael Dolin of the University of Rochester (New York) Medical Center and colleagues at several other US research centres. They published their result in Annals of Internal Medicine [114, 119 (1991)]. (Reprinted with permission from Chemical and Engineering News, 21 January 1991, p. 17. Copyright (1991) American Chemical Society)

"Biocoating" seen as way to outwit immune system

Millions of dollars have been spent in the search for materials compatible with internal use, but with limited tangible results. Now, however,

Beacon Research Inc., thinks there is a better approach than has been tried before. The company calls it "biocoating".

As the word suggests, biocoating involves a coating that is biologically compatible with the body of mammals and acceptable to the immune system. It can be applied to almost any material, concealing its true identity from the system. It also makes the material smooth and slippery, reducing irritation to tissues.

Beacon has devised a way to permanently anchor the coating to plastics, rubbers, glasses and metals, giving the designers of synthetic organs an unprecedented choice of existing materials, including new light-weight, high-strength composites. The company has successfully tested the coating in animals. (Source: Chemical Marketing Reporter, 18 February 1991)

"Kamikaze" drugs

A class of protease-blocking drugs is being developed that are designed to self destruct or neutralize themselves after activation, thus avoiding problems caused by lingering or excess drugs in a patient's system. The "kamikaze" drugs are designed to be activated by a specific enzyme, to which they will bond, making enzyme and drug both inactive. James Powers of the Georgia Institute of Technology has tested an anti-clotting drug in rabbits, and found no drug residue detectable after five minutes. Targets for the new class of drugs will be enzymes that consume proteins. (Extracted from Discover, February 1991)

Agricultural applications

Field testing of genetically engineered corn

Biotechnica International has submitted an application to the US Department of Agriculture for permission to conduct multiple field tests of corn genetically engineered with a commercial gene for improving nutritional quality. Tests are planned from early spring in Iowa, Illinois, Minnesota and Nebraska. The genetically engineered corn is intended to add value to existing grain for feed, a $10 billion market, by reducing the need for synthetic supplements. (Source: European Chemical News, 11 March 1991)

Approval for use of fungus on plants

W.R. Grace (New York) has received approval from the US Environmental Protection Agency to use a fungus to control a pair of common plant diseases. The Grace product - a strain of Gliocladium virens - is formulated into pellets that are applied to the soil to control two disease-causing fungi, Rhizoctonia solani and Pythium Ultimum. Grace aims to commercialize its biocontrol fungus in two years. While the EPA approval is for use on greenhouse plants, Grace says it could eventually seek federal approval for the fungus's outdoor use. Grace has exclusive license to the technology, which was developed by the US Department of Agriculture. (Source: Chemical Week, 5 December 1990)

Pheromone to control beet armyworm

Shin-Etsu Chemical (Tokyo, Japan) has synthesized the female sex pheromone of the beet armyworm, a hard-to-control vegetable pest. The firm is marketing Yotoucon-S for control of Spodoptera exigua by setting time-release tubes of the agent in vegetable fields where it diffuses, confusing the male insects and reducing their mating opportunities. The short 30-day life cycle of the insects has made them difficult to control with insecticides. The pheromone agent is said to be harmless to humans and plants, and is in widespread use in Japan. (Extracted from New Technology Japan, January 1991)

Natural pesticides growing; biotechnology comes of age

Natural pesticides and biologically engineered crops are gaining ever-wider interest, and producers say these will alter world agricultural production in coming decades. Sales of natural pesticides are rising, and a wave of new products is expected for the second half of the 1990's, but the market is still in its infancy and producers have no idea of its eventual size.

Environmental concerns and a need to improve pesticides are fueling interest in biotechnology. Producers say natural pesticides are safer, cheaper and more effective than conventional ones. Insects are developing resistance to many conventional pesticides, and tighter EPA regulations are shrinking the number of available pesticides because producers are often unwilling to pay for environmental testing and reregistration of niche products.

Biologically engineered crops are also being developed and should be commercialized towards the end of the 1990's. These are plants that have been genetically altered to produce more food, withstand diseases or chemical pesticides, or produce toxins that kill insects. Such crops may eventually reduce the need for pesticides, but environmentalists are skeptical of them and they face considerable testing before they can be commercialized.

"Three factors account for the rise of biological pesticides", a producer says. "Safety concerns are driving the industry to look for environmentally-benign replacements for traditional pesticides. That is the main factor. But stricter EPA regulations are eliminating small-volume products too expensive to reregister, and insects are developing immunities to older pesticides."

"Biotechnology is enabling us to attack problems that cannot be controlled or are controlled only with chemical pesticides", he adds. "It is a low-cost means of control for farmers. Chemical pesticides aren't always used efficiently. Farmers tend to bomb their fields. Biological pesticides can be used by even the most basic farmer in any Third World country."

Producers say bioengineered pesticides will never replace traditional ones completely, but they are expanding the $20 billion world-wide pesticide market and taking an ever widening share of it.

Another producer adds, "Biological pesticides work only on specific families of pests. They are not effective against all pests, and they can never replace chemicals completely, but the two work well in conjunction with each other, and bioengineered products will take an ever larger share of the pesticide market." (Extracted from Chemical Marketing Reporter, 21 January 1991)

The future written in a grain of rice

In Asia rice is more than a mere food, though it does provide the main source of calories for 2.7 billion people. One crucial achievement of the past 30 years has been to increase production of rice faster than Asia's population has grown. Over this period the real price of rice has halved and the disastrous famines predicted by so many people never happened.

It was the green revolution, rather than any form of divine intervention, which caused this success; it would have been impossible without new high-yielding varieties of rice. The first of these, IR8, was made available in 1966 by the International Rice Research Institute (IRRI) an independent organization based at Los Banos, in the Philippines. A cross between a dwarf Chinese rice and an Indonesian variety, IR8 changed the architecture of the rice plant. It had shorter and stronger stems so that it would not fall over when increased use of nitrogen led to bigger heads of seed (panicles). Improved varieties have been developed since then. IR36, made available in 1982, was bred from 13 parents to have genetic resistance to 15 pests and a growing cycle of only 110 days (compared to 180 days for traditional varieties), thus permitting up to three crops a year. It is now the most widely grown crop variety in the world.

Gurdev Khush, IRRI's chief plant breeder and the creator of IR36, believes that existing techniques could be used to increase rice production by 25-30 per cent over the next decade. The world's population is forecast to continue to grow for at least the next 30 years, by which time there will be perhaps 4.3 billion rice eaters.

To feed all of them, the world's rice production will have to grow by at least 10 million tons a year every year between now and then. Circumstances make it more difficult to achieve than it might sound. Without heavy and continuous investment, irrigated land deteriorates as its salinity rises. Soils asked to yield two or three crops a year rapidly run out of nutrients, while bugs living in them thrive. Even on IRRI's 252-hectare model farm, yields are showing a long-term decline. Outside that farm, the problem of stagnant or declining yields is compounded by a loss of prime land to rapidly expanding cities.

Mr. Khush and his colleagues are trying to breed a new super-rice, capable of feeding many more mouths from less land. It will look very different from existing varieties, which typically have 20-25 stalks (or tillers), of which only 15-16 produce panicles. Super-rice will have 3-4 tillers, each of which will produce a large panicle. It will need sturdier stems, dark green leaves (with more chlorophyll and so better growth), more vigorous roots and genetic resistance to a multitude of diseases and insects. Farmers will be able to seed it directly, rather than having to transplant seedlings, which is what makes rice farming so laborious now. This paragon will produce 13-15 tons per hectare from each crop, compared with a maximum output of current varieties of 9-9 tons.

Biotechnology may hold the key to developing this new variety. Since 1985 the Rockefeller Foundation has spent $7 million a year on a rice biotechnology network whose aim is to ensure that genetic techniques to improve cash crops of interest to rich consumers, such as tomatoes and tobacco, are also developed for rice. Members of the network have already made steps forward.

The most promising avenue for genetic research in the short term is increasing rice's resistance to pests. This is because usually only one gene is needed to confer resistance to a specific pest. The next major hurdle to overcome will be to refine the tools available so that they are capable of identifying and manipulating a number of genes at the same time. Only then will geneticists be able to tackle more complex questions such as what makes rice more tolerant of salt in the water in which it grows or, most important of all, which groups of genes govern its yield. (Extracted from The Economist, 9 March 1991)

Herbal secrets

The Hong Kong Institute of Biotechnology has joined forces with the American pharmaceuticals company Syntex and the Chinese Academy of Sciences to track down the active ingredients of Chinese herbal remedies.

The three-year-old institute and Syntex have formed a joint company to screen compounds for their potential as new pharmaceutical products. They will be looking at samples of Chinese herbs and other medicinal products collected by members of the Chinese Academy. The project also breaks new ground in its liaison with Chinese scientists. (Source: New Scientist, 27 April, 1991)

Improving the sweet potato

Agricultural Genetics (AGC) (UK) will jointly research the transfer of the cowpea trypsin inhibitor (CpTI) gene into the sweet potato in an effort to render sweet potatoes genetically insect resistant. AGC will work with the International Potato Center in Lima, Peru, and Durham University (UK) on a project funded by the UK Overseas Development Administration (ODA). The sweet potato may be able to play a leading role in the alleviation of famine, since the crop can be grown under a variety of conditions, but it is prone to damage from a number of insects. Conventional breeding has not produced a sweet potato strain resistant enough, while agrochemical options are not economically tenable. Researchers predict novel strains of sweet potato will be available in the mid-1990s. (Extracted from European Chemical News, 24 February 1991)

Food and Food Processing Applications

Shellfish stop the rot in fruit

Crabs, lobsters, shrimps and other shellfish could provide a cheap and abundant raw material for a preservative that extends the shelf-life of fruit. Because the preservative is derived from natural sources, it may be more acceptable to consumers than existing synthetic preparations.

In February 1990, the US Environmental Protection Agency withdrew Alar, a synthetic preservative and growth regulator sprayed on apples, after receiving reports that a breakdown product of Alar caused tumours in mice. Christina Anne Carolan, a researcher at Queen's University Belfast, and colleagues have developed a preservative from chitin, the hard component within the shells of

crustaceans. "Chitin is second only to cellulose as the most abundant biopolymer in nature", she said.

Carolan and colleagues have chemically modified chitosan, a derivative of chitin, so that it dissolves in water to form a transparent gel. Apples coated with the gel stayed fresh for at least six months.

Carolan and colleagues make the preservative - which has the chemical name N,O-carboxymethyl chitosan (NOCC) - by reacting chitosan with monochloroacetic acid under alkaline conditions. A patented synthesis for NOCC already exists, but the product from this route has only limited application as a preservative because it biodegrades after two months. NOCC that has been produced using this technique has been approved by the Environmental Protection Agency as a seed coating to increase crop yield. But by varying the reaction conditions, the Irish team succeeded in making the biopolymer with slightly different structure. This type of NOCC had a shelf-life of at least six months.

The new gel is permeable to some gases and vapours but not others. It traps carbon dioxide, which prolongs the shelf-life of the apple, and excludes oxygen which rots the fruit. (Source: New Scientist, 19 January 1991)

Reishi mushrooms

A San Antonio wholesale nursery has been able to capitalize on a Japanese health trend by producing the Far East's most precious health food: the Reishi mushroom. Reishis are a rare and expensive commodity in Japan and Lone Star Growers is one of the few places in the world to master the plant's meticulous growing techniques. After harvest, the mushrooms are pulverized into pills and exported to Japan, but demand for the Reishi tablets has also spread to the domestic market. The nursery originally began growing the Ganoderma lucidum to aid researchers from the University of Texas Health Science Center at San Antonio who were studying the anti-inflammatory properties of the mushroom - long used in Oriental medicine to relieve a wide range of ailments. including hypertension, diabetes, insomnia, inflammation, arteriosclerosis, high cholesterol, baldness, and attacks on the immune system. (Source: BioBytes San Antonio Biotechnology News & Information. Produced by Dublin-McCarter & Associates, April 1991)

Looking for the natural edge

The large-scale production of natural beta-carotene is a fast-growing business. While a company in Australia is literally reaping the profits, British scientists are looking for new ways to coax the pigment from micro-organisms in a controlled environment.

Beta-carotene has traditionally been used as a food colouring agent. More recently medical studies have suggested that consumption of beta-carotene could help prevent certain diseases.

Synthetic beta-carotene has been manufactured for 30 years, but since 1985, one Australian company has been exploiting the increasing market for products from natural sources. Total sales for the company, Betatene Ltd., of Victoria, were A$2.27 million last year, almost double the earnings achieved the year before.

At the heart of the operation lies the alga Dunaliella salina. In conditions of high salinity and light intensity, and in arid climates, it produces elevated concentrations of beta-carotene, which aggregates as bright red droplets within the cells.

At its site in Whyalla, Betatene operates three algal cultivation lakes totalling 260 hectares. The company's harvesting plant can process brine at the rate of 1 million litres per hour. A spray drier produces algal meal powder, used as a prawn feed supplement by Japanese clients.

The technological side of the operation has not been without its teething troubles. For instance, it has been difficult to achieve consistent densities of viable alga, and high beta-carotene yields.

Because Dunaliella farming requires specific climatic conditions, biotechnologists are seeking alternative systems for the commerical production of pigments from natural sources.

At Liverpool Polytechnic's school of life sciences, Andrew Young has launched a project aimed at identifying microalgae which are capable of generating large quantities of important carotenoid pigments such as beta-carotene and astaxanthin.

Studies have indicated that high pigment concentrations are produced when the organism is under stress. Young is therefore systematically screening a large number of marine and freshwater microalgae for their ability to produce elevated quantities of pigment, by stressing the cultures in other ways - limiting nutrients, varying the pH, and so on.

Algae that do not require light will be of particular interest, because they should be cheaper to grow under artificial conditions. When a potential candidate has been identified, the tests will be scaled up to near-commercial levels. (Source: Chemistry & Industry, 1 April 1991)

An explosive start to fast-maturing cheeses

Cheeses that mature in days instead of months are now in prospect thanks to the development of so-called "exploding starter cultures", which may also lead to new types of cheeses. These new cultures are identical to the conventional bacterial cultures that cheese makers add to milk to make it ferment into cheese, except that the bacteria have been endowed with an extra gene that makes the cells of the culture disintegrate, liberating enzymes that give cheese its flavour.

Normally, the bacteria take months to break down after the preliminary phase of fermentation, so the enzymes that impart flavour are locked away during that time. Mike Gasson, Claire Shearman and Karen Jury at the Agricultural and Food Research Council's Institute of Food Research in Norwich have engineered a viral gene into the bacteria in the cultures which, when activated, makes the bacteria self-destruct. The investigators are now seeking a "switch", such as a temperature change or a variation in salinity, to trigger the foreign gene into action.

The source of the gene is a virus that naturally infects the lactococcus bacteria used in

cheese manufacture. Ironically, the virus is normally considered a difficult industrial problem. Some cultures are vulnerable to the virus, called a bacteriophage, and this limits a cheese maker's choice of starter culture.

Gasson's team have turned the characteristics of the bacteriophage to their advantage. They isolated the gene within the phage that codes for the manufacture of lysin, an enzyme that causes the walls of an invaded bacterial cell to break open. Gasson's team is seeking regulatory approval before testing the genetically engineered lactococcus in cheese maturation experiments. (Source: New Scientist, 16 March 1991)

Protecting our food supply

An International Standard has been issued which gives general guidance for the detection of Vibrio parahaemolyticus, a food pathogen that can be present in products intended for human consumption or animal feeding stuffs.

The standard was prepared by ISO/TC 34/SC 9, Agricultural food products - Microbiology.

Vibrio parahaemolyticus stems from a genus of short, rigid, motile bacteria that include a few important pathogens that are the cause of Asiatic cholera and abortion in cattle and sheep. Vibrio parahaemolyticus, which is a food pathogen, is mostly found in seafood and shellfish and is a problem particularly in Japan. Its effects include diarrhea and it can be life-threatening for the very young and old.

The standard, ISO 8914, Microbiology - General guidance for the detection of Vibrio parahaemolyticus, defines Vibrio parahaemolyticus as halophilic micro-organisms which form characteristic colonies on solid selective media, and which display the biochemical characteristics described when the tests mentioned in the standard are carried out.

The standard contains provisions relating to ISO 6887, Microbiology - General guidance for the preparation of dilutions for microbiological examination, and ISO 7218, Microbiology - General guidance for microbiological examinations.

In general, the detection of the micro-organism is carried out in three successive phases: enrichment in selective media; plating out and identification; and confirmation. The standard gives specifications for the culture media and reagents as well as for the test apparatus and glassware to be used. Other sections deal with sampling, preparation of the test sample and procedures to be followed.

Normative annexes show a diagram of the procedure to be followed and the composition and preparation of culture media and reagents. A bibliography has been included as an informative annex. (Source: ISO Bulletin, February 1991)

Energy and Environmental Applications

Battelle scientists dig deep for answers to waste clean-up

Micro-organisms living hundreds or even thousands of feet beneath the eastern Washington desert may hold the secret to cleaning up part of the contamination at the US Department of Energy's Hanford Site and other areas polluted with hazardous and/or radioactive wastes.

Microbes in the subsurface environment may be able to break down some of the wastes produced during nearly 50 years of nuclear materials production at Hanford. Scientists recently began drilling a deep bore hole on the Hanford site to search for microbes that can survive in a low-oxygen environment by consuming other materials, including hazardous substances. They expect to reach a depth of 350 feet. The drilling is part of the US Department of Energy's Subsurface Science Program.

Already researchers at Battelle's Environmental Sciences Research Center, based at the Pacific Northwest Laboratories, have shown that some organisms can render some chemical compounds harmless. One type of organism can neutralize potentially toxic nitrates in ground water while simultaneously destroying carbon tetrachloride, a carcinogenic solvent extensively used over the years at many industrial sites.

To ensure that micro-organisms are not inadvertently introduced from the surface, workers take special precautions during coring to disinfect the drilling and sampling tools and use other techniques to extract undisturbed core samples. Details from: Pacific Northwest Laboratories, Battelle Boulevard, P.O. Box 999, Richland, Washington 99352, USA. In the UK, talk to Renate Siebrasse, operations manager, Battelle Institute Ltd., 15 Hanover Square, London W1R 9AJ or on 071-493 0184. Fax: 071-629-9705. (Source: Biotechnology Bulletin, Vol. 9, No. 12, January 1991)

Uranium-hungry microbes filter toxic waste

Microbes with the modest name GS-15 may be the secret to removing uranium from toxic waste dumps and polluted water around uranium mines. The bacteria acquire energy by converting a form of uranium that dissolves in water into one that is insoluble.

Derek Lovley, a microbiologist with the US Geological Survey in Reston, Virginia, says he went looking for uranium-eating bacteria to clean up toxic waste at plants where nuclear weapons are made. Lovley tried GS-15 bacteria because they can live on another metal - iron - and they also break down the poisonous hydrocarbons toluene and benzene. These bacteria were first isolated in 1987 from sediments in the Potomac River.

The microbes are not useful for removing iron pollution from water, because they turn particles of insoluble ferric iron into ferrous iron, which dissolves in water. But they have the opposite effect on uranium.

If water polluted with uranium passes through a "bioreactor" filled with GS-15 bacteria, the microbes will transform the uranium into particles that precipitate out and settle to the bottom. Collection and disposal is then much easier.

Naturally occurring bioreactors may be the source of a mineral form of uranium called uranite. The uranite could be the remains of large colonies of uranium-eating microbes that lived in streams containing dissolved uranium. (Source: New Scientist, 6 April 1991)

Will viruses vanquish the Adriatic's algae?

Algae blooms that have regularly covered the beaches of Italy's Adriatic coast with a frothy scum could be controlled using naturally occurring viruses, according to research by scientists at the University of Göttingen in Germany.

Algae belonging to two groups, the Chysophyceae and Dinophyceae, are the main culprits for algal blooms in the Adriatic and North Seas. A team from the university's Institute of Plant Physiology, led by Werner Reisser, has already isolated and identified viruses capable of killing strains of freshwater Chlorella algae. They intend to use this information as a model system for other virus-algae interactions.

According to Reisser, the viruses that infect Chlorella attach to specific sites on the cell wall of the algae. Reisser thinks the virus breaks into the algae by releasing enzymes which digest the carbohydrates in the cell wall. Then, by some unknown mechanism, the virus DNA penetrates the interior of the algal cell and hijacks its genetic machinery for reproduction. As the viruses multiply, the cell eventually breaks open, releasing the viruses to infect other cells.

Reisser and his colleagues have isolated viruses capable of killing some species of Chlorella. Under laboratory conditions, the Göttingen group has been able to use these viruses to infect other samples of Chlorella.

The prospect of genetically modifying a virus in order to enhance the killing of algae is still a long way off, however. It is also unlikely that any authority would want to take the risk of releasing such a modified virus into the environment.

With support from the government-funded German Research Organization, the Göttingen team is trying to understand how the virus infects plant cells, in particular those physical conditions under which the virus is most harmful to the algae.

Reisser believes this approach could also provide opportunities to kill toxic algae and cyanobacteria (blue-green algae) in drinking water and in fish farms. In the longer term, he sees the potential to control the growth of large-scale marine algal blooms such as those seen in the Adriatic and North Seas. (Source: New Scientist, 23 March 1991)

Safe drinking water for the developing world

Despite the best efforts of the United Nations and its agencies, the 1980s did not bring clean drinking water to the millions who need it. According to the United Nations Economic and Social Council (ECOSOC), one of the main reasons for the failure of the Decade was the use of technology too sophisticated and expensive for the target communities. Instead of using expensive imported technology, cheap local materials should have been used. Work being done by the Engineering Departments of the Universities of Malawi, and Leicester, in the UK, has identified just such a material. The seeds from a tree.

The idea is not new; it was reputedly discovered by Sudanese women carrying water many years ago. They would place leaves on the surface of the water to stop it splashing out of the container. In time they discovered that some leaves made the water taste sweeter.

In India, seeds of the tree Strychnos potatorum have been used to clarify muddy water for some 4,000 years. One researcher on natural water purifiers, Samia Jahn, has identified hundreds of natural purifiers ranging from seeds, nuts and saps to clays which have been used for centuries in rural communities all over the world. Now the joint university project is investigating the feasibility of commercial scale production of a natural coagulant from the seeds of the Moringa oleifera tree.

The first phase of the Malawi/Leicester project involved a study of the efficacy of the Moringa oleifera seed as a coagulant. Its efficacy was compared with the seed of a similar tree, Moringa stenopetala which was known to be an effective coagulant, and with alum.

Both trees are indigenous to many parts of the world. Moringa oleifera was introduced into Malawi by people from the Indian sub-continent who prized its edible seed-pods, which are similar to okra but two or three times the size. Some Malawians also eat the leaves as a relish.

Water purification can simply be achieved by crushing the seeds and adding the powder to a pot of water. It is then allowed to stand for a few hours so the suspended particles can coagulate and sink to the bottom.

Tests in Malawi at the Polytechnic in Blantyre have found little difference in the efficacy of the two seeds. The reduction in turbidity (cloudiness) of water obtained by using either seed was equal to and sometimes better than the results obtained from alum, particularly in the case of heavily turbid water.

The tests on bacterially contaminated water showed that both were significantly effective in inactivating bacteria and preventing regrowth. Further study is planned on the effects of these seeds on specific viruses often present in water, for example polio and herpes simplex.

The real breakthrough came with the discovery of the efficacy of co-coagulation. When a small amount of alum is added to the crushed seed its effectiveness equals that of a much larger quantity of alum alone. It is estimated that a 75 per cent reduction in the use of alum could be obtained by substituting the crushed seed of oleifera.

Phase two of the Malawi/Leicester project involves growing oleifera on a commercial scale. Three different sites with varying soil, rainfall and drainage characteristics have been identified. The nursery stage is complete and the seedlings will be planted out in the first rainy season of 1991. The trees are expected to start bearing seeds within ten months and may reach maturity within five years.

Moringa trees seem to grow easily and quickly in a variety of different conditions. If rural communities could grow their own trees they could provide themselves with substantially cleaner water than they have been used to. Then, there are the added bonuses of edible leaves and seed pods, and wood for building and fuel. The small scale needs

of many rural communities make this form of water purification particularly attractive.

On a national scale, there are many economic and technological advantages of this renewable resource, particularly savings in foreign exchange and transport costs. The only disadvantage is that the crushed seeds are organic and subject to decay if poorly stored. Production on a commercial scale is viable, however, if the seed is crushed and freeze-dried, although this significantly increases the storage and transportation costs. This then raises the possibility of export returns from widespread use of the seed throughout the developed world, with health benefits and economic advantages to producers and consumers alike. (Source: Our Planet, Vol. 3, No. 1, 1991)

Monsanto uses bacteria to clean waste streams

Researchers at Monsanto have developed a unique process that uses immobilized bacteria to treat complex industrial waste streams in the presence of salt.

The process has been used successfully to treat up to 100 gallon/day of effluent at Monsanto's WG Krummerich plant in East St Louis. Typical waste chemicals include p-nitrophenol, o-nitroaniline, p-nitroaniline, 4-nitrodiphenylalanine, 4-aminophenylalanine, ethylbenzene, xylene, methyl ethyl ketone, aniline and potassium formate.

Science fellow at Monsanto, Bill Adams and his team are putting together a proposal, including a design for a full-scale treatment unit, in order to make a presentation to Monsanto's vice president. If approval is given, Adams predicts construction of a full-scale plant could begin in 1992.

Monsanto is in the process of taking out patents on the bacterial species used in the process. The researchers found suitable bacteria by taking those already being used to treat chemicals at a nearby waste treatment facility and gradually exposing them to increasing salt concentrations in the laboratory.

Adams said bacteria probably survived the salt conditions better because they were immobilized by attaching them to a support of activated carbon or a porous inorganic barrier made from diatomaceous earth.

Laboratory and on-site pilot plant data showed that the bacteria removed around 90 per cent of the dissolved organic carbon (DOC) and chemical oxygen demand (COD) from the waste, with reactor hydraulic retention times as short as six hours.

The experiments found that activated carbon was a better support to use than an inorganic biocarrier in the presence of chemicals that adsorb to carbon. Using a carbon support produced visually clear effluent, although a carbon system required a longer period of acclimatization.

The researchers concluded that the process of combining adsorption and biodegradation appears to provide a useful approach for treating industrial chemicals.

They also concluded that problems of volatilization of chemicals, such as methyl ethyl ketone (MEK), and biomass build-up are problems that require special handling. (Source: European Chemical News, 14 January 1991)

Industrial Microbiology

Degradation path for dichlorophenol found

The pathway by which the fungus Phanerochaete chrysosporium degrades 2,4-dichlorophenol has been characterized in detail for the first time. The findings should aid in the development of bioremediation strategies for chlorophenols, which constitute a significant category of environmental pollutants.

P. chrysosporium is the best studied of the white rot basidiomycetous fungi, which are capable of degrading lignin, the heterogeneous, random, nonhydrolyzable, phenylpropanoid polymer that is a major component of wood. P. chrysosporium secretes two heme peroxidases-lignin peroxidase and manganese peroxidase - that appear to be primarily responsible for the oxidative depolymerization of lignin. Several studies have shown that this fungus is also capable of breaking down a variety of chlorophenols.

At Oregon Graduate Institute of Science & Technology, Michael H. Gold, professor and chairman of the department of chemical and biological sciences, has been studying P. chrysosporium and its peroxidases for a number of years. In work supported by the Department of Energy and the National Science Foundation, Gold and postdoctoral scientist Khadar Valli have now shown that the pathway by which P. chrysosporium degrades 2,4-dichlorophenol involves several cycles of oxidation and subsequent quinone reduction and hydroquinone methylation, leading to the removal of both chlorine atoms from the substrate before cleavage of the phenolic ring occurs. The same general pathway is probably used for the degradation of tri- and pentachlorophenols. Efforts are under way in Gold's laboratory to isolate and characterize the individual enzymes that are implicated in the pathway. (Abstracted with permission from Chemical and Engineering News, 7 January 1991, pp. 22-23, by Rudy Baum. Copyright (1991) American Chemical Society)

Algae to the rescue

Tadashi Matsunaga and Shigetoh Miyachi, two of Japan's leading microbiologists, believe that tiny, genetically engineered photosynthetic micro-organisms may help to solve worries about global warming by mopping up carbon dioxide emitted from power stations and industrial plants. Japanese industry and MITI are prepared to back their ideas.

Matsunaga, who heads the department of biotechnology at Tokyo University of Agriculture and Technology in Koganei in the outskirts of Tokyo has built a 2-litre prototype "biosolar reactor" that can absorb all the carbon dioxide out of ordinary air bubbled through the reactor at 300 millilitres per minute. The reactor contains a genetically engineered marine cynanobacterium, Synechococcus sp., and is filled with a stack of 600 light-diffusing optical fibre cables that ensure even lighting and optimum growth of the bacterium throughout the vessel.

Matsunaga's reactor, however, is still a long way from providing a practical means of absorbing carbon-dioxide emissions from power plants and

industry because the levels of carbon dioxide in such emissions are much higher than the 0.03 per cent in air. And high levels of carbon dioxide usually inhibit growth of photosynthetic micro-organisms.

But researchers working under Miyachi, who heads MIT's marine biotechnology laboratories in Shimizu and Kamaishi, may have found a solution. They recently isolated a strain of marine green algae off the coast of Kamaishi that grows happily at concentrations of up to 20 per cent carbon dioxide. By isolating the genes responsible for carbon dioxide tolerance, they hope to genetically engineer strains of micro-organisms that can efficiently assimilate carbon dioxide at high concentrations.

Even so, it would require an enormous biosolar reactor to cope with the output of a power plant. Matsunaga says a typical megawatt-class power plant emits about 200 tons of carbon dioxide per hour. And if the biosolar reactor absorbed only a few per cent of this it would produce several tons of algal sludge per hour.

Matsunaga and Miyachi differ on how to deal with the sludge. Miyachi hopes to create strains of calcareous algae that can mop up the carbon dioxide and convert it into calcium carbonate that can be dumped at sea. His laboratories have been searching for suitable strains of calcareous algae in coral reefs in Palau and the Great Barrier reef off Australia.

Matsunaga, on the other hand, is trying to create strains of photosynthetic micro-organisms that produce useful extracellular products that are released into the green brew of the reactor. For example, the Synechococcus in Matsunanga's prototype reactor has been genetically engineered to produce the amino acid glutamate. And his team have other strains that produce antibiotics and plant growth hormones.

A remarkable feature of the research by the two groups is the enthusiastic backing it is getting from industry. Matsunaga's research is supported by six companies, including a cement manufacturer, and a maker of ball-point pens, through a new co-operative research centre at Matsunaga's university that was established by the Ministry of Education, Science and Culture in April 1990 to encourage collaboration with industry. (Source: Nature, Vol. 350, 28 March 1991)

Enzymes produce SB intermediates

SmithKline Beecham has announced it is to invest £9 million in replacing chemical production with enzyme production for intermediates of augmentin and Amoxil, the company's main semi-synthetic penicillin products.

The company says the new enzyme technology, which is jointly owned with another company, is signficantly more efficient than chemical processes and has made possible sizeable reductions in manufacturing costs and an increase in capacity. Also, enzyme production is carried out in mild conditions, not involving noxious chemicals and is therefore cleaner.

The project is expected to be completed by mid-1992. (Source: European Chemical News, 31 December 1990/7 January 1991)

Industry turns to oyster shells, plaice and nuts

Environmentally friendly compounds which come from nature's own laboratory are coming under the scrutiny of chemists. At the annual meeting of the American Chemical Society, held in Atlanta, Georgia, researchers presented novel uses for proteins from oyster shells and winter flounder (plaice), and for the fine flour from the shells of pecan nuts.

Oyster shells contain polyaspartic acid, which is a polypeptide, a segment of a protein. The molecule is useful because it binds crystals of calcium carbonate. This material forms the mineral scale in pipes, valves, pumps, tanks and other equipment used to handle water. Erich Mueller of the Univeristy of South Alabama and Brenda Little at the Stennis Space Center in Mississippi have synthesized a version of polyaspartic acid. They find that it retards the build-up of calcium carbonate scaling on metal equipment. It is also not toxic and is easily degraded, unlike other water-treatment chemicals.

Another sea creature - the winter flounder, or plaice - inspired the work of Thomas Caceci and his colleagues at Virginia Tech University in Blacksburg. The winter flounder can tolerate water at -2°C without freezing. It achieves this feat with the aid of a natural antifreeze - a relatively simple polypeptide. The polypeptide stops the fish's tissue freezing at a level of between only 1 and 3 per cent.

Caceci believes that molecules of the polypeptide bind to the face of an ice crystal, stopping water molecules from inserting themselves and building up an ice lattice. He says that this natural chemical is probably less harmful than today's antifreezes, or even salt, which corrodes metal.

Another chemist, Ramaswamy Raj of the University of Quebec, Canada, has come up with a use for pecan nutshells. Ground into powder, they can be added to polyethylene. When the nut flour is substituted for 40 per cent of the plastic, it improves the material's tensile strength by almost 50 per cent, though it reduces its resistance to impact. Raj says that the flour will make the bags more easily degradable as well. (Source: New Scientist, 27 April 1991)

Industry shells out for chitin

Many chemical, medical and pharmaceutical companies are now researching and in some cases developing and patenting chitin-based products. Protan, a Norwegian company, has been producing and selling chitin and chitosan from shellfish waste since 1984. It lists 13 broad areas for its products, from "personal care" to detoxification of industrial waste.

Other applications include treatment of sewage, dairy waste, paper mill effluent, food-factory waste, liquid radioactive waste and purification of drinking water. In Japan about 500 tons of chitin are used every year as a water purifier, and the US Environmental Protection Agency rates chitosan as acceptable for the purification of drinking water.

Using chitosan to remove suspended solids from food-processing wastes, such as cheese whey, has an additional benefit. As well as purified effluent, the method yields coagulated by-products rich in

proteins which can be added to feed for domestic animals. This seems to make the feed more digestible.

Chitin and its derivatives also have some very useful properties in the medical field. Between 1968 and 1975 researchers working for the American pharmaceuticals company Lescarden of Goshen, New York, filed five patents for the use of chitin and chitosan to accelerate wound healing. They found that chitin mats, fibres, sponges, sutures and films were much better than standard cartilage-based ones. The pharmaceuticals company Katakurachikkarin based in Hokkaido makes an artifical skin - a chitosan-collagen composite - that appears to enhance recovery from surgical wounds or burns. In 1983, doctors working for the Veterans Administration Medical Center in Omaha discovered that chitosan could also speed up blood clotting and used it to reduce the loss of blood following blood vessel grafts.

Chitosan can be produced in numerous forms - powder, paste, solution, film, fibre or spray - giving manufacturers huge scope for incorporating it into bandages, dressings, salves, sutures or disposable contact lenses. The body does not seem to reject these and they break down slowly to harmless carbohydrates, carbon dioxide and water. Because chitosan is absorbed completely in the body, it is an ideal carrier for drugs that must be released slowly. After tests on rats in 1978, some Japanese researchers claimed that chitosan reduces serum cholesterol. In Japan one can buy biscuits and noodles sold for the alleged benefits of the chitin they contain.

The food industry is developing ways of exploiting the emulsifying properties of chitosan to make mayonnaise and peanut butter. Chitosan could eventually find its way into any area where non-toxic, high strength films are required, from sausage casings to oven wraps and food packaging.

Some researchers even think these chemicals will be the basis of a biodegradable plastic. Technics, the hi-fi manufacturer, of Shizuoka in Japan has even made the vibrators of flat-panel audio speakers from chitosan, an idea which is supposedly based on the acoustic properties of crickets' wings. (Source: New Scientist, 9 February 1991)

Plastic from crab shells

Shikoku of Japan has developed a biodegradable plastic using superfine cellulose and chitosan from crab and lobster shells.

The translucent, pliable, composite film, which decomposes in soil within two months, is produced by dispersing superfine cellulose in water and mixing with an aqueous solution such as chitosan acetic acid.

Flexibility may be improved by adding a plasticizer such as glycerine although this may result in a slight loss of strength. (Source: Manufacturing Chemist, April 1991)

Monoclonal detectives

One of the difficulties faced by manufacturers is how to label a product subtly enough to make it difficult for counterfeiters to copy, yet not so subtly that it takes an age and costs a small fortune to identify the product as genuine.

Now a small subsidiary of Shell believes it has the answer. Biocode Ltd., based at the University of York, has used its expertise in the generation of monoclonal antibodies to develop a unique marking system that is applicable to almost any commercial product. Biocode's research director, Colin Garner, says the company's system is tamper-proof, simple to operate and can confirm the identity of a product at the point of sale, bypassing the need for laboratory analysis.

The technique involves selecting suitable marker chemicals for the product and generating antibodies to the marker. The marker chemical is added at tiny concentrations to the product during the manufacturing process. To test whether a product is genuine - that it contains the marker - it is brought into contact with the appropriate antibody.

One system uses a tiny syringe in which the antibody has been immobilized on a gel support. As the product - in this case in solution - is passed through the syringe, the marker chemical is drawn out and concentrated by the antibodies in the gel. If the marker is a dye, for example, the gel changes colour.

The system can also be used for surface marking. The marker is applied to the surface and can be developed by the antibody solution. Because the marker is used in such low concentrations - a few parts per billion - it is undetectable by other means. Only the manufacturer has the antibodies that can recognize it.

Each marker must be chemically stable within the particular product, acceptable on health and environmental grounds and must allow antibodies to be generated against it. To date the company has assembled around 30 marker chemicals.

But because an antibody can be generated to a combination of more than one chemical marker, the number of possible permutations is vast. Biocode believes the anti-forgery potential of the system is significant; an estimated 3 per cent of world trade is in counterfeit goods. (Source: Chemistry & Industry, 15 April 1991)

E. PATENTS AND INTELLECTUAL PROPERTY ISSUES

Cech wins first patent

More than four years after the first application for ribozyme technology was filed, the US Patent Office has granted the first patent (Number 4,987,071) to Thomas Cech and the University of Colorado.

Ribozymes, RNA catalysts that can specifically cleave other RNA molecules, are likely to have important pharmaceutical and biotechnological applications because of their ability to destroy RNA molecules that code for individual proteins.

Thomas Mann, chairman of United States Biochemical Corporation (USB), which holds an exclusive licence to Cech's work, says the patent covers "a broad range of catalytic RNA molecules, methods of using them and methods of synthesizing

[them]". This includes RNA enzymes that cleave RNA at any site except a specific four-nucleotide sequence, CUCU, for which USB already has a commercially available ribozyme product.

The new patent contains 63 separate claims, 10 fewer than when the application was first filed, and has been extensively revised since that time. Other applications are still under consideration, and according to Richard Warburg, a patent lawyer with Fish and Richardson in Boston, a second patent may be awarded to Cech later this year. (Source: Nature, Vol. 349, 7 February 1991)

Appeals court rules on biotech patents

The US Court of Appeals for the Federal Circuit has ruled on patents held by Amgen and Genetics Institute for erythropoietin (EPO). Although affirming that certain claims of Amgen's patent are valid and infringed by Genetics Institute, the appeals court's finding that Genetics Institute's claims are invalid partially reversed a US District Court in Massachusetts decision from late 1989. Both companies appealed following this earlier decision and a subsequent court ordered cross-licensing. Amgen's patent covers host cells and genetic sequences used in producing recombinant EPO. Genetic Institute's claims were on the purified natural protein. As a result, Genetics Institute is unable to manufacture EPO in the US. However, its overseas licensees, Chugai Pharmaceuticals and Boehringer Mannheim, still can manufacture and market EPO in countries granting approval. Amgen's US sales of EPO, which stimulates red blood cell growth and is used to treat certain forms of anaemia, reached more than $300 million in 1990. On news of the ruling, Genetics Institute stock fell $21.75 to $40-1/4 per share. Amgen's stock rose $12 to $113 per share, the second big jump for the company's stock following approval of its second major drug product. (Reprinted with permission from Chemical and Engineering News, 11 March 1991, p.15. Copyright (1991) American Chemical Society)

Synergen and New York University awarded patent on basic fibroblast growth factor

19 February 1991 - Synergen, Inc. and New York University Medical Center announced that they have obtained US Patent 4,994,559 for human basic Fibroblast Growth Factor (bFGF). Synergen is developing bFGF, a human protein, under the trademark TROFAX™, as a treatment for chronic skin ulcers. The company also has a joint venture with Syntex (USA) Inc. to develop bFGF to treat Alzheimer's disease, Parkinson's disease and other neurological disorders.

The patent, issued by the US Patent and Trademark Office, covers the human bFGF protein, first purified and characterized by Synergen and NYU Medical Center scientists working in collaboration. The patent is jointly owned by Synergen and New York University. Synergen's bFGF product, which is currently being manufactured for clinical trials in Synergen's pilot production plant, is the natural human protein described in the Synergen/NYU patent.

The company's bFGF is in Phase III human clinical trials for treatment of chronic skin ulcers. The initial study, with nearly 200 patients, at 13 medical centres, is now nearing completion. Since bFGF is also a potent neurotrophic factor, the Syntex-Synergen Neuroscience Joint Venture is developing bFGF as a therapy for treatment of Alzheimer's disease, Parkinson's disease and other neurological disorders. (Source: News Release, 19 February 1991)

Cetus wins patent victory

Cetus scored a major victory against Du Pont recently, when a US jury upheld the validity of two Cetus patents covering its GeneAmp polymerase chain reaction (PCR) technology. Patent infringement issues and the question of damages will be raised in another trial.

The polymerase chain reaction allows small amounts of DNA to be selectively amplified for analysis. It can be applied as a sensitive and rapid assay for diagnostic tests, forensic analysis and research. PCR also has potential applications in agriculture and food safety.

Du Pont initiated litigation in 1989, arguing that two Cetus patents, covering the PCR process and certain applications, were invalid. Du Pont claimed that earlier work published by Gobind Khorana, now at the Massachusetts Institute of Technology, had anticipated Cetus's 1985 invention by a decade. The jury, however, disagreed. The US Patent Office had already reaffirmed the validity of the patents before the trial, Cetus said.

In a separate but related counter-suit filed last December, Cetus has charged Du Pont with infringement of another PCR-related patent. Cetus says it will also seek a preliminary injunction, barring Du Pont sales of PCR materials.

Scientists at Cetus, Roche and the University of California used GeneAmp in a study which indicates that human papilloma virus, a sexually transmitted disease which has been associated with cervical cancer, is more prevalent than once believed. Cetus said that its method allowed researchers to identify previously unknown HPV types. (Source: Chemistry & Industry, 18 March 1991)

F. BIO-INFORMATICS

Biotechnology: EEC policy on the eve of 1993

Recent developments suggest that the European Community is beginning to make the political choices needed to fulfil its biotechnology potential. On 22 April 1990, the Member States adopted two Directives which go a long way towards establishing a regulatory framework for the biotechnology industry. A review of this framework can be found in **Biotechnology: EEC Policy on the Eve of 1993**, priced at BF 11,800 (including postage and packing). Details from: European Study Service, 43 Avenue Paola, B-1330 Rixensart, Belgium. Chapter headings are:

- An EEC strategy for biotechnology
- The regulatory framework
- Twelve agree on common rules on the contained use of genetically modified micro-organisms
- Protection of workers from the risks related to exposure to biological agents: Commission proposals

- Member States adopt a directive on the deliberate release into the environment of genetically modified organisms

- EEC partners pave the way for a common market in medicinal products arising from biotechnology

- A directive on the legal protection of biotechnological inventions on the way

- Cheaper agricultural raw materials for the manufacture of biotechnological products

- Research, training, concertation: on going initiatives

- Prospects.

These chapters, which also have detailed subheadings, are accompanied by an extensive list of annexes which detail various Council documentation and decisions. For those marketing into Europe, this is obviously a "must". (Source: Biotechnology Bulletin, Vol. 9, No. 12, January 1991)

Plant-derived chemicals subject of renewed interest

Riding a wave of interest in all-natural ingredients, biodegradability and environmental protection, the plant-derived chemicals business is expected to see renewed vigour, after a period of decline earlier in the century due to competition from petrochemicals.

Industry after industry is looking at plant-derived chemcials, says a BCC report, Plant-Derived Chemicals - Performance Requirements, Applications and Manufacturing (distributed in Europe by RauCon), providing opportunities for suppliers of plant-derived chemicals and for plant biotechnology. Among the products considered are rubber, lignin, alkaloids, enzymes, allelopathics and lectins.

But the challenge, RauCon concludes, will be to stay ahead of the competing new alternative of stereochemical chiral technology, which seeks to duplicate natural substances with synthetic chemicals. Details of the report, which costs $2,850.00, from: Dr. Norbert Rau, RauCon GmbH, POB 1069, D-6912 Dielheim, Germany or on +49 (6222) 73562. (Source: Biotechnology Bulletin, Vol. 9, No. 12, January 1991)

ESF Reports on Genome Research

The European Science Foundation (ESF) has published a report on genome research outlining the scope of genome research throughout the world, and the likely future directions of human genome research.

They also put forward recommendations for European research, including:

- Consolidation and enhancement of existing coordinating mechanisms, such as the EC Human Genome Analysis Programme, and HUGO.

- Development of shared European facilities for high volume or large scale experimental procedures e.g. characterization of gene functions; and automated approaches to DNA analysis.

- Urgent consideration of the practical consequences of genome research.

Further information from: European Science Foundation, 1 quai Lezay-Marnesia F-67000 Strasbourg, France. Telephone: 88 35 30 63; Telex: 890 440; Fax: 88 37 05 32.

EBIS to provide bio-information services across Europe

The European Biotechnology Information Service (EBIS) is edited by staff of CUBE, the Concertation Unit for Biotechnology in Europe. CUBE is a small team based in the Directorate-General for Science, Research and Development (DG XII) of the Commission of the European Communities.

The service is likely to be both paper-based and available on an electronic bulletin board. Details from: Dr. M. F. Cantley, CUBE, DG XII, Rue de la Loi, B-1049 Brussels, Belgium or on +32 2 235 8145. Fax: +32 2 235 5365. Email Telecom Gold DB10538. (Source: Biotechnology Bulletin, Vol. 9, No. 12, January 1991)

CUBE + ERICA initiative on consumers and biotechnology

A series of workshops promoting a dialogue with consumers on the subject of biotechnology has been organized by the European Foundation for the Improvement of Living and Working Conditions, in association with CUBE, the European Commission's Concertation Unit for Biotechnology in Europe.

The Foundation and CUBE have worked with Ms. Eirlys Roberts of ERICA (European Research into Consumer Affairs) in putting together the workshops. Following the first workshop, Ms. Roberts wrote a booklet, The Public and Biotechnology, which is available from the Foundation in English, French, German, Spanish or Italian - and in effectively unlimited quantities. Details from the Foundation on +353 1 826888. (Source: Biotechnology Bulletin, Vol. 9, No. 12, January 1991)

Agribusiness monitors agricultural biotechnology

CAB International and CPL Scientific have published what they believe to be the first news quarterly to focus extensively on the impact of technical change for the prospects of agricultural biotechnology.

Impact AgBioBusiness is based on the technical resources of the CAB ABSTRACTS database, a compilation of some 150,000 research summaries per year created by scientists scanning over 10,000 scientific journals, reports, conferences and books. Details from: Dr. Christina Cunliffe, CAB International, Wallingford, Oxon OX10 8DE or on 0491-32111. Fax: 0491-33508. (Source: Biotechnology Bulletin, Vol. 9, No. 12, January 1991)

ATCC catalogues on yeasts and plant viruses

The ATCC has also published a new catalogue "ATCC Catalogue of Yeasts, 18th edition, 1990". This 230 page reference catalogue lists over 4,000 yeast strains available from the ATCC. The catalogue provides strain descriptions which include genotypes, source of isolation, literature

references, media formulae, special applications, and more. New to the catalogue is a section of chromosome maps of overlapping continuous genomic clones (contigs) from Saccharomyces cerevisiae. Available for $US 9.00 outside the USA. Copies from: ATCC Marketing, 12301 Parklawn Dr., Rockville MD 20852 USA.

The new Catalogue of Plant Viruses and Antisera, 6th edition, 1990 lists over 500 virus and viroid strains, 200 polyclonal antisera and 90 molecularly cloned viruses. The catalogue contains strain descriptions, source references, and host plant names. The catalogue also has a taxonomic listing, index to molecular clones, and crop susceptibility table. This publication is available for $US 5.00 to all foreign locations. Copies from the same address as above.

Biotechnology business news

The British publication Financial Times has commenced publication of this twice monthly review of the international biotechnology industry. We have not seen a copy yet, but the Financial Times usually offers newsletters of good quality. Those wishing to subscribe should contact Carolyn McNamara, Biotechnology Business News, Financial Times Newsletters, London UK (Fax: (071) 240 7946).

Animal Biotechnology Bulletin

The Animal Biotechnology Bulletin is a new quarterly publication published by the Regional Coordinating Centre of the UNDP/FAO Asian Network for Biotechnology in Animal Production and Health. This Bulletin aspires to serve the scientific community in general world wide and Asia specifically. It reflects current biotechnological developments in relation to animal production and health, and the challenges facing biotechnology and molecular biology in the decades ahead. Short review papers and research notes, as well as national news on important research results and development, extension work to educate farmers and other users of biotechnology are welcome. Further information from the editor, Animal Biotechnology Bulletin, Regional Coordinating Centre, ANBAPH, c/o Institute of Animal Science, CAAS Malianwa, Haidaa 100094, Beijing, People Republic of China.

BioINVENTION: Comprehensive review of biotechnology patents, published by: BioSource, Inc., P.O. Box 550, Howell, NJ 07731

Each month's issue provides a comprehensive and cost effective means for technology managers, researchers and marketers to keep abreast of the vast wealth of information contained in patents in biotechnology and related fields. Cross referenced by keyword, inventor and assignee, BioINVENTION provides users in industry, academia and government full text information on the latest patents covering the Healthcare, Diagnostics, Agriculture, Chemical, Food industries and more.

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Price includes delivery by First Class Mail. For more information: Thomas J. Puskar, 908-905-5728.

Scitech Technology Directory 1991

This excellent annual comprehensive guide to Technology and Industry Development Assistance in Australia is now available in its 1991 edition. It has been extensively updated to take into account the numerous changes to Federal and State Government programmes, the venture capital industry and the higher education sector over the last year and includes all new Government, education and private sector programmes which have been set up since the previous edition.

The Directory is available for $95.00 (plus $5 postage and packing) from Scitech Publications Pty. Ltd., GPO Box 1915, Canberra, ACT 2601 (Tel: (06) 247 7220; Fax: (06) 249 6648)

Risk Assessment in Genetic Engineering: Environmental Release of Organisms. Edited by M. Levin and H. S. Strauss. McGraw-Hill: 1991, pp. 403, $39.95, £37.95.

Risk Assessment in Genetic Engineering gives a good picture of the state of the risk-assessment industry in the United States, where environmentalists, government agencies, firms of private consultants, lawyers and academics, not to mention the companies attempting to test and market their products, are locked in expensive (or lucrative) controversy and negotiation. Levin and Strauss's compendium consists of 17 chapters by different authors, writing from a variety of different standpoints - scientific, technological, administrative and social/political. The subject matter is confined to plants and the control of plant pests, presumably because it is only in this area that environmental release of manipulated organisms is in prospect.

The earlier chapters review the conceivable hazards from different applications of genetic engineering - engineered organisms and toxins for pest control, safety of transgenic plants as food, use of viruses to mitigate viral infections, horizontal gene transfer, the cultivation in open fields of transgenic plants. Several of the authors make recommendations on precautions, either during preliminary tests to assess hazards or after full-scale release.

Miracle or menace: Biotechnology and the third world. Robert Waldgate. Panos Institute, 1990

Biotechnology, the manipulation of plant and animal species by controlled breeding and genetic engineering, raises scientific, legal, ethical and commercial questions, and much acrimony. For example, Mexico provides a quarter of the genes used in the main US wheat varieties, yet receives no financial return for this contribution. The potential for future conflict between developed and developing nations is enormous when it is considered that developing nations harbour approximately 65 per cent of the world's genetic resources.

Waldgate's book aims to improve debate on the control over, and benefit from, genetic resources.

And there are very real benefits in settling this conflict as soon as possible. For example, the yield of cassava, the staple food crop throughout much of Africa, could be quadrupled if disease-resistant strains could be developed. The main obstacle in the development of such strains is that much of the experience, knowledge and laboratory equipment needed for this work belongs to the developed world, and the returns from this kind of research are insufficient to attract research staff and companies.

The book outlines not only the debates but gives basic background material on the science and economics of biotechnology. Particular emphasis is given to the role of biotechnology in crop plants like cacao and cassava, and in medicine. Chapters are devoted to impacts on the use of animals in farming, the engineering of microbes (for example, a microbe has been developed to digest spilt oil), farmers' rights, the relationship between public and private interests, and the environmental hazards posed by the release of engineered species and varieties.

Waldgate does not hesitate to point at the developed world for using genetic resources from developing countries for highly lucrative food and medicinal materials, yet failing to pay for the use of this material.

The book is well laid out with clear chapter breakdowns, and boxes of salient facts for easy reference throughout the text.

First the Seed: The Political Economy of Plant Biotechnology. Reviewed by Sheldon Krimsky.

Agriculture is poised for a restructuring as a result of the biotechnology revolution. That is the conventional wisdom. But what will be the effect of the changes? Who will be the winners and the losers? What are the tradeoffs? How will the biosphere fare?

Jack Kloppenburg's probing study which he subtitles "The Political Economy of Plant Biotechnology" provides a structure and logic to address these questions. In part, the answers can be found in the historical analysis of agricultural developments. To reveal the forces of technological innovation that have led to modern agriculture, Kloppenburg takes us through a 500-year examination of humankind's oldest system of production - the farm and its primary unit of production, the seed.

Through a discussion of ownership, development, and global distribution, Kloppenburg shows the seed's special role as the material basis of social and technological change in the agricultural sector. The history of the seed reveals the political economy of agriculture, an economy that reflects the underlying logic of capitalist development. Seeds are no longer simply the capsules of germ plasm that regenerate the protein sources. Seeds are commodity futures; seeds are "patentable products of manufacture", seeds are co-conspirators in a colonial warfare against nature.

Kloppenburg's book sets high standards for continued debate in this area. Further, his analysis draws attention to many unresolved issues deserving of continued study. Will the new bio-rational pesticides lessen agriculture's dependency on toxic chemicals? Will the new generation of seeds provide sufficient variability in the germplasm as insurance against future blights? Will we be able to improve yields and move toward sustainable agriculture? Biotechnology is still too young to evaluate its contributions to agriculture.

Starvation and plenty. Shattering: Food, Politics and the Loss of Genetic Diversity. By Cary Fowler and Pat Mooney. University of Arizona Press, pp. 295, $24.95 hbk, $12.95 pbk.

Fowler and Mooney trace the development of gene banks from botanic gardens, of plant breeding from selection by peasant farmers, and of our present-day, global agrochemical industry. Reading one of their books is like reading several books at once; science, history and development politics meld to form an illuminating and absorbing story.

Shattering is written for the general reader. It sets out to link developments in agriculture, biotechnology, industry and United Nations politicking.

Modern agriculture is big business. It relies on high inputs of fertilisers, pesticides, irrigation and intensive marketing. Its seeds are bred to respond to fertilisers, producing better harvests and bigger profits for breeders. Biotechnology promises, among other things, to cut the time that it takes to breed new varieties.

During the 1970s multinational companies, such as Shell and Pioneer, Sandoz, ICI and Upjohn, bought up thousands of small seed companies. Research by the Rural Advancement Fund International, which employs the authors, found that at least 65 research programmes around the world are trying to breed herbicide tolerance into agricultural crops. The herbicides that threaten these crops are usually the same ones manufactured by subsidiaries of the multinational companies.

The outwardly humanitarian aims of feeding the hungry mouths of the Third World by setting up International Agricultural Research Centres (IARCs) in the 1950s concealed other less altruistic motives, suggest Fowler and Mooney.

Today there are 13 IARCs, all funded and, the authors imply, therefore controlled by industrialized countries. Most have gene banks, stocked largely with the genetic resources of the crops of the South. This germ plasm should be freely available to any breeder that wants it, whether in the private or public sector, but it is often restricted. Commercial gene banks are not even obliged to exchange germ plasm.

The IARCs were responsible for the "green revolution" but, say the authors, that revolution itself increased genetic erosion as farmers in the Third World replaced their traditional varieties with the new "high-yielding" ones. Those new varieties are continually ousting old varieties from the farmer's fields. Because extinction is for ever, write Fowler and Mooney, conservation must also be for ever.

The International Board for Plant Genetic Resources (IBPGR), was set up in the 1970s to combat genetic erosion. It is the international rescue team for the world's plant genetic resources that are threatened with extinction. But, according to the authors, it has failed in its task.

The Board has favoured collection of crops of global economic importance at the expense of crops of national or local importance. Even crops valuable to the global food trade, such as wheat and rice, have not been adequately collected. Moreover, the material in its gene banks is not well maintained.

The authors make a case for the Third World being paid in full for being guardians of the world's genetic diversity. IBPGR and the IARCs have so benefited the developed nations that the status quo is maintained, and the imbalance of expertise and funds between the North and the South remains firmly in place. But there is not much discussion of possible modes of compensation for Third World farmers.

Like all good books, Shattering does not answer nearly as many questions as it raises. But it raises them in an entertaining and stimulating way.

Biosensors: Applications in Medicine, Environmental Protection and Process Control, R. D. Schmid and F. Scheller, eds. ISBN 0-89573-955-0. DM 128.00 (VCH Publishers, Heidelberg: 1989).

Biosensors: Elizabeth A. H. Hall. ISBN 0335-15894-3 £50.00 (cased) (Open University Press, Milton Keynes, UK: 1990).

Readers wishing to access the current state of play in biosensor research would be well advised to start with a copy of the Open University Press' Biosensors. For those already in the area or with the facilities and inclination to build their own biosensors, Biosensors: A Practical Approach (Oxford University Press) may be a useful addition to their library. This is a do-it-yourself handbook of biosensor construction with detailed instructions on how to build a variety of working biosensors for a range of applications. Many promising prototype biosensors are also described in Biosensors: Applications in Medicine, Environmental Protection and Process Control, the proceedings of a 1989 workshop held under the auspices of GBF (Braunschweig, Germany). Among the most ambitious projects is a collaboration involving researchers at Dusseldorf, Frankfurt, and Halle which aims to develop home screening for phenylketonuria. Environmental sensors, too, abound: whole-cell sensors for biological oxygen demand and pesticide sensors based on acetylcholine esterase are just two examples.

Bamboos: Current Research, by I. V. Ramanuja Rao, R. Gnanaharan, and Cherla B. Sastry (editors).

This study is a condensed version of the Proceedings of the International Bamboo Workshop in Cochin, India. Bamboo remains a vastly underresearched subject of forestry in developing countries. This collection of papers by specialists in bamboo is an attempt to understand this resource better and suggest measures for its proper utilization, management, and conservation. Published jointly by the Kerala Forest Research Institute in Peechi, India, and the International Development Research Centre (IDRC) in Ottawa, Canada.

Vaccines 91: Modern approaches to new vaccines including prevention of AIDS. Edited by Robert M. Chanock, NIAID, National Institutes of Health; Harold S. Ginsberg, Columbia University College of Physicians and Surgeons; Fred Brown, Plum Island Animal Disease Center; Richard A. Lerner, Research Institute of Scripps Clinic.

Vaccines 91 presents information at the cutting edge of vaccine development with examples of common infectious agents of critical importance to humans and many other animal species. This volume contains the latest data on the immunological, molecular, genetic, and pathogenic properties of important human and animal pathogens with particular attention paid to those critical for the development of vaccines. Other approaches are also described for preventing or ameliorating the diseases these pathogens cause.

Prominent among the exciting advances presented in this volume are fundamental findings on the devastating human immunodeficiency virus (HIV), the etiological cause of AIDS: features of the envelope structure critical to developing protective, humoral immunity; antigens that appear to provide cellular immunity, which may be essential for a vaccine to be effective; and the use of antisense RNA, which may provide a unique therapeutic approach to AIDS (this approach is also described for other viral infections). The utilization of several viral vectors, and even bacterial vectors, is demonstrated for expressing a variety of viral and parasitic antigens that may provide practical delivery systems for vaccines. Innovative immunological studies are described revealing the ability to utilize combinatorial expression libraries to obtain specific monoclonal antibodies demonstrating the danger of producing antibodies that enhance rather than prevent viral infections if the wrong antigen is used for immunization, and presenting methods to engineer T-cell-presenting epitopes.

1991 448 pp. (approx.), ISBN 0-87969-367-3 illus., colour plates, indexes, Paper $85

Available from Cold Spring Harbor Laboratory Press, Fulfillment Department, 10 Skyline Drive, Plainview, NY 11803-9729.

The molecular biology of Alzheimer's disease: Current communications in molecular biology. Edited by Caleb E. Finch, Andrus Gerontology Center, University of Southern California; Peter Davies, Albert Einstein College of Medicine.

Alzheimer's disease (AD) has been the subject of intense biochemical and molecular research for a number of years. That many aspects of this research are in a state of healthy controversy was evident from this meeting, the third Banbury Centre conference on AD. The neuropathological changes in acute AD have been known for many years, but the relationship of these changes to the symptoms of the disease is not clear. The

biochemical nature and the role of plaques and tangles in the pathogenesis of AD are still controversial. There was considerable debate about the involvement of the β-amyloid protein and the structural relationships of Tau protein to neurofibrillary tangles. Another subject of discussion concerned the molecular genetics of AD studied using the new methods of RFLP linkage analysis and whether early cases of AD demonstrate genetic heterogeneity. The participants in the meeting critically reviewed the latest findings. This book is exciting reading for all interested in Alzheimer's disease and degenerative brain disorders.

1988, 197 pp., illus. ISBN 0-87969-319-3. Paper $25

Available from Cold Spring Harbor Laboratory Press, Fulfillment Department, 10 Skyline Drive, Plainview, NY 11803-9729.

Hints on electronic record keeping offered

There are pitfalls that should be recognized and precautions that should be taken in maintaining research records in computers and data storage devices. To help researchers in recognizing them, the American Chemical Society's Committee on Patents and Related Matters has published a free pamphlet. "Electronic Record-Keeping for Patent Purposes: Cautions and Pitfalls".

The committee points out that there is no precedent in patent case law where computer-stored data have been used to establish priority of a claim. Hence, it says, computer record keeping cannot be assumed to serve as a substitute for maintaining an original, permanently bound, handwritten research notebook.

Nevertheless, the committee notes that computers are increasingly being used for gathering original data directly from instrumentation, storing data, and maintaining research records. The pamphlet deals with the issues of permanence, accuracy, contemporaneity, and protection against loss.

The pamphlet is available by sending a self-addressed mailing label to American Chemical Society, Department of Government Relations and Science Policy, 1155-16th St., N.W., Washington, D.C. 20036. Or telephone (202) 872-4479. (Reprinted with permission from Chemical and Engineering News, 18 February 1991, p. 34, by James Krieger. Copyright (1991) American Chemical Society.)

Derwent and intelligenetics offer GENESEQ

GENESEQ is a new database that contains information on nucleic acid and protein sequences from patent applications and granted patents. It is the product of a cooperative effort between IntelliGenetics Inc. and Derwent Publications. GENESEQ records all nucleotide sequences longer than nine bases, all proteins longer than three amino acids and probes of any length. The database is used in conjunction with the IntelliGenetics Suite sequence analysis programmes.

Details from: Derwent Publications Ltd., Rochdale House, 128 Theobalds Road, London WCIX 8RP or on 071-242-5823. Fax: 071-405-3630.

Hitachi America announces new CD-ROM database for micro-organism information

CD-STRAINS is Hitachi America's current line of biotechnology related PC-based software/database programmes. CD-STRAINS allows users to retrieve information from the three major micro-organism culture collections.

These culture collections are provided by the American Type Culture Collection (ATCC), the Institute for Fermentation, Osaka (IFO), and the Japanese Collection of Micro-organisms (JCM).

These culture collections are now available from Hitachi on CD-ROM, compact disk, read-only memory, which permits the storage of large amounts of data (550 megabytes) on one disk. Micro-organism information can be retrieved within seconds by name, culture designation, growth temperature, or GC content, depending on the database searched. The introductory subscription costs $700.00.

Details from: Kathy Padgett, Hitachi America Ltd., Computer Division, Hitachi Plaza, 2000 Sierra Point Parkway, Brisbane, CA 94005-1819, USA or on +1 (415) 589-8300. Fax: +1 (415) 583-4207. (Source: Biotechnology Bulletin, Vol. 9, No. 12, January 1991)

Hybridoma data bank update

An updated and greatly enhanced version of the CODATA/IUIS Hybridoma Data Bank (HDB) will soon be available via the Microbial Strain Data Network (MSDN). The entire HDB file, consisting of over 20,000 records describing individual hybridomas and/or their monoclonal antibody products, will be accessible through an MSDN gateway to the Canadian Scientific Numeric Database System (CAN/SND). CAN/SND is managed by the Canada Institute for Scientific and Technical Information (CISTI) of the National Research Council Canada.

Access to HDB on CAN/SND will be selected from the MSDN menu just as the previous version of HDB was selected. However, the new file is much more comprehensive than the original one and the CAN/SND software allows for preliminary browsing through lists of terms contained in the database and field specific searching. Those familiar with the original HDB on MSDN should have no trouble using the new capabilities, as the field names and database format remain the same. User documentation will be available online and in hard copy which will be mailed to MSDN registered users. CAN/SND also contains "help files" which will guide new users as they search the system. Periodic updates will provide MSDN subscribers with the latest information on hybridomas and their immunoreactive products.

All records in the CAN/SND version of the HDB will contain pointers to further information about the hybridomas either through literature citations and/or developers' and distributors' names and addresses. Those hybridomas available through the American Type Culture Collection (ATCC) or the

European Collection of Animal Cell Cultures (ECACC) may be ordered directly online by submitting order messages to ATCC-SERVICES (42:CDT0109) or ECACC-SERVICES (75:DBI0222).

General biotechnology information available through the MSDN network

Bioindustry association databases, which include:

- BIA Bulletin
- Diary of events
- The European Community and Biotechnology
- Summary of EC Directive on the contained use of genetically manipulated organisms
- Summary of EC Directive on the protection of workers from biological agents
- Summary of EC Directive on the deliberate release of organisms into the environment
- Export assistance from the UK Department of Trade and Industry.

Biotechnology in Europe, Manpower, Education and Training (BEMET)

The first (UK) part of a European-wide database on the education, training and manpower opportunities in biotechnology is available online. Data on other countries will be added as it becomes available. Further information from D. Bennett (Cambridge Biomedical Consultants, 21 Mill Street, Cambridge CB1 2HP on DBI0531)

Data-Star databases

The Data-Star host makes available over 200 databases that can be accessed via the MSDN network. The databases contain bibliographic and commercial information of importance to biotechnology and medical science.

Biological databases

Widely dispersed data on the location and strain behaviour of micro-organisms and cultured cells has been linked by the MSDN to provide a comprehensive service that complements the above general databases. Electronic mail, fax and telex facilities, together with training and software distribution complete the MSDN's international services.

MSDN, 307 Huntingdon Road, Cambridge CB3 0JX, UK. Tel: 0223 276622

Databases that can be accessed through the MSDN (Microbial Strain Data Network)

1. MSDN Bulletin Board.
2. European Biotechnology Information Service (EBIS) bulletin board.
3. MSDN Central Directory to laboratories or data centres with information on properties of micro-organisms or cultured cells.
4. Hybridoma Data Bank on commercially available cloned cell lines and their immuno products.
5. UK Culture Collections databases (MiCIS) (MiCIS database with primary data on strains held in UK).
6. UK National Collections of Yeasts and Food Bacteria (NCYC/NCFB) databases.
7. Netherlands Culture Collections databases (CBS/NCC).
8. Deutsche Sammlung von Mikroorganismen databases, including Approved List of Bacterial Names.
9. World Data Center for Collections of Microorganisms (RIKEN, Japan), including world-wide culture collection information and species list of holdings, the Hybridoma Data Bank, the World Directory of Algae, bibliographic information on plant tissue culture research.
10. DATA-STAR databases, including bibliographic information such as Chemical Abstracts or SCISEARCH (for current contents), medical and commercial databases. All available at reduced costs to MSDN users.
11. French databases on lactic bacteria and filamentous fungi (MINE).
12. Brasilian Tropical Database (BDT)
13. a. ATCC collection of bacteria
    b. ATCC collection of algae and protozoa
    c. ATCC collection of animal cell lines
    d. ATCC recombinant clones and libraries
14. European Collection of Animal Cell Cultures.
15. UK BioIndustry Association databases (BIA)
16. Biotechnology in Europe – Manpower, Education and Training (BEMET) database.