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UNITED NATIONS INDUSTRIAL DEVELOPMENT ORGANIZATION

Genetic Engineering and Biotechnology Monitor

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A. POLICY, NEWS AND OTHER EVENTS

UNIDO News

International Centre for Genetic Engineering and Biotechnology

The initial programme in starting up the International Centre for Genetic Engineering and Biotechnology (ICGEB) was presented to the press at a recent UNIDO Forum, a monthly TV feature, by three key figures who were instrumental in creating it - Ambassador A.R. Taylhardat, Permanent Representative of Venezuela to the UN Organizations in Geneva and Chairman of the ICGEB Preparatory Committee; Ananda Chakrabarty, Professor of Microbiology and Immunology at the University of Illinois and Chairman of the ICGEB Panel of Scientific Advisers; and Krishnaswamy Venkataraman, Senior Technical Adviser in the UNIDO Department for Industrial Promotion, Consultations and Technology.

UNIDO is assisting the ICGEB member countries in establishing the Centre and is currently implementing the interim programme. After ratification of the statutes by a minimum of 24 countries, it should function as an autonomous intergovernmental organization. To date, 13 of 39 States have ratified: Algeria, Bhutan, Bulgaria, Cuba, Egypt, Hungary, India, Iraq, Kuwait, Panama, Senegal, Venezuela and Yugoslavia.

In this start-up period, the Director, Irwin C. Gunsalus, Professor of Biochemistry at the University of Illinois, was responsible to the ICGEB Preparatory Committee, on which all member countries were represented. Once the centre was legally established, the Committee would be replaced by a Board of Governors. The Panel of Scientific Advisers would also continue to advise the Board, the Director and the Heads of Components. A Forum of Scientists would be convened to aid further elaboration of a five-year programme of co-operation in research with member countries.

The Trieste component, headed by Professor Arturo Falaschi, is actively recruiting support staff and the first 900 sq. m building will be in operation this summer. Additional facilities would be ready by mid-1989. Trieste in the start-up phase would comprise three research groups: on DNA replication, virology, and biomass conversion and upgrading.

Trieste would also work with the Centre's affiliated bodies in their areas of special interest:

Algeria	vaccines, diagnostics, monoclonal antibodies and enzyme engineering
Argentina	vaccines, diagnostics, monoclonal antibodies, cellulose waste and enzyme engineering
Bulgaria	vaccines, diagnostics, monoclonal antibodies and enzyme engineering
Chile	lignocellulose waste, metal leaching and food fermentation
Cuba	vaccines, diagnostics, cellulose waste and enzyme engineering
Greece	vaccines, diagnostics, monoclonal antibodies and enzyme engineering
Nigeria	vaccines, diagnostics, monoclonal antibodies and enzyme engineering
Senegal	vaccines and diagnostics
Venezuela	vaccines, monoclonal antibodies and diagnostics
Yugoslavia	monoclonal antibodies

New Delhi, headed by Professor K.K. Tewari, had an approximately 1,200 sq. m interim facility at the National Institute of Immunology; additional space was being made available in Jawaharlal Nehru University's biology building. In the early phases, the work was planned to be organised in three groups - covering plant biology, malaria and hepatitis.

Affiliated centres working with New Delhi were:

Algeria	nitrogen fixation
Argentina	trypansones
China	agricultural plants and hepatitis B vaccine
Cuba	genetic transformation of Graminaceae
Egypt	plant cell culture and propagation
Nigeria	hepatitis B vaccine, plant pathogens and malaria chemotherapy
Venezuela	Chagas disease, malaria, schistosomiasis, Leishmaniasis, and nitrogen fixation
Yugoslavia	gene engineering, plant cell and pollen propogation.

Regarding funds for the Centre itself, latest figures presented to the Preparatory Committee indicated sufficient resources for the interim three-year programme. Funds were made available through a $10 million contribution of the Government of Italy, with an additional Lire 10 billion (appr. $7 million) provided by the Research Area of Trieste. The Government of India had contributed in kind to the value of $17 million and made a convertible contribution of around $500,000. Contributions had also been received from Argentina and Panama; China, Kuwait, Venezuela and Yugoslavia had indicated forthcoming contributions.

The purpose of the Centre was twofold - training and industrial promotion. Developing countries had to have people who knew how to apply genetic engineering technology to manufacture products that would be unique to their own countries and using the resources of those countries. At the same time, it was necessary to sensitize developing countries' industries to the need to produce genetically engineered products and compete in world markets. This would require a nucleus of people capable and experienced in the methodology and applications of genetic engineering technology.

The Centre was not in the business of making money by selling products, but rather its business was training people and doing research and development. If certain unique products resulted from the R & D, then the patents for those products would be licensed to the member countries to exploit in ways they deemed suitable.

Formal training at the two components would begin in 1987 with short-term (three to eight week) courses, workshops and conferences. Where appropriate, training would also begin in non-ICGEB institutions.

The programme in New Delhi would support agriculture, and human and animal health. The effort to obtain high-yield plant varieties would include cytoplasmic male sterility studies, potential herbicide and pesticide resistance and plant protein quality investigations of Amaranthus, an important crop in developing countries. Nitrogen fixation, a critical problem throughout the world, would emphasize studies of slow-growing Rhizobium strains associated with legumes grown in developing countries.

The health field at New Delhi would focus on two areas: malaria and hepatitis - with emphasis on vaccines critical to diverse problems of developing countries. The malaria parasite provided an example of several life-cycle stages with antigenic differences and thus potentially interruptable by a series of vaccines. The antigenic variety among hepatitis viruses would require screening within the developing countries.

In Trieste a parallel programme of industrial applications of biotechnology would investigate typical viral diseases in developing countries. Human papilloma virus (a main cause of genital cancer death in women especially in Africa) and rotaviruses (representing a family of RNA-based viruses, and a main cause of infant mortality in tropical areas) were targeted as important problems. The studies would combine cell and molecular biology methodologies with molecular studies on human DNA replication, and immunological and pharmacological approaches.

A microbiological approach - including fermentation, biochemistry and genetics - would be taken

to lignocellulose degradation - a possible new source of food, feedstocks and chemical intermediates. An excess of lignocellulose feedstocks was less than optimally used and occurred in many developing countries. Both pure cellulose and lignin by-products were scarce and could be of enhanced use and economic value, it was pointed out.

A protein engineering group would orient the studies of both the human health and the microbiological efforts.

Trieste would also develop the industrial applications of research results emanating from both the New Delhi and Trieste components - including production of diagnostics, and new and traditional vaccines and drugs in small- and medium-scale industries of importance to developing countries.

Other activities of UNIDO in the field of biotechnology are continuing. There will be a workshop on Protein Structure to Protein Engineering to be held at Trieste from 21 to 25 March 1988, and another on Molecular Biology of Photosynthesis to be held in New Delhi in July or August 1988. Two other workshops are foreseen for 1988, one in Cuba and another in Saudi Arabia. More information on these two workshops will be supplied in later issues of the Monitor.

UN and other organizations' news

Obsolete policies hamper development of Asian livestock

Asian governments are under pressure to streamline obsolete livestock policies as the sheer number of people, rapidly changing diets and incomes push the demand for meat, milk and eggs ahead of limited supplies.

"The projected output of meat, milk and eggs would not come close to meeting the demand for these products by 1990," experts from 13 Asian and Pacific countries concluded at a recent meeting of the United Nations Food and Agriculture Organization (FAO). They added: "By the year 2000, the supply-demand imbalances could be even worse, particularly in milk or meat."

The FAO organized the week-long consultation in Bangkok. It sought to examine how price policies and other measures could help close the gap. It is a tough job, delegates admitted. Although fertility rates have started to decline all over Asia, the region has a massive population base.

Complicating the task is the grim fact that over 300 million men, women and children remain ill-fed, while the undeniable progress achieved in livestock production over the past decade masks wide disparities in the industry.

Prior to the 1950s, most Asian livestock were raised under a primitive scavenger system. It was adequate only for subsistence consumption. However, production surged as modern technology began to flow in. Main features of today's livestock scene, as noted by the experts, were:

- Total meat production for the 27 FAO member-countries in the region grew at 5.8 per cent over the last decade. It lost some momentum recently and dropped to 4.8 per cent. The slowdown was most marked in the advanced countries.

- Such growth permitted the region to be a net exporter of meat. These exports are largely due to production gains in countries such as Australia, New Zealand or Thailand. Lagging production forced 12 out of 26 countries to import ever-larger shipments of meat. The importers were Cook Islands, Laos, Malaysia, Fiji, Pakistan, Papua New Guinea, Philippines, Samoa, Solomon Islands, Sri Lanka, Tonga and Viet Nam.

- Despite the production gains livestock contributed a shrinking share of the calories that make up the diets of people.

Ideally, livestock products should provide at least 10 per cent of the calorie intake, but data, painstakingly compiled by the FAO for 43 countries of Asia and the Pacific shows that in the early 1970s, livestock provided only 6 per cent of the calories. This has now dropped to 5.4 per cent.

"Although not substantial, this decrease is an undesirable trend in the region," a FAO study notes. "The proportion of calories from animal products in most of the developing countries is already low, in comparison with the developed countries of the region."

A Japanese, for example, draws 30 per cent of calories from meat and other forms of livestock products. This percentage falls to only 2 per cent for an Indonesian.

An appreciable improvement occurred in the availability of milk and milk products. It rose from 23 per cent to 26 per cent through home production or import. Indians and Malaysians appeared to have substantially increased their intake of milk.

The production figures for milk are cheerful - and misleading. It is true production increases by 3.4 per cent. This outpaces the 1.4 per cent rate set for the rest of the world. However, Asia's share of milk production is miniscule. It produces only 16 per cent of the world's milk.

Delegates to the FAO meeting observed that many countries have not, as yet, written out comprehensive price policies for major livestock products. This policy vacuum persists despite widespread recognition of the need for price policy mechanisms in these countries.

The experts also stressed that prices for agricultural and livestock products have an impact on government efforts to alleviate poverty and reduce malnutrition. Hence, price policy should not be considered on a fragmented ad hoc basis, as far too many governments do today. (Source: Agricultural Information Development Bulletin, March 1987)

'Benign neglect' stunts growth of vegetable industry

Despite an upswing in vegetable output in Asia and the Pacific, over 300 million men, women and children remain ill-fed. Hence, many governments see vegetables as a practical means to curb the ravages of malnutrition. But how to accomplish this still remains a big question mark.

Why are many Asian farmers able to coax only nine tons or so of potatoes from a hectare of land? In contrast, nearby agricultural schools often harvest up to 65 tons from their experimental plots.

Why do yields in major vegetables, like cabbage, vary so widely? The Republic of Korea reaps 35 tons of cabbage-heads from a hectare, but Thailand is hard put to raise five tons.

And why is the production of root crops - so vital for improving the diets of the poor - locked into stagnation?

These questions bother countries seeking to boost vegetable production. Despite recent bumper harvests in cereals, over 300 million men, women and children in Asia remain ill-fed. Hence, many governments see vegetables as a practical means to curb the ravages of malnutrition.

To track some of the answers, the week-long meeting at the FAO regional office at Bangkok found, among other things, that:

- Vegetable production in Asia and the Pacific is on the upswing. The statistics are still patchy, but there is enough data to show that output of vegetables surged from 143 million tons in 1975 to 196 million tons last year. This is almost half (48 per cent) the world's production.

- The region grows a rich and bewildering variety of vegetables. They range from the common egg-plant to spicy chillies and protein-rich wing beans.

But the overall statistics also mask the fact that in nine countries, population growth outstripped vegetable production. The lagging nine were Bangladesh, Bhutan, Burma, Democratic Kampuchea, Fiji, Indonesia, Malaysia, Papua New Guinea and Thailand.

"In these nine countries, per capita production - and most probably availability - of vegetables declined between 1975 and 1985," the experts said.

- Country production differs widely. In 1984, the Republic of Korea raised 224.6 kgs of vegetables for every person. But Bhutan could grow only 7.6 kgs.

China accounted for 52 per cent of the region's output by producing over 100 million tons, both from large farms and household plots. India (45 million tons) and Japan (16 million tons) came second and third. Mongolia and the People's Democratic Republic of Laos appeared to have the fastest expanding vegetable production.

- Average yields of most vegetables are far below potential. Japan and New Zealand, for example, harvest 30 to 40 tons of tomatoes per hectare. But the average yield of tomato farms elsewhere is only 15 tons. Australia harvested 27 tons of cauliflower per hectare compared with eight tons in India.

"There is ample scope for improving yields," the report of the FAO meeting noted. "There are wide gaps between the yield of farmers' fields and those from experimental plots of national research institutions.

- Consumption statistics also display the same wide disparity. Koreans and Mongolians apparently consume 225 kgs and 210 kgs each per year. The lowest were the Bhutanese (8 kgs) and Bangladeshis (14 kgs).

"An annual consumption of 125 kgs vegetables per person is recommended," the FAO meeting report noted. "Of the 26 countries, for which data was available, only five met the recommended levels of production/consumption." These were the Democratic People's Republic of Korea, the Republic of Korea, Mongolia, New Zealand and Japan.

- An overall "benign neglect" blanket stunts growth of the vegetable sector. Among the major technological constraints identified by the experts were lack of research, reflected in the limited number of improved varieties; insufficient supply of quality seed; high incidence of pests, diseases and weeds.

Overburdened and poorly-trained extension workers fail to communicate technology to vegetable growers. Post-harvest losses are also high.

"Research is the backbone for all future improvement in vegetable crops," FAO said. "But the funds and personnel assigned to vegetable research are a fraction of those assigned to other fields."

Asia and Pacific countries lack appropriate vegetable breeding facilities at the national level, the report added. Several international institutions like the International Crops Institute for Semi-arid Tropics have been developing promising varieties.

"But their effective adoption to suit local agro-ecological conditions is often weak. Introduced varieties soon succumb to local pests and diseases. There are hardly any varieties which could be claimed to be resistant."

To break out of sluggish production, the experts called for urgent support to develop new varieties adapted to tropical temperatures with built-in resistance to disease. Arid upland farms needed drought-tolerant varieties.

There is also need to produce, on an urgent basis, quality seeds of high yielding cultivars.

There are, however, success stories that relieve this otherwise bleak situation.

Farmers in Sri Lanka and the Philippines, for example, scored breakthroughs in producing potatoes under rice-based systems. Thais successfully produces baby corn. Chinese and Indian horticulturists have advanced technology for hybrid seed production.

"A technical corporative arrangement for sharing experiences of the countries would constitute a giant step forward," FAO said. (Source: Agricultural Information Development Bulletin, March 1987)

Biogas presents bright hope for fuel-starved Asia

Until the first oil crisis in 1973, the idea of alternative energy sources seemed to many people more a subject for leisurely intellectual musing. It was stimulating and interesting but not really so relevant, practical and necessary.

Today, the so-called non-conventional sources of energy, especially renewable ones, are getting to be more conventional and their use is spreading. The use of biogas is one alternative energy idea which is getting increasing attention in the Asia-Pacific region. The technology involves the use of animal waste for the production of methane gas (through anaerobic (oxygen-less) fermentation.

Animal waste, mainly in the form of cowdung cake, has been used as fuel particularly by villagers in India and Pakistan. However using waste in this form is considered wasteful as it burns valuable fertilizer which could have been used in farm production.

Worldwide, the use of livestock droppings as fuel is estimated to lower annual grain production by some 20 million tons, enough food to minimally nourish 100 million people.

Biogas promises to meet the demand for both fuel and fertilizer. The extraction of methane gas from animal wastes leaves a by-product - a thick slurry which can be spread in the fields as fertilizer.

Extracting biogas from the wastes does not lessen the qualities of the residues as a good fertilizer. The slurry contains the basic ingredients of natural fertilizer, it aerates the soil, retards the moisture evaporation in dry weather, sustains life of vital micro-organisms and buffers the soil's acidity level.

Essentially a process of recycling waste, the biogas technology also means the safe disposal of waste which can prevent the spread of diseases and control pollution. It can help minimize the destruction of forests by offering an alternative to wood as fuel.

Despite its great potential for agricultural third world rural areas, biogas still has very limited

application. The pioneers in this field are the two countries with the world's largest populations - China and India.

India began work in this field in the 1930s although up to now the number of biogas digesters has not reached 100,000. This despite estimates by the Indian Planning Commission that there are enough wastes to operate 19 million family-size units in the country and 569,000 community plants. Installation of these units will mean a 44 per cent drop in electricty use, 15 per cent drop in the use of coal, and a saving of 79 per cent of the firewood.

In China, on the other hand, there are already more than seven million biogas digesters serving about 35 million people. The Chinese intend to increase the number of digesters 10 times.

Member countries of the Association of South East Asian Nations (ASEAN) have biogas facilities in one form or another. The member countries are Brunei Darussalam, Indonesia, Malaysia, Philippines, Singapore and Thailand. It is estimated that in the ASEAN countries biogas potential of livestock and poultry wastes is equivalent to 32,653 million barrels of oil.

In 1981, biogas production in Singapore was about 32,000 cubic metres a day. Thailand, by that time, had installed more than 400 units mostly in the central and northern parts of the country. Biogas was mainly limited to Thai rural villages and was used primarily for cooking and lighting. A few were used for irrigation and electricity generation.

The Philippines' Maya Farms pioneered in the adoption of biogas technology on an industrial scale, making it Asia's largest biogas establishment. Fourteen 800-cubic-foot digesters and eight 128-cubic-foot digesters have been installed using dung from 15,000 pigs. One 128-cubic-foot digester alone can operate a 46-horse power generator or 34 kilowatts capacity for four hours per day.

There are problems however which prevent biogas from being the overnight success which some proponents expected it to be. Cultural resistance seems to be a setback in India. The subcontinent has a large cattle population whose dung is made into fuel cakes. Other sources of non-conventional energy - such as pig and human wastes - present cultural barriers.

Rural Indonesians do not seem to find a need for biogas, as conventional forms of energy - like wood and kerosene - are cheap and readily available to most of them.

Cost appears to be a major factor in the Malaysians' lack of enthusiasm for biogas. The installation cost does not make biogas appealing to rural villagers. Many rural families, to whom the biogas technology is expected to appeal, may not be aware of an energy crisis and thus of the need for an alternative fuel. To them, biogas may seem a solution to a non-existent problem.

UNESCO, together with other United Nations agencies, has worked to bring not only the energy problem to the attention of the world's population but also the possible solutions to it.

Through the Regional Office for Science and Technology for Southeast Asia (ROSTSEA) and national commissions in participating countries, UNESCO supports groups such as the Regional Network for Development of Alternative Sources of Energy in Southeast Asia and the Pacific. This network aims, among other things, to promote activities which will be relevant to local needs and which will find solutions to local problems.

UNESCO also established in 1983 the Information Network on New and Renewable Energy Resources and Technologies in Asia and the Pacific. INNERTAP is a network designed to facilitate information exchange on new and renewable sources of energy among non-Commonwealth countries in the Asia-Pacific region.

It was set up in line with the goal of UNESCO's Energy Information Programme to establish a worldwide network of institutions which will share and use energy information particularly on new and renewable sources of energy.

INNERTAP, which when fully developed is expected to serve 16 countries, is complemented by the 19-nation Commonwealth Regional Renewable Energy Resources Information System (CRRERIS). (Source: Agricultural Information Development Bulletin, March 1987)

Asia needs technologies to convert farm residues into cheap energy

Asia has abundant supplies of farm residues, but lacks appropriate technologies to convert them into low-cost energy to meet the fuel needs of people in the rural areas.

Efforts to develop residue energy conversion (REC) technologies have so far reached only the experimental or pilot testing stage, according to a report issued by the United Nations Economic and Social Commission for Asia and the Pacific (ESCAP). The slow progress result from insufficient co-ordination between private and public sectors, it noted.

The report said that in the Asia-Pacific region most research in REC technologies have received little support from the private sector, which views investment in them to be "risky and less attractive". On the other hand, "when private enterprises have developed such technologie there has been little input from the research institutions," it added.

The report contains the findings and recommendations of a four day meeting held last November organized by ESCAP with financial support of the United Nations Development Programme (UNDP).

Attended by energy experts from 10 ESCAP countries, the meeting explored the use of agricultural wastes as low-cost energy sources to help reduce the region's dependency on oil import and, at the same time, develop its rural sector.

According to the report, the abundant agricultural residue supplies in rural Asia are converted, to a limited extent, into domestic fuel by low-income households and industrial raw materials.

China, said the report, produces some 150 million tons of agricultural residues per annum, and India's yearly output is 20 million tons of rice husk.

"Agricultural residues have long been used in the rural areas of Nepal as fuel for cooking and heating, animal feed, manure, etc.," said the report, adding that in Thailand a considerable amount of them is either left unused or burnt away.

Through gasification, pyrolytic conversion, carbonization, direct combusting, densification and anaerobic fermentation methods, the report pointed out that agricultural by-products could be converted into energy forms.

"Many of the REC technologies bear a direct relevance to meet the energy needs of the household, agriculture and other utility needs of the (region's) rural sector," it said.

Of all REC techologies, the report identified the gasification method of rice husk as showing "a high potential for widescale application for productive activities" and is "commercially viable in generating electricity for rice milling operations". This technology also offers considerable scope for water pumping systems and electrification of remote areas and for direct thermal applicaton.

In Indonesia, for example, the report noted that the energy generated from rice husk could save the equivalent of as much as 228 million litres of diesel fuel per year or, based on 1986 diesel prices, nearly 45,650 million rupiahs.

To promote their wider use, it asserted that more capital should be invested in the research and development of REC technologies. "The extent to which the use of REC technologies can help contribute to the country's energy supply," it said, "needs to be estimated and continuously reviewed and updated."

In addition to establishing data banks at both national and regional levels, the report suggested that Governments should adopt "a definite policy" to promote the use of agricultural residues as sources of energy for rural consumption.

For more information, write to: Agriculture Division, ESCAP Secretariat, United Nations Building, Rajdamnern, Nok Avenue, Bangkok.

Regulatory issues

New US biotechnology regulations in first trial

The US Department of Agriculture (USDA) and the Environmental Protection Agency (EPA) have received their first outdoor-release application from a biotechnology company under the new guidelines co-ordinating federal regulation of biotechnology. Biotechnica International of Cambridge, Mass., applied to USDA under the Plant Pest Act for a permit to conduct outdoor tests of a strain of Rhizobium meliloti that was genetically altered to increase its ability to fix nitrogen on alfalfa. The company also sent the EPA a premanufacture notification of the proposed environmental release as required under the Toxic Substances Control Act. The guidelines, published in the Federal Register on 26 June 1986, give the two agencies overlapping authority to review proposed field tests of non-pesticide agricultural micro-organisms. Officials in both agencies say they are co-ordinating their reviews. (Extracted from Chemical Week, 18 February 1987)

The new US drug export law

The drug export bill signed by President Reagan in December 1986 creates a number of opportunities for biotechnology companies to increase their export earnings. Getting the most out of these opportunities, however, requires strategic planning.

Although the new law contains some ambiguities it has remedied the inequities imposed for most of this century upon US pharmaceutical manufacturers. The law now permits the export of new drug and biological products intended for human or animal use to any of 21 developed countries once the Food and Drug Administration (FDA) has approved an export application. The statute also relaxes restrictions on exporting partially processed biological products. In fact, one of the most important decisions that biotechnology company executives need to make is whether to export finished or partially processed products. Another significant issue is what strategy to pursue if the company wants to export to an unlisted country.

There are circumstances when a company may be eligible to export an intermediate but not the final product, as well as circumstances when a company is eligible to export either but should prefer to export the intermediate. But what strategy should a company pursue if it wants to ship to an unlisted country?

The obvious strategies predate the drug export law: vigorously pursue FDA approval of the product for marketing in the US, produce the product abroad, or license the technology to a foreign producer. But there is now another option for some products: seek approval to export under the tropical disease provisions of the new law.

A drug or biological product that is to be used in the prevention or treatment of a tropical disease may be exported on more liberal terms than other unapproved products - and exports are not limited to the 21 countries specified in the law. These products may be exported to any country which FDA finds that the product would be safe and effective in the prevention or treatment of a tropical disease. Furthermore, a company need not be pursuing US marketing approval to export a tropical-disease product, though active pursuit of domestic approval is required for other products. Because tropical diseases are not defined in the law, FDA has considerable latitude in determining product eligibility. One option that is not available is petitioning FDA to add the desired country to the approved list. (Extracted from Biotechnology, Vol. 5, March 1987)

General

Biomedical grants for international study

Several fellowship programmes for advanced international study in the biomedical sciences are available from the Fogarty International Center of the National Institutes of Health. US scientists may apply for support to conduct basic or clinical research at foreign institutions for up to one year. Support is also available for two- to 12-week exchange visits between the US and Hungary, Poland, Romania, Yugoslavia, or the Soviet Union. Applicants are required to have a doctoral degree in one of the behavioral, biomedical, or health sciences and some post-doctoral experience. Further information is available from the International Research & Awards Branch, Fogarty International Center, NIH, Bethesda, Md. 20892. (Abstracted with permission from Chemical and Engineering News, 26 January 1987, p. 17. Copyright 1987, American Chemical Society)

Donation for drug research

The transfer of basic research into human health-care products is the aim of a $7.8 million collaboration between Stanford University and SmithKline Beckman. SmithKline will contribute $5 million for construction of Stanford's new Center for Molecular and Genetic Medicine and $2.8 million for research support. The center - for which Stanford has raised $86.6 million - is scheduled for completion late next year. It will house departments of biochemistry, developmental biology, molecular and cell physiology and the Howard Hughes Medical Institute unit. (Source: Chemical Week, 11 February 1987)

Battelle offers multi-client bioequipment study

Complementing its multi-client programme on bioproducts, Battelle's Columbus Division is offering a multi-client study of the opportunities in supplying bioequipment to biotechnology-related industries. The programme will examine such areas as new products and technologies, market sizes and

growth rates and timing for market entry. Four main categories of product will be covered: biosepurations equipment and consumables; instruments such as DNA sequencers/synthesizers and peptide synthesizers; cell culture and other novel bioreactors; and traditional fermentation equipment. Companies may participate in the programme for $30,000, with entry to a single product segment costing $12,000. Details from: Renate Siebrasse, manager - operations, Battelle Institute Ltd., 15 Hanover Square, London W1R 9AJ or on 01-493 0184. (Source: Biotechnology Bulletin, Vol. 6, No. 1, February 1987)

Top scientists predict future drug advance

The most important health problems in the developed world in the year 2000 will be those stemming from the aging population, typically cardiovascular disease and cancer. In the developing world, infectious diseases and malnutrition will remain the major killers. This is the view of over 200 leading medical researchers interviewed as part of a study commissioned by Bristol-Myers.

The study points to AIDS, measles, polio, malaria and hepatitis as being the diseases most likely to be eliminated by 2000. As far as AIDS is concerned, the experts reckon that there will be over 1 million sufferers of the disease in the US alone by that time. Six out of 10 researchers are optimistic that a safe and effective vaccine will be available by 2010.

New diagnostic techniques will become increasingly important in the fight against cancer. Advances in cancer therapy will vary according to the disease. Lung cancer will see the highest degree of improvement, with smoking cessation playing a key role. Leukemia and non-Hodgkin's lymphoma will see the greatest advances.

In the field of cardiovascular disease, blood-clot dissolving drugs and other techniques will eliminate most coronary bypass operations by the end of the century although prevention will play the major role.

The most promising target for research in the central nervous system area is increasing the understanding of the brains's molecular biology. The greatest advances are expected for the treatment of depression while modest improvements are expected in the treatment of Parkinsonism, epilepsy and tardive dyskinesia (a side effect of antipsychotic drugs).

Scientists working in the central nervous system area agree that molecular antibody diagnostics and DNA probes will be widely used to detect conditions like Alzheimer's disease at their earliest stages. Treatments which delay or prevent loss of brain neurones during diseases like Alzheimer's and Parkinsonism will play an important role by 2000.

In the treatment of infectious diseases, most of the scientists polled reckon gene-spliced vaccines hold promise for use by 2000. Malaria vaccine is seen as a top priority for the third world.

Products from biotechnology will also help in the treatment and prevention of cancer, according to 58 per cent of the scientists. The vast majority of the researchers feel that the risks of genetic engineering have been greatly exaggerated and there is no need for stricter regulation. (Source: European Chemical News, 30 March 1987)

New study on biotechnology scale-up

Biotech enters scale-up phase:

Biotechnology is entering the scale-up phase of its development. Investments of the order of $5.1 billion will be required in the US alone, in the view of Business Communications Co., the Norwalk, Connecticut-based market research firm.

Based on current development projects, a conservative estimate of average annual growth for the US market is put at 9 per cent for the remainder of this century. Globally, biotechnology scale-up projects will total $8.5 billion during 1986-1990, $13.1 billion for 1991-1995 and $20.1 billion in 1996-2000, according to the BCC study, "Scale-up in biotechnology: a strategic analysis."

The industry has yet to confront a number of critical questions, however, concerning potential market size for its products, cost of production plants and their size.

Although many observers suggest that genetic engineering will be widely used for the production of high-value products such as pharmaceuticals, BCC maintains that gene-spliced drugs will be produced in much smaller quantities than conventional products made by organic synthesis and thus capital investment on biotechnology projects may not be as high as assumed earlier. On the other hand, biotechnology products should find wider application than conventional drugs. (Source: European Chemical News, 30 March 1987)

Gene banks for preservation of plants

Human civilization is inseparably related to the world of plants. The present population explosion accompanied with rapid industrialization and other processes have threatened our ecological stability, and affected plants in their quantity and variety.

Out of 2,500,000 different plant species, some are already lost and nearly 20,000 seed plants are threatened with extinction. With these fast disappearing natural resources, their invaluable genetic variabilities will also be lost for ever, which, in turn, may put man's future in serious danger. Some varieties of our staple crops like

Projected biotechnology scale-up market ($m)

	1986-1990 US	1986-1990 World	1991-1995 US	1991-1995 World	1996-2000 US	1996-2000 World	Average annual growth rate (%)
Biopharmaceuticals	1 410	5 950	2 169	9 155	3 338	14 086	9
Speciality chemicals	410	1 750	631	2 693	971	4 143	9
Agriculture-related/other	180	800	275	1 231	426	1 894	9
Total	2 000	8 500	3 075	13 079	4 735	20 123	9

Source: Business Communications Company, Inc.

rice, wheat, maize, etc., with high yielding, disease resistance and better adaptability characters have been developed from their wild counterparts. The naturally occuring plant species in different parts of the world are genetic treasuries and unless the germplasms or the genetic potentials of the plants are preserved, the new varieties needed to feed the hungry mouths of the world will be far from reality. Thus, establishment of genebanks for different crops and plants of economic, scientific, aesthetic and ecological value is of more importance than ever.

Objectives of genebanks:

A genebank or germplasm bank (germplasm is the sum total of genes) is a scientific institution for the exploitation and preservation of plant genetic resources (PGR) collected from different parts of the world. It is otherwise known as Genetic Resources Centre or GRC. The potential value of PGR in different geographical centres of the world was first expressed in the first decade of this century by a Russian scientist, N.I. Vavilov. After the International Biological Programme (IBP) 1964, a global concern was raised. The main objectives of these centres are: (a) exploration and collection; (b) evaluation and storage; (c) regeneration; and (d) documentation and utilization.

Survey and exploration:

There are three main categories of genetic resources: (i) wild and weed species; (ii) primitive or traditional cultivars; and (iii) advanced or bred cultivars, of which the primitive cultivars are more threatened with extinction than wild and weed species. Basically, the main approaches in the survey and exploration for genetic resources include the study of geographical distribution, location of danger spots and search for primitive cultivars of plants based on importance and degree of urgency. Based on these aspects, exploration for genetic resources has already been started in some countries for cereals like Triticum, Hordeum, Oryza, Secale, Avena species; grain legumes like Cicer, Lens, Phaseolus, Vigna, etc., species; forage crops like Trifolium, Medicago, Lolium, Phalaris, Dactylis, etc; vegetables like Cucumis, Raphanus, Daucus, Solanum species, etc., some spices and industrial crops including oil and fibre plants, medicinal and perfume plants.

Conservation and storage:

Genetic resources of plants are collected either as seeds, pollen grains, vegetatively propagating plant parts or as plant tissues. Collection varies depending on the nature of a crop and consequently the methods for conservation are specific.

As seeds are compact and easy to handle, seed collection and preservation is a common method in the conservation of PGR. Besides, a large quantity of seeds representing thousands of genotypes of plant population can be stored at one place. The PGR of many crop plants are conserved by this process. During storage of genetic stocks of seeds two aspects are considered: (i) long-term storage to avoid cost expenses, complications and risks involved in growing plants at frequent intervals, and (ii) no, or a minimum, amount of genetic alteration in seeds takes place. The second aspect is important and is generally achieved by maintaining the moisture content of seeds between 5 to 10 per cent and the temperature at 10°C. In these conditions, viability lasts for 50 years or more. Such a condition of seeds can be achieved by storing them in sealed hermatic containers which have been dried to a desired moisture content and maintained at the desired temperature by air-conditioning.

Pollen grains show different viability periods. The group of families noted for the highest longevity of pollen grains consists of Rosaceae, Primulaceae etc. As in seeds, so in pollen some important environmental factors such as temperature, moisture and oxygen pressure affect viability. Lowering of any of these factors tends to increase longevity. The longest period of pollen storage recorded is 9 years at -20°C for apples. Besides, storage of pollens at an extremely low temperature (-180°C to -190°C) and in liquid nitrogen to ensure low moisture content increases viability. However, pollen storage seems to be a far less promising method than seed for long-term conservation of genetic resources.

Tropical roots and tubers of different plants like yams, potato, sweet potato, some aroids, etc., are staple foods and important sources of calories. As they are all perennials and grown as annuals and maintained by vegetatively propagated clones, long-term storage of their vegetative parts (e.g. corms, tubers, stem cuttings, etc.) is a significant step towards conservation of genetic resources. A combination of different methods like lower temperature, modified atmosphere, chemical applications, etc., have been employed to prolong their storage, reduce sprouting and maintain the quality.

However, like seed preservation, the plant tissue culture technique has also proved to be a promising one for long storage of PGR. In this technique, the plantlet can be grown in controlled conditions from any tissue of the plant. In general, maintaining PGR by tissue culture technique has the following advantages.

1. The space required is relatively small;
2. Maintenance is relatively simple and cheap;
3. Propagation potential or multiplication rate is high;
4. Problems of genetic erosion of stocks which can be serious under field conditions are absent.

Besides, cold storage of woody plant materials has also been suggested for long-term conservation of PGR.

Documentation:

Documentation is the most active function in any GRC because information about the plant material rather than the material itself is necessary for its utility by the user or other GRCs. Every item that goes into GRC, whether a seed collection, a living plant or its parts, a dried herbarium or a photograph, requires that some records be kept. That record is documentation.

In order to facilitate description and communication, description of characters has been coded as scaler information and denoted by some numbers to indicate intensity of expression. Variability of expression of descriptors dealing with reactions to pests and diseases is indicated as 'H' for hyper-sensitivity, 'I' for immunity, 'R' for resistance, 'S' for susceptibility, 'T' for tolerance, etc. Several standard computer programmes have been set up for different crops to store and handle information.

World GRCs:

The first GRC of the world was established in the USSR in 1920. In the last two decades several regional and international GRCs have been set up in different countries. The International Rice Research Institute (IRRI) established in 1960 in Manila, Philippines, has a rice germplasm bank. Here, more than 25,000 varieties of rice germplasms from all over the world have been collected and are being maintained. Similarly maize germplasms have been stored at three important GRCs. They are the International Maize and Wheat Improvement Centre (CIMMYT) in Mexico, the Instituto Colombiano Agropecuario (ICA) in Columbia and the Instituto Nacional de Investigaciones Agricolas also in Mexico. Germplasms of more than 4,000 varieties of potato have been collected and are being maintained at the International Potato Centre (CIP) at Lima, Peru. There are also a number of regional seed storage laboratories and GRCs for different crops which function in collaboration with FAO, and other GRCs.

Inaction over species loss decried at AAAS meeting

The annual meeting of the American Association for the Advancement of Science was opened with a warning: The global decrease in forests and biological species spells danger for all citizens of the world.

P.H. Raven, director of the Missouri Botanical Garden and Engelmann Professor of Botany at Washington University, St. Louis, was the keynote speaker for the week-long meeting held in Chicago.

From any point of view, Raven felt the situation to be extremely serious. He outlined a number of strategies that could help stabilize the world ecosystem and reverse the current trend of destruction. Besides calling for accelerated international development aid and mitigation of payments on international debt, Raven urged that biological diversity be surveyed as a matter of urgent priority and conserved to the extent possible so that future generations will have the most extensive set of options available to them. He also urged that modern biotechnology be applied to development of new kinds of crops for the tropics and subtropics. Tropical deforestation is proceeding rapidly, although some recent steps have been take internationally to slow the destruction. At least 40,000 square miles are being cut each year and if the clearing were to continue at the rate at which it was occurring 10 years ago, the forest would be gone in about 60 years.

The most serious, long-term global problem that is resulting from deforestation, Raven says, is the loss of a large portion of the biological diversity on Earth within a few decades. However it is viewed, he says, "It is unquestionably the most serious problem of all those that confront us and the one that will have the most lasting consequences."

Among the considerations developed nations derive many material benefits from the genetic resources of the tropics. Examples include oral contraceptives that were for many years produced from Mexican yams; muscle relaxants used in surgery worldwide that come from an Amazonian vine; a drug for Hodgkin's disease that comes from the rosy periwinkle, a native of Madagascar; and the gene pool of corn recently enriched by the finding of a perennial wild relative in a small area in the mountains of Jalisco, Mexico.

Only about 500,000 species of tropical organisms have been named, but there are at least 3 million, and perhaps 10 times that many, yet to be discovered. It was difficult to chart the actual rate of extinction of tropical organisms quantitatively, Raven pointed out, but the dimensions of the problem can be approximated. For example, at a minimum estimate of 3 million species of tropical organisms, and assuming that the patterns of diversity in poorly known groups approximate on average those of well-known ones, the number of species can be determined that occur only in those forests expected to be severely damaged in just the next 15 years or so. For plants, the figures work out to about 120,000 of an estimated total number of about 165,000 tropical species. Just under half of the total number of species in the world occur only in forests that are rapidly being destroyed. (Reprinted with permission from Chemical and Engineering News, 23 February 1987. Copyright 1987, American Chemical Society)

Biotechnology firms report losses

Bictechnology companies continue to report losses, as high research expenditure hits profits. At the end of 1986 two companies, the Genetics Institute and Genentech, both posted net losses.

Genetics Institute reported a net loss of $4.5 million for the year to 30 November on revenues of $19.3 million. In the fourth quarter the company reported a net loss of $961,000 on sales of $7.[illegible] million versus a net profit of $122,000 on sales of $5.1 million in the previous year. The increases losses were apparently due to greater spending on research and product development, as well as on group expansion.

In May last year Genetics Institute raised $79 million via a public share issue and in September formed a joint venture with Burroughs-Wellcome for the manufacture of biotechnology-based human pharmaceuticals. The subsidiary plans to announce the location of its manufacturing and research facility later this year. The firm's products include tissue plasminogen activator, granulocyte monocyte colony stimulating factor and erythropoietin, which are all in clinical trials. The company has also produced a human macrophage colony stimulating factor using recombinant DNA technology for the first time.

Meanwhile, Genentech Inc. reported losses at the end of last year to the tune of $352.2 million, despite sales improving by 50 per cent to $134 million. This compares with a 1985 profit of $5.6 million. Genentech, however, says its operating profit more than doubled to $12.8 million.

The net loss stemmed from Genentech's decision to take a $365 million charge for the purchase of the assets of two limited partnerships which were formed to finance the group's research. It is hoped the repurchase will boost earnings by preserving all anticipated profits from three key products awaiting approval - gamma interferon, tissue plasminogen activator and human growth hormone. TPA alone could have a market worth some $1 billion. (Source: European Chemical News, 2 February 1987)

Prognosis on biotechnology sales

Biotechnology-related sales are expected to total $25 billion by the year 2000, including $15 billion in pharmaceuticals, $5 billion in agriculture, $3 billion in chemicals and $2 billion in foods, according to Consulting Resources. The high stakes involved will probably keep companies investing in biotechnology research in 1987, despite losses by seven of the top ten biotechnology firms in 1986. Major drug and chemical companies are expected to continue to fund the research. Biotechnology product sales were up to 81 per cent of corporate income, but in no case did product sales cover company expenses. Most biotechnology

success to date has been in diagnostics. Genetic improvement of crop plants and animals offers another major field for biotechnology.

Furthermore, the total annual market for biotechnology equipment in Europe will nearly double in the next eight years, according to a 353-page report by international market researchers, Frost and Sullivan. The report, Biotechnology process plant market in Europe, predicts that demand will grow from £127 million in 1986 to reach £233 million by 1995.

Spain is cited as the market which will grow the fastest and it is envisaged that Germany will exceed the market average in yearly volume growth, paralleled closely by the UK. Chemical firms are said to be purchasing more than 60 per cent of all products sold, followed closely by the food and beverage industry. (Extracted from Chemical Marketing Reporter, 12 January 1987 and Engineering, February 1987)

World Resources Institute sees positive role for biotechnology in the third world

"Like any other major industry, the emerging biobusiness has a major stake in the sustainable development of the world's natural resources," notes a new US report from the World Resources Institute, "whether or not it recognizes the fact." At a time when the downside of biotechnology is constantly in the headlines, with activists like Jeremy Rifkin keeping the media spotlight firmly on the biotechnology industry in the United States, the WRI report is designed to help policy-makers think through both sides of the equation.

Written by Biotechnology Bulletin editor John Elkington following extensive visits to US biotechnology companies in 1985 and 1986, Double Dividends? US Biotechnology and Third World Development reviews the work under way in the USA and concludes: "Of all the emerging technologies biotechnology - or the cluster of technologies that go by that name - probably has the greatest long-term potential for promoting environmentally sustainable development in the Third World." Profiles of companies doing relevant work are included. Details of the report, priced at $7.50, from: Dr. Janet Welsh Brown, Senior Associate, World Resources Institute, 1735 New York Avenue, NW, Washington, DC 20006, USA or on 0101 (202) 638 6300.

The International Scientific Committee for Biotechnology (COBIOTECH)

The General Assembly of the International Council of Scientific Unions (ICSU) at Bern (Switzerland) in September of 1986 resolved to establish an International Scientific Committee for Biotechnology (COBIOTECH) and provided initial core funding. Terms of reference for COBIOTECH are contained in a report of an ad hoc ICSU study group on biotechnology and in a draft constitution.

COBIOTECH has the goal of serving as a focal group for the promotion of biotechnology for the benefit of humankind and to provide information and advice on biotechnology for the international community as a whole.

The initiative for establishing COBIOTECH arose among scientists actively engaged in biotechnology and from disciplinary and regional international organizations concerned with the field. They recognised the interdisciplinary nature of biotechnology which involves engineering, industry, agriculture and medicine as well as the basic sciences. They also recognised the role of ICSU to relate science to society and the special concern of ICSU for developing countries.

COBIOTECH is to serve as a clearing house for information on biotechnology-related activities such as meetings, courses, fellowships, culture collections, data banks, governmental regulations, international projects, standards and nomenclature.

The Committee is also to function in an advisory role, evaluating biotechnology projects on request from national governments or international institutions and presenting the opinion of the scientific community to the public sector in matters that affect biotechnology.

A third main function of COBIOTECH is to stimulate activities that result in international co-operation, such as the organization and sponsorship of scientific meetings, conferences for public education, workshops on specific topics and laboratory training courses. The Committee also will issue appropriate publications.

COBIOTECH is to work in close collaboration with other ICSU scientific bodies and national members as well as with outside scientific and industrial organizations having an interest in biotechnology internationally.

An Interim Steering Group has been appointed consisting of Jorge Allende (Chile) and Philipp Gerhardt (USA), Isao Karube (Japan), and H. Ringpfeil (GDR) as Co-chairmen.

The Interim Steering Group is to organize and communicate an agenda for the first meeting of COBIOTECH, invite interested ICSU and non-ICSU bodies to designate a representative to COBIOTECH, initate certain activities in 1987, and raise additional interim funding. The Group met on 2 and 3 February 1987, at the International Centre for Genetic Engineering and Biotechnology of the United Nations Industrial Development Organization in Trieste, Italy.

An organizational first meeting of the full International Scientific Committee for Biotechnology was held on Saturday, 13 June 1987, just before the European Congress on Biotechnology at Amsterdam, the Netherlands. COBIOTECH convened at the International Centre of the Royal Tropical Institute.

Further information is obtainable from the following sources:

ICSU Secretariat, 51 bd. de Montmorency, Paris 016, France. Telephone: 33/1/4525-0329
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Prof. Jorge E. Allende, Departmento de Bioquimica, Facultad de Medicina (Norte), Universidad de Chile, Casilla 70086, Santiago 7, Chile. Telephone: 56/2/376-3 20
Telex: UNESCO CK 340258.

Prof. Philipp Gerhardt, Michigan Biotechnology Institute and Michigan State University, P.O. Box 27609, Lansing, MI 48909, USA.
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Scientists seek crops to help feed the world's hungry

Dr. Richard Felger sees more in the desert than most people do. Where they see forbidding desolation, he sees a rich and varied ecosystem. Dr. Felger is one of America's ethnobotanists and his specialty is new food crops that could thrive in those areas of the globe where hunger is now ever-present.

A young discipline that appeared around the turn of the century, ethnobotany has come into its

own in the last 10 years. It lies at the confluence of botany and anthropology and involves gathering information about plants and their uses from native peoples, usually isolated cultures that have lived in harmony with their environment for hundreds or even thousands of years.

Ethnobotany's leading practioners include researchers at the Harvard Botanical Museum, the University of Illinois, the University of Arizona (including Felger) and the University of New Mexico.

The most immediately significant research in ethnobotany is in the area of new food crops. Yet its significance goes far beyond the need for more food.

As Felger puts it, "I'm not only talking about more food, but crops better adapted to the environment. Right now, we're changing the environment to fit a narrow range of plants. My basic philosophy is to change the crops to fit the environment. We'd use fewer pesticides, less energy, less water."

Ethnobotany is often the best avenue to ecologically sound new crops because indigenous cultures know about the plants native to their regions, plants that have adapted naturally to those regions over time and generally don't need as much irrigation, fertilizer or other aids. Ethnobotanists can learn about promising native food plants and then figure ways in which to adapt them for modern agriculture.

Felger's work has taken him all over the globe, but his passion is the desert. He lives in the Sonoran Desert and from there he roams Arizona and Mexico, gathering the knowledge that has made him a prominent figure in ethnobotany.

Felger and his colleagues estimate that local people have used at least 450 species of the Sonoran Desert's flora as food.

Originally more of a pure botanist, Felger added the "ethno" to his job description when he encountered the Seri Indians, an isolated race of some 5,000 individuals who live in a few villages along the Gulf of California.

Felger's work with the Seris includes documentation of their use of eelgrass as food.

Eelgrass is a grain that compares favourably with major grains of nutritional value. What makes it special is that it grows in the ocean. The only known grain from an ocean plant that is used as human food, it exists in great masses along the coasts of North American and Eurasia. Because of the staggering potential, research is currently being done to develop eelgrass and other crops that can grow on or in saltwater.

Felger expects great things of his and others' ethnobotanical work. For example, he believes that the foothill palo verde, a Sonoran desert plant used for food by the Seris, is the "legume of the future." From the Cocopah Indians of the Colorado River Delta has come knowledge of palmer saltgrass, which Felger thinks could become an important grain.

But he *places the greatest faith* in mesquite, which he predicts will become one of the world's major crops, joining vital grains such as wheat and rice, by the year 2000. (Source: Agricultural Information Development Bulletin, March 1987)

The effect of AIDS on Europe

Like a wave starting with a deceptively gentle build-up, AIDS has crashed upon Europe. The force of the impact shows itself both in the rising numbers of those who have caught the disease and in the vigorous reaction it has brought from most West European governments. At present America still has five times more victims in proportion to population than even the worst-hit country in Europe. Yet the complacent notion that this is "an American disease" or something out of Africa has been exploded in Western Europe, and is fast being deflated in Eastern Europe.

The epidemic has hit all of Western Europe's larger countries, France in particular. It is proportionately most severe in three smaller states: Switzerland, Belgium and Denmark. After appearing as what seemed to be limited danger in Europe in 1983 - two years after it began alarming American doctors - AIDS has become one of Europeans' deepest concerns.

People over much of the continent have come to see the disease as something that could affect them personally, according to the World Health Organization's AIDS-control specialist, Dr. Jonathan Mann. It is no longer "they" but "us" and "our children" who are at risk. In Western Europe, the previous disposition to minimise the threat (by arguing that AIDS is not as dangerous as driving a car, and so on) has pretty well vanished. West Europeans have been shocked by loud, frank and repetitive reporting of the facts into recognising that this plague spreads quickly.

As in America, 50-100 times more Europeans are thought to be infected with the virus than have died or are suffering from the disease. According to Dr. Mann, the experts think that by the end of next year the number of European victims will have reached the present American total: close to 30,000, which does not include the much larger number of carriers who have not yet developed the disease.

The disease has come to Europe by a variety of routes. France and Belgium have close post-colonial links with black Africa; two-thirds of Belgium's cases are non-residents, predominantly Africans. The Swiss have Europe's highest per capita rate of diagnosed cases, officials in Bern contend, because they are rich enough to travel a lot, especially to the United States, and also get many foreign visitors. In both Italy and Spain an overwhelming proportion of victims are drug-users. That contrasts with the northern countries - Federal Republic of Germany, the UK, Scandinavia, Holland and to some extent France again - where the disease seems to have mainly taken the homosexual route from America.

Countries in the communist part of Europe officially report to the WHO a mere handful of cases. These countries have indeed had less contact with infected parts of the world. They also have stiffish conventions about sexual behaviour of all kinds, and fewer opportunities to inject themselves with drugs.

Still, a widespread growth of AIDS-testing in Eastern Europe, notably of blood-donors and African students, and an explosion of AIDS committees, councils and co-ordinating teams, suggests that the communist states are more affected than some of them care to admit. In Hungary, the government is sending information leaflets to all families.

A message for everybody:

Most governments in Western Europe are preparing, or have already launched, publicity campaigns.

Testing, or screening, for AIDS has put

European governments in a dilemma. It has been carried out systematically among blood-donors, yet nowhere are the authorities ready to make it a general requirement. Still less are governments ready to list known carriers. That would discourage people from seeking medical help for fear of being identified. Calls for the naming and quarantining of carriers have so far come mainly from fringe political parties of the far right. By contrast, the authorities are increasingly overcoming scruples about offering free disposable needles to drug-users. Amsterdam pioneered this; Spain is considering issuing them in its prisons.

In the hunt for a cure, the French lead the European field. The Russians say dozens of their scientific institutes are at work on an elusive vaccine. (Extracted from The Economist, 24 January 1987)

Chemical resistance

Resistance is one of the clearest instances of Darwinian natural selection. Bacteria are evolving resistance to antibiotics and insects resistance to pesticides faster than new chemicals are being invented. Resistance spreads from bug to bug because most of the resistance genes lodge themselves in plasmids: small loops of DNA that bacteria swap with each other. Resistance is usually irreversible. It can also move between species of bacteria: a harmless soil organism made resistant by antibiotics on a farm can pass the resistant plasmid to a strain of Salmonella.

Again for Darwinian reasons, the enemy gets better at developing resistance: selection encourages the quick evolvers. Five successive generations of pesticides have passed since DDT was first used in the 1940s. The time it takes for the number of species of insects resistant to each new generation to double has fallen from 6.3 years for DDT to one year for the newest generation of pesticides, pyrethroids. Colorado potato beetles have beaten almost everything thrown at them. In the beginning, it took them many years; today, they can beat a new insecticide in a season. Meanwhile, many of the insects that eat Colorado beetles are still susceptible. Spraying simply encourages the beetles.

More than 450 species of insect are now resistant to DDT. The most famous is the mosquito, which turned the World Health Organization's 21-year, $2 billion campaign to stamp out malaria into a rout. In 1963 the programme had worked so well that there were only 17 cases of malaria in Sri Lanka. By that year resistance appeared and by 1968 the country had an epidemic of more than 1 million cases.

Antibiotic resistance has yet to produce such a medical disaster but it will do so before long. Dr. Stuart Levy of Tufts University has found that more than half the benign bacteria in human guts in Massachusetts are resistant to at least one antibiotic. Benign bacteria can pass on resistance to harmful ones. In the United States, the first case of penicillin-resistant gonorrhea appeared in 1976; by 1985 8,500 cases were reported.

Multiple resistance is a new worry. Dr. Levy has done experiments raising chickens on tetracycline. Within 12 weeks, their gut bacteria were resistant not only to tetracycline, but to several other antibiotics as well. In Tanzania, cholera has evolved resistance to several drugs, though only one was used. The same is happening among insects. In 1976 only seven species were resistant to all five classes of insecticide; now 17 are, including house-flies, cockroaches and mosquitoes.

Nor is genetic engineering much of a help yet. The first genetically-engineered crops will have genes conferring resistance to herbicides (so that farmers can spray more herbicide on nearby weeds), and resistance to insects conferred by a gene taken from bacteria. Both will simply encourage resistant weeds and bugs to appear quicker.

The number of new kinds of pesticides and antibiotics invented each year has fallen fast over the past quarter-century. Between 1980 and 1985, no new pesticides were introduced at all. Meanwhile, costs have climbed relentlessly. Synthetic pyrethroids cost 100 times as much in real terms to develop as did DDT (and the best of them, deltamethrin, 1,300 times as much). The ever more rapid appearance of resistance has put chemical companies in a squeeze. They have less time in which to recoup greater costs, so they encourage wider use, which accelerates the appearance of resistance.

The chemical industry may find a way out of its dilemma by developing chemicals that fight resistance. For example, Dr. Samuel Martin and his colleagues at the Walter Reed Army Medical Centre in Washington, DC have recently shown that they can reverse resistance in malarial parasites to chloroquine, an antimalarial pill. They did so by learning from cancer cells, which can also develop resistance to drugs. Cancer cells achieve resistance by becoming more efficient at getting rid of the drug and so preventing it accumulating: hence, the cell can resist various kinds of drug after being exposed to only one.

A chemical called verapamil fights this excretion and so reverses resistance. In the laboratory, it also works for chloroquine-resistant malaria. Perhaps one day it will be possible to give people penicillin together with a chemical that reverses resistance to penicillin.

At the moment the only answer for both pesticides and antibiotics is to use them sparingly. This not only postpones the spread of resistance, but in some cases can head it off altogether. Antibiotics, Dr. Levy says, should not be used in farms, nor be used indiscriminately for weeks before surgery, and should not be available over the counter for all sorts of unsuitable ailments, as they are in many poor countries. In Mexico, scientists have found that the amount of resistance co-relates neatly with the availability of antibiotics.

Similarly, insecticides, used carefully, need not produce resistance. In Australia, it is illegal to use synthetic pyrethroids on Heliothis, a cotton pest, except during a 40-day period each year when the bug is most vulnerable. After five years of prohibition, no evidence of resistance to synthetic pyrethroids has appeared in Australia. In the rest of the world, cotton growers profligate in their use of the stuff have had no trouble producing resistance.

In another case, Dr. Brian Croft of Oregon State University has persuaded the chemical industry to leave off its label any suggestion that pyrethroids be used in summer against a pest called Psylla. Again, resistance has been avoided. In Italy and East Europe, which have used the pesticide in summer, resistance is rife.

Such practices are hard to introduce. Farming will survive - it can breed plants in the right rather than the wrong direction but human health will suffer. The only hope is that genetic engineering can deliver weapons that evolve as fast as the enemy. (Extracted from The Economist, 21 March 1987)

B. COUNTRY NEWS

Australia

r-DNA Monitoring Committee submits report

Australia's Ministry of Industry, Technology and Commerce has completed a report that identifies ways to manage any hazards associated with recombinant DNA technology. The report, prepared by the Recombinant DNA Monitoring Committee, recommends minor changes to the non-statutory monitoring system. The government's reaction to the report is not expected until autumn this year. (Source: European Chemical News, 19 January 1987)

Bangladesh

Report on international workshop

The International workshop on Basic Molecular Biology and Recombinant DNA Technology organized by the Department of Zoology, University of Rajshahi, in collaboration with the Centre for Advanced Molecular Biology, University of the Punjab, Pakistan, was held at the Laboratory of Genetic Engineering, Department of Zoology, Rajshahi University from 4 to 18 April 1987. The course was designed to introduce the young and initiated researchers at the post MSc level to modern techniques commonly employed in genetic engineering research. An emphasis was placed on those methodologies which could be routinely carried out under local conditions and enabling future scientists to practice modern approaches in their teaching and research assignments.

Ten post-MSc researchers (two were observers) from various universities and different R&D institutions in Bangladesh participated as trainees in the workshop. In addition, four scientists from third world countries were invited to attend the course. The scientists from Sri Lanka, India, and Pakistan participated in the course as trainees. Four experts, three from the Centre for Advanced Molecular Biology, University of the Punjab, Pakistan, and one from the Department of Zoology, Rajshahi University, demonstrated the laboratory work programmes of the workshop very successfully. The experiments planned in the workshop were the methods for isolating DNA (procaryotic) and plasmid, preparation of competent cells and transformation in E. Coli, molecular cloning, restriction endonuclease analysis and gel electrophoresis, colony hybridization, southern blotting and other methods of molecular biology. In addition to course lectures, guest professors delivered special lectures on molecular mechanism of DNA repair, cloning and characterization of the dcm locus of E. Coli K-12 and expression of chemically synthesized yeast ubiquitin gene under copper metallthionein promoter. The workshop was sponsored by ISESCO, TWAS, the British Council and Rajshahi University.

Canada

New tissue culture plant in Nova Scotia

Based on Nova Scotia, Canada, Nova Biotechnology Inc. plans to exploit tissue culture methods to boost production of a range of plants. A lack of highbush blueberry plants in Nova Scotia led the company to experiment with the propagation of blueberries and strawberries and it has since expanded into 29 different crops, including apples, pears, herbs and ornamental plants. A new tissue culture facility due to open soon is being built near Upper Canard, in the Annapolis Valley, with financial assistance from Canada's National Research Council. (Source: Biotechnology Bulletin, Vol. 5, No. 12, January 1987)

Denmark

Danish company buys into US firm

Denmark's Novo Industri, a leading maker of enzymes and pharmaceuticals, has bought a 20 per cent holding in Idetek for $3.3 million. Based in San Bruno, Calif., Idetek, a small privately owned concern set up in 1983, has developed novel tests using monoclonal antibodies for application in three broad areas. One is in meat inspection, such as the identification of the pathogenic organisms that cause trichinosis in pigs. Another is in food analysis, typically the characterization of the bitter constituents of citrus juices. The third is in the evaluation of plant growth hormones. The move gives Novo production and marketing rights for Idetek's products outside the US. Novo already has a team of some 50 people studying the application of monoclonal antibodies to human diagnostics. (Abstracted with permission from Chemical and Engineering News, Copyright, 16 February 1987, p. 8, American Chemical Society)

EEC

Two reports on the impact of biotechnology within the EEC

Members of the European Parliament debated two reports on the impact of biotechnology within the Community during January.

Dutch Socialist Phili Viehoff warned that the EEC will have to adapt and revise all its programmes for biotechnology if Europe is not to fall behind US and Japanese efforts.

In a report, drawn up by the Parliament's Energy, Research and Technology Committee, there was a call for an integrated policy with sufficient funds for this sector. By comparison the US spends about $2 billion annually, while the European community has only spent Ecu15 million ($16.8 million) on its biomolecular engineering programme in the past four years.

The Energy, Research and Technology Committee acknowledges the positive results of the first two Community programmes in biotechnology which stimulated transnational co-operation and industry support, but points out that more than 80 per cent of proposals for the four-year research programme launched in 1985 had to be rejected because of insufficient funds.

The Committee has called on the Commission to set out a list of priorities for research focusing on healthcare and environmental considerations. Furthermore, harmonization of patent laws allowing innovations to be treated uniformly throughout the Community is expected.

More controversial was the European Parliament's Agriculture, Fisheries and Food Committee's report on the consequences of the introduction of biotechnology into European agriculture. While conceding that biotechnology will probably allow the EEC to cut fodder imports there is a danger that small and medium-sized agricultural enterprises will disappear. There appeared little regard by the Commission for the social consequences of biotechnology. The Committee has highlighted a number of problems and risks that biotechnology could throw up and is concerned that agricultural research is becoming concentrated in the hands of a few chemicals giants. Since the start of the 1970s about 900 seed firms have been taken over by the large agrochemical companies. "By the year 2000 the seed market will be controlled by a dozen seed and chemical multinationals," the

report warns. Concern has also been raised about the environmental risks and consequences for the developing nations, warning that commercial applications of biotechnology are diametrically opposed to the objectives of the common agricultural policy (CAP) and Third World development.

Another of the committee's concerns is the effect of biotechnology on the diversity of animal and plant species. It is also anxious that bioethanol production should be be seen as a solution to the problem of surpluses as the permanence of these surpluses would be a precondition for production.

Not surprisingly, most of the chemical industry and particularly those companies with oil interests are also against the use of agricultural surpluses for bioethanol production. Industry observers estimate that the price of crude oil would have to rise to about $75/barrel for bioethanol production to be economically feasible.

However, after debating 39 amendments to the Parliament's Energy, Research and Technology Committee report and 53 amendments to the report from the Agriculture, Fisheries and Food Committee there were not enough members present to vote on the reports.

Votes on the two reports, which assess the impact of biotechnology have now been postponed.

In an attempt to keep to its own deadline for the introduction of two biotechnology directives the European Commission hopes to meet representatives of European industries this month. The two directives will cover deliberate release of genetically manipulated organisms and hazard controls similar to the Seveso directive.

Officials in Brussels are anxious to discuss EEC plans for regulating guidelines with the European Committee on Regulatory Aspects of Biotechnology (ECRAB), a body involving five European industry federations interested in biotechnology. Likely to be the most contentious issue is the Commission's plans for deliberate release guidelines, which will affect firms developing microbial pesticides.

The European Parliament has called for stringent testing of potential ecological consequences of deliberate release and has requested the Commission to present forecasts on the structural and social consequences of biotechnology on European agriculture.

In addition, the Commission has been asked by the Parliament to revise its biotechnology programme to give an effective strategic programme which respects ecological principles. (Source: European Chemical News, 26 January 1987, 2 February 1987 and 9 April 1987)

EUREKA consortium posts first 1987 bio-investments

EUREKA, short for the European Research Co-ordinating Agency, a consortium of 18 continental countries plus the European Economic Commission's executive board, has released its first list of 37 research projects approved for 1987. Five of the multinational undertakings are clearly in the fields of biotechnology and account for some $42 million in funding. They are described below.

A brainchild of the French, EUREKA was created in 1985 as a civilian counter-project to the US invitation for European research to aid the Strategic Defense Initiative. EUREKA describes itself as a multilateral "information conduit" to promote cross-frontier scientific collaboration. Participants agree to share expertise and research results, but not necessarily commercial benefits. Funds come from each project-participant's member-government. In addition, there may be considerable private-sector contributions to the financing, but these are usually confidential.

EUREKA's 19 members includes the twelve Common Market countries and the European Free-Trade Association states - Austria, Switzerland, Sweden, Norway, Finland, Iceland. Non-European parties may join in an activity, but all work must take place on EUREKA territory. About 10 per cent of all projects since EUREKA's inception have involved biotechnology; these five are the latest:

- Venereal-disease diagnosis: A two-year collaboration between the UK's PA Technology Ltd., Royston, Herts. and Spain's Biokit SA, Barcelona, to develop monoclonal-antibody-based kits for rapid detection of gonorrhea. There are roughly 450 different strains of gonorrhea; present methods require two to three days of extended laboratory analysis to diagnose a gonorrheal infection. Research funds - 2.4 million Ecu (US$2.7 million) will be divided according to each participant's stake in the project, 70 per cent for Biokit; 30 per cent for PA Technology.

- Mammalian cell culture: This EUREKA project aims to develop high-productivity, animal-cell bioreactors for mass production of vaccines, antibodies, enzymes and hormones.

Approximately 25 million Ecu ($28.25 million) will be allocated along national lines: France, 43 per cent; Federal Republic of Germany, 2 per cent; Italy, 25 per cent. To date, four French firms are participating: Bertain Cie., Paris; the Vandoeuvre branch of France's National Science Research Centre, (CN-RS); Rhône-Poulenc Recherches, Saint Fons, Institut Merieux, Charbonnieres-Les-Bains. Austria is represented by Immuno AG, Vienna.

- Super-sunflowers: French and Spanish entities have joined to develop new varieties of high-oil-content sunflowers which can weather Mediterranean climates. Participants in the US$4.2 million project are: Rhône-Poulenc Agrochimie, Lyon (12.4 per cent); Insecticidas Condor, SA, Madrid (72.2 per cent); CIDA (Centro de Investigacion y Desarrollo Agrario) - the Agricultural R&D Centre - Cordoba, (15.4 per cent).

The goal of their seven-year project, says Rhône-Poulenc's seed project leader, Jean-Louis Arnault, is to cross - via genetic manipulation - wild sunflowers that withstand drought and cold weather, but have low oil-yield, with more fragile but higher-yield commercial species.

- Root-symbiosis: This quadripartite, US$3 million plan aims to identify and mass produce rhizobacteria for natural growth promotion and fungal-disease control in sunflower, sugar beet, soy-bean, corn and wheat. Participants are: Belgium's SES (Societé Europeenne de Semences SA) in Tienen, and Plant Genetic Systems NV of Ghent; Italy's Societa Europea del Seme, Rome; Spain's Sociedad Europea de Semillas SA, Zaragoza; Austria's Chemie Linz AG, Linz.

- Artificial tomato seeds: A joint Franco-Swiss effort aims to perfect somatic tomato embryos, which can be pelleted in a permeable, biodegradable film to eventually yield a plant. The project will initially research embryogenesis-inducing cell markers, then explore genetic information-transfer techniques. Ultimately, the group hopes to create encased seedlings of uniform size, genetically protected against disease, which can be planted quickly and economically with conventional agricultural drilling equipment.

The five-year, $3.7 million programme has three partners: France's Limagrain SA, based in Gerzat; Rhône-Poulenc Agrochimie, Lyon; and Switzerland's Nestle subsidiary, Nestec SA, Vevey.

The following industrial proposals have been submitted on a national level for possible co-operation under the EUREKA label.

The Netherlands

1. Development of biotechnology for production of vaccines.

2. Augmentation of the nutritional value of feedstuffs derived from agricultural products for increased productivity and growth in dairy cattle and beef and of foodstuffs for human use, using biotechnological processes such as fermentation and precipitation.

3. Development of technology for processing residuals such as dung.

Denmark

1. Plant cell culture (A/S Dansk Gaerings-Industri).

2. Protein engineering (NOVO Industri A/S).

3. High-level technology in plant and animal production and related industries (Carlsberg Research Laboratory).

Finland

1. Root growth inducers and hormones in plant engineering (Orion Corporation Limited).

2. Application of DNA probe technology to animal and plant disease diagnostics and improvement and commercialisation (Orion Corporation Limited).

3. Automation of liquid manipulation operation in genetic engineering, biotechnology, biomedical, and medical fields (Fluilogic Systems Oy).

4. Genetic engineering methods for plants (Kemira Oy).

5. Development of a method to produce anticancer anthracyline antibiotics with a streptomyces strain modified by genetic engineering (Huhtamäki Oy).

6. Environmental gas monitoring by biosensors (Vaisala Oy).

7. Antigen-antibody sensors for rapid diagnosis of infectious diseases (Orion Corporation Limited).

Greece

1. Production of metabolic products and energy (cell immobilization and bioreactors).

2. Production of monoclonal antibodies by means of hybridoma immobilization and bioreactors for medical purposes.

3. Production of peptides for synthetic vaccines and as novel reagents.

4. Production of hybrids by means of genetic engineering for agricultural applications.

5. Development of fermentation technologies for utilization of by-products (Bio-Hellas).

6. Second generation bioreactors for biosynthesis and biotransformations.

7. Pheromones (isolation, identification, synthesis).

8. Plant growth factors.

9. Production of high added secondary metabolites (pharmaceuticals, flavours, fragrances).

10. Fusion of protoplasts.

11. Dormancy in plants and optimization of plant production (Viroryl S.A.).

Ireland

1. Synthetic seeds: control and regulation systems (University Colleges at Dublin and Cork).

Portugal

1. Development of seeds by genetic or synthetic processes.

2. Development of biofertilizers.

3. Utilization of new vegetal protein sources (Favorita-Industria, Agro-alementar Lda).

4. Process development for enzymatic products and immunomodulator agents.

5. Process development for extraction under supercritical conditions to be applied for aromatics and essences (Franco Farmaceutical).

Belgium

1. Control systems applied to the field of medicine (SABCA).

2. Development of biospecific detection systems for biological compounds (ARBIOS).

3. Industrialization and automation of in vitro cultivation (Belgonucleaire).

4. Development of genetic engineering technology to improve sugar beet cultivation and characteristics such as resistance to disease (virus, mould) and to herbicides (Plant Genetic Systems).

5. Genetics of plant varieties in view of a selective reforestation (BIAGRAL).

6. Artificial seeds (Plant Genetics Systems).

7. Development of a computer-aided protein design system (Plant Genetic Systems).

8. Separation processes (Oleofina).

9. Production of food products by micro-organisms (ANVIOS).

10. Continuous fermentation reactor technologies (including fungi culture technologies) (ARBIOS)

France

1. Artificial seeds (Rhône Poulenc).

2. Animal mass cell culture (Bertin et Cie).

3. Fine regulation of inoculation in medicine (ELF).

4. Construction of "host-vector" pairs leading to micro-organisms or genetically modified animal cells (ORGANBIO).

(Source: McGraw-Hill's Biotechnology Newswatch, 2 March 1987 and European Science News, February 1987)

Federal Republic of Germany

Gene study calls for laws

The Federal Republic of Germany's parliamentary committee on the risks posed by genetic engineering is calling for the establishment of a legal framework for research into and exploitation of the new technologies before areas of application are technically or economically feasible.

In its report, which took two years to complete, the 17-member parliamentary committee makes a number of concrete recommendations for coming to grips with the possibilities offered by genetic engineering. Among other things, the paper recommends legal safety guidelines for basic and applied research, the establishment of registration procedures for new products and a legal framework for questions of data protection and manufacturers' liability. (Source: European Chemical News, 9 February 1987)

Finland

NASH technique

Finnish Orion Pharmaceutica has developed a technique called the "Nucleic Acid Sandwich hybridization" technique (NASH), which makes it possible to accurately identify various organisms and genetic structures based on the absolute specificity of the genes. The method has wide applications both in medicine and in other branches of science and has been patented worldwide. Orion has now signed an agreement with the Du Pont Group on product development and marketing co-operation on the NASH technique, suitable for the diagnosis of human diseases, microbes and for all cell identification. (Source: Biotechnica '87, Hannover, Journal No. 2)

US firm licenses system to Finnish company

Panlabs, Inc., Seattle, has licensed its "proprietary recombinant technology" to Finnish Sugar Co. Ltd., Espoo, Finland, for an initial term of one year. The Finnish firm will use the US company's process for enhancing product synthesis by recombinant filamentous fungi to increase output of certain enzymes. One feature of the Panlabs process that attracted the Finns is its method of transforming a host organism, such as Aspergillus niger to synthesize an enzyme of interest, then enhance its yield by strain improvement. An advantage of fungal hosts is that cloned genes are integrated into the cell's chromosomes for greater stability. Also, a gene of interest produced by a host - for example, one encoding alpha-amylase - can be re-introduced in multiple copy-number to increase secretion level. (Extracted from McGraw-Hill's Biotechnology Newswatch, 16 March 1987)

France

Panel set up to review proposals

France has also made major, though tentative, moves regarding the deliberate release of genetically modified micro-organisms into the environment. In Paris, the Ministry of Agriculture has just set up a top-level 15-member panel of scientists "to reflect on the question globally, review proposals case by case, and weigh the orientation of future jurisdictions" in the matter.

Chairing the French body will be Pierre Royer, honorary president of the Pasteur Institute's board of directors. The commission was set up at the behest of scientists, led by France's foremost official figure in biotechnology, Daniel Thomas, who directs the Ministry of Research's four-year-old Biotechnology Impetus Programme. (Extracted from McGraw-Hill's Biotechnology Newswatch, 16 February 1987)

Public R&D funding for biotechnology

France, like Europe, while possessing basic research of international quality and fame in numerous branches of biology, has been long in evaluating its results. The transfer of scientific accomplishments from public basic research to the private domain and its exploitation have come about only partially and later than in the United States and Japan.

Various measures encouraging research do exist in France and since 1981, specific aid has been given to industrial biotechnologies through the promotional "Boom in Biotechnologies" programme. Except for this programme, most government participation in research and development in

R&D budgets in France
(in millions of French francs)

	1982	1983	1984	1985	1986
Total public and private R&D budget	74,800	84,800	95,000	104,000	
Public R&D budget	42,636	48,336	54,150	58,240	
Public R&D budget for biotechnologies		680	800	1,000	1,000
Minimal public aid to biotech. R&D of industry		34.5	40	57	50

Source: Ministry of Research

biotechnology comes in the public research centres and institutes (the CNRS [National Centre for Scientific Research], INSERM [National Institute of Health and Medical Research], the INRA [National Agronomic Research Institute], etc).

Incentives and nonspecific aid to bioindustrial research include mainly tax-research credit, aid to innovation of ANVAR (National Agency for the Implementation of Research) and co-financed scholarships. ANVAR credits, because of their mode of distribution, do not help all enterprises engaged in active, high-performance industrial research. It has a budget which, compared with other major organizations, remains modest, considering its strategic mission and the scope of its task. The credits it allocates can only complete other measures.

The following table gives the main figures for the French public R&D budgets and the share allocated to biotechnologies, which is low. Public aid for biotechnological research and development in industry come mainly from the MRT and is granted through the "Programme" to Promote Biotechnologies." Aid given by ANVAR is very little in this field. Public aid for research and development in the bio-industries represents less than 6 per cent of the public budget devoted to biotechnologies and under .01 per cent of the overall public R&D budget.

France boosts AIDS research funding

France is committing FF 100 million for research into AIDS, 10 times the amount allocated last year. In addition, a new research centre to define viral and immunology treatments for the disease is to be established by Institut National de la Santé et de la Recherche Médicale at the Pitié-Salpêtrière hospital in Paris.

Research on retroviruses at the Institut Pasteur is also expected to be completed, according to Jacques Chirac, France's prime minister. Currently France has the highest number of AIDS sufferers in Europe, over 1,000.

Meanwhile, Diagnostics Pasteur has announced a number of developments in the AIDS diagnostics field. the joint subsidiary of Institut Pasteur and Sanofi hopes to market a test that detects antibodies directed against the HIV-1 and HIV-2 viruses both rapidly and simultaneously. Approval is expected in France for a new test which detects the HIV-1 virus directly by the summer.

Researchers at the French firm are conducting several types of tests on a synthetic HIV-1 virus in co-operation with US partner Genetic Systems. The synthetic substitute is based on peptide chemistry which has proved successful on available serum collections. (Source: European Chemical News, 16 March 1987)

German Democratic Republic

GDR researchers produce AIDS monoclonal antibodies

The Institute of Clinical Immunology at East Berlin's Charite hospital has produced monoclonal antibodies against the (HIV) human immunodeficiency virus responsible for AIDS (acquired immune deficiency syndrome). The Charite team see this as a step towards developing antibody-linked drugs to combat the virus. The announcement was made by Professor Roedigar von Baehr, head of the research team.

The German Democratic Republic has a well-developed AIDS information service and was prepared to discuss the risks earlier than other socialist countries. (Source: Nature, Vol. 326, 26 March 1987)

Hungary

Hungary and Japan sign agreement for lysine plant

A plant to produce lysine from genetically modified bacteria is the biggest single foreign investment in Hungary since that country permitted foreign equity participation in partnerships in the mid-70s. Kyowa Hakko Kogyo Co., Ltd. and Toyo Menka Kaisha Ltd. and a consortium of Hungarian shareholders - Nagy Hajdu Agricultural Industrial Association, Hadadvar, National Commercial and Credit Bank Ltd., and Grain Trust, both of Budapest - put up a total of $18 million to build the factory in the eastern Hungarian town of Koba. The Hungarians hold 60 per cent interest in the project; the balance of the $45 million project's cost will be covered by long-term loans from the International Finance Corporation, an arm of the World Bank. Kyowa Hakko will provide production technology, and receive royalties for use of its microbial strain. (Source: Newsam-Hill's Biotechnology Newswatch, 2 March 1987)

India

Centre for Advancement of Biotechnology

Activities:

The Centre for Advancement of Biotechnology at Bangalore, India is a non-profit voluntary scientific research organization committed to bring awareness of the unique position that biotechnology occupies in shaping human society in the areas of health, food, chemicals, environment and energy, indeed it may turn out to be the basic pervasive technology for the future of mankind.

The CAB is the result of a common desire of a number of young scientists and engineers from all over India, who would like to disseminate information to universities, research institutions and industry on the progress of biotechnology and its relevance to society in improving the quality of life with modest outlays, especially in the developing countries.

As a first step the CAB publishes a News Monitor free of charge to acquaint scientists from research institutions, universities and industries with the latest information on developments in biotechnology. The CAB has also published a special News Monitor entitled "Biotechnology in India" which highlights biotechnology work activities at various institutions in India.

The CAB plans to conduct mission oriented research on the application of biotechnology to the problems of agriculture, environment, energy, food, etc., of special relevance to India in collaboration with the RV Institute of Plant Tissue Culture at Bangalore.

Some of the aims and objectives of the Centre are:

- To stimulate research in the field of biotechnology and bioconversion with regard to its application in India;
- To promote biotechnology by organising symposia, seminars, workshops and short courses for the exchange of knowledge and advances in the field;
- To create a nucleus for the development of industries based on biotechnology;

- To establish a research and development unit where applied biotechnology research can be carried out;

- To associate with national and/or international bodies connected with promotion of biotechnology.

India considers establishing AIDS institute

The Indian Council of Medical Research (ICMR) is advocating a National Institute for AIDS for research and to treat patients. By 1 March 1987, 104 cases of infection had been detected in India out of 30,000 people so far screened at ICMR's referral centres. At least four new cases are detected every two weeks.

Because many of the infected cases are expected to develop the disease, a hospital exclusively for AIDS is now considered necessary; existing hospitals are overcrowded and are not equipped to deal with AIDS patients. (Extracted from Nature, Vol. 326, 26 March 1987)

New research centre established

In what is described as a unique collaboration, the Swedish pharmaceutical company AB Astra and the Indian Institute of Science (IISc), Bangalore, have joined forces to establish a centre for basic research in genetic engineering and biotechnology. Located in Bangalore, the immediate aim of the Astra Research and Development Centre is to recruit a group of outstanding Indian scientists involved in biotechnology research in India and abroad. The long term objective of the centre is to develop drugs, diagnostics and prophylactics for such tropical diseases as malaria and diarrhoea, using recombinant DNA and hybridoma technologies. AB Astra will fund the research while the IISc will provide the back-up infrstructure and laboratory facilities as well as training personnel. The new centre's director is Prof. J. Ramachandran, currently director of the protein chemistry division of Genentech Inc., USA. (Extracted from Business World, 19 January 1987)

Japan

Japanese biotechnology budget increases 15 per cent; up for fourth straight year

The Japanese government has increased its overall budget allocations for biotechnology. Virtually all of the government departments with biotechnology interests are funding new programmes for 1987.

GOVERNMENT ALLOCATIONS FOR BIOTECHNOLOGY	Millions of Yen 1986	1987	% Increase
Ministry of International Trade and Industry (MITI)	5400	6100	13
Biotechnology section of "Next-Generation" project	1280	1232	-4
Biomass technology development	1312	874	-33
Bioindustry safety	115	167	45
Organic acids from petroleum	313	504	38
Biotechnology projects with STA	249	239	-4
Large-scale industrial water recycling - "Aqua-Renaissance 90"	1072	2123	98
Sci. Tech. Agency (STA)	10000	12800	28
Technologies promotion	2200	2200	0
Cancer, nuclear medicine	240	375	56
Inst. Physical, Chemical Research:			
International frontier research	231	386	67
Life-science projects	325	255	-22
Genetic sciences	1094	1201	10
Cell depository	226	367	38
R&D Corp. of Japan:			
Hepatitis B. vaccine	1145	1589	39
Super-molecules; generative genes	1245	1797	44
Nat. Inst. Radiological Sciences	2390	3257	36
Japan Information Center	744	901	21
Ministry of Agriculture, Forestry and Fisheries (MAFF)	3100	3200	3
Plant breeding	445	449	1
Local biotechnology R&D	234	256	9
Infrastructure Technologies	320	421	31
Gene bank	915	879	-4
Food technologies	548	721	32
Livestock	530	408	-23
Ministry of Health and Welfare (MHW)	3400	5000	32
Health and Welfare research:			
10-year anti-cancer program	1570	1820	16
Longevity research	785	860	10
Research on the elderly	1	300	29900
AIDS	1	3	200
Biological resources	1032	979	-5
Ministry of Education, Culture and Science (MECS)	20000	14100	-
Recombinant DNA	25	pending	-
Animal experimentation facilities	1557	pending	-
Bioscience facilities	1113	pending	-
Bioscience equipment	1729	2201	27
10-year anti-cancer strategy	8792	8848	1

MITI: Although the ministry announced that it was slowly phasing out bioreactor research and cutting its 'Next-Generation Project' it had a 13 per cent overall increase in allocations for 1987. MITI has started a six-year plan to improve continuous yeast-alcohol fermentation by cell fusion and recombinant DNA. It increased funds for bio-safety by nearly half and all but doubles its three-year-old Aqua Renaissance programme.

STA: Its 25 per cent budget increase is the largest among government agencies. Three projects will begin at the Institute of Physical and Chemical Research: genetic structures, recombinant expression of components of the immune and nervous systems.

MAFF: Even though MAFF suffered a 4 per cent budget decrease, funding of its biotechnology projects increased 3.2 per cent. New programmes include development of enzymatic food conversions and enzyme production by gene splicing and protein engineering; gene mapping, cloning and chromosome isolation in rice.

MHW: The newly established financing/investment system will recive ¥1 billion ($6.4 million), only a quarter of its initial request. It will offer support to joint corporate ventures in development of pharmaceuticals by biotechnology, drug delivery, Phase I and II clinical trials and gene banks.

Selected budget items for fiscal 1987 and 1986 are compared in the table on the left. Expansion of biotechnology into new agencies, and rearrangement

of line items, account for differences from the previously published 1986 budget. (Source: McGraw-Hill's Biotechnology Newswatch, 16 March 1987)

Hepatitis B vaccine

Meiji Milk Products claims that its hepatitis B vaccine has passed the World Health Organization's (WHO) safety standards. The remnant of DNA in the vaccine is one hundred thousandth of the WHO standard. The firm started clinical trials last November and plans to begin marketing the vaccine in 1989. (Source: European Chemical News, 26 January 1987)

Japanese link on biochip R&D

Eight leading Japanese electronics firms are to join forces to develop a biochip, the key to the potential development of organic computers. The companies have been selected by the industrial technology council, an advisory body to Japan's Ministry of International Trade and Industry (MITI). MITI will invest some Yen 5 billion in the venture over the next 10 years.

The eight firms - Mitsubishi Chemical Industries, Fujitsu, NEC, Hitachi, Mitsubishi Electric, Sanyo Electric, Sharp and an R&D subsidiary of Matsushita Electric Industrial - will set up a committee and invite researchers at various institutions to take part in the venture. (Source: European Chemical News, 5/12 January 1987)

Japan plans to sequence human genome

Japan's Science and Technology Agency has taken its first formal step towards setting up a programme for sequencing the human genome.

The agency, in collaboration with Seiko and Fuji Film, has for several years been developing an automatic DNA-sequencing machine under the leadership of Professor Akiyoshi Wada of Tokyo University and a move to begin processing long DNA sequences, such as the human genome, has been expected.

The biotechnology sub-committee of the Agency's Council for Aeronautics, Electronics and other Advanced Technologies will chart policy during the next year and its working group, composed of fifteen scientists will draw up a detailed research programme.

Among the issues to be resolved are the relative weights to be placed on mapping and sequencing and the priority of genes sequenced. Members of the sub-committee and the working group will visit the Seiko and Fuji Film factories to see the automatic DNA-sequencing machine.

There have been suggestions that sequencing of the human genome should form part of the Human Frontiers Science Programme being organized by the Ministry of International Trade and Industry, the Science and Technology Agency and five other ministries. But Prof. Wada, who chairs one of the Frontiers working groups, does not expect genome sequencing to figure prominently in Frontiers, although the development of DNA-sequencing machines may well form part of the programme. The present feasibility study, on the other hand, is devoted specifically to sequencing of the human genome. (Extracted from Nature, Vol. 326, 26 March 1987)

Bioelectronics

Five Japanese government ministries and more than 50 companies have moved into one key area of bioelectronics research, biosensors. Companies like NEC Corp. and Mitsubishi Electric Corp. are developing biosensors and see them as "stepping-stones" that could lead to "a chip or computer that's entirely organic".

Although companies elsewhere are also moving into biosensors, Japan is boosting its investment in biotechnology almost twice as fast as the US, although the US still spends about five times as much.

Biosensors consist of biological molecules (of a substance such as an enzyme, antibody or whole cell) linked to a transducer (e.g. an electrode or field effect transistor), so that an electrical signal is produced when a chemical reaction takes place. A 10-fold increase in the value of the European biosensor market is predicted by 1990, to be $8.6 million.

New applications of biosensors are constantly being found in the field of industrial process control. Asahi Breweries Ltd., for example, is developing a yeast-based biosensor which can sense alcohol levels in beer-brewing vats, to help control uneven fermentations. The problem has been that this alcohol sensor only survives around three days in the vat, whereas an economical device would need to last at least a month. Kirin Brewery Co. dropped its work in this field and switched to work on a sensor which does not use organic material.

There is no doubting the growing Japanese enthusiasm for biosensors. Fujitsu is thinking in terms of a biosensor that could detect chemicals in fish, to assess its freshness. Other researchers are looking at the use of biosensors to test for air and water pollutants. (Extracted from Biotechnology Bulletin, Vol. 6, No. 2, March 1987)

Laser beams to cut DNA selectively

The research laboratory of the Tokyo Institute of Technology has developed a new technology that uses laser beams to cut DNA selectively and efficiently. The third harmonic component (355 nm) emitted by a YAG laser cuts DNA when it is radiated onto a mixture of alpha-phage DNA and a photoreceptor protein composite or semiconductor-photocatalyst. This technology is designed to promote gene therapy, breeding of animals and plants, and industrial use of recombinant-DNA technology. (Source: Bio/Technology, Vol. 5, February 1987)

Monoclonals detect plant viruses

Japan Plant Quarantine Association (JPQA) has finalized a plan for replacing antisera with monoclonal antibodies to detect viruses in plants. Working jointly with the Ministry of Agriculture, Forestry and Fisheries, JPQA will begin distributing a monoclonal against rice stripe virus (RSV), followed in 1988 by an antibody to southern dwarf virus of citrus trees. In late February through early March, leafhoppers in the Kanto area will be tested to determine what percentage are carriers of RSV, and hence predict the size of the outbreak of the rice disease this summer. (Source: McGraw Hill's Biotechnology Newswatch, 2 February 1987)

Cosmetics company to manufacture drugs

Shiseido, Japan's largest producer of cosmetics, is to diversify into the pharmaceuticals business utilizing biotechnology. Shiseido scientists have been looking into the use of biotechnology in the cosmetics area, in the bacterial production of hyaluronic acid, the polysaccharide used as an eye surgery aid and a moisturizer in expensive cosmetic creams, for instance.

According to Japanese press reports, Shiseido plans to launch its first therapeutic, an epidermal agent for treatment of skin disorders in the spring of 1988, to be followed by analgesics, anti-inflammatories and an antifungal for treatment of athlete's foot. (Extracted from European Chemical News, 9 April 1987)

Sweden

Proposal to develop Swedish biotechnology

During the next ten years Sweden could invest 3.5 billion kronor into its national biotechnology programme.

The suggestion is that the State contributes the main part of the funding, with additional support from industry.

The national biotechnology programme was developed by a committee consisting of representatives from industry and research societies such as the Research Council, the University and Institute Office and the Committee for Technological Development with the aim of organizing the resources within Swedish biotechnology into a national strategy in a manner similar to that in which information technology was organized into a national microtechnology programme.

The organizations that are participating in the Swedish National Committee for Biotechnology have maintained from the beginning that their current resources cannot be used for this kind of programme. There had to be new, "fresh" funds from the State. The Committee emphasized a couple of areas where it felt the Swedish capability to be especially pronounced and could be strengthened further. These were immunology and separation technology.

"White spots" are also indicated, areas where Sweden is clearly behind other countries. Such an area is micro-biology. Other areas considered most suitable for investment of the Swedish resources were agriculture, forestry, environmental control, health and hospital care as well as equipment.

Furthermore, the Committee felt that research education had to be reinforced. The lack of competent personnel in Sweden causes businesses to look to other countries for their research and development. Pharmacia is starting a gene technology company in the United States, Astra a development company in India, etc.

The biotechnology programme has been submitted to the Government for consideration in the research and industry-political bills. (Extracted from Bioteknik & Biokemi, No. 4, November 1986)

Genes from 10,000 Nordic plants preserved for future generations

Seeds from more than 10,000 Nordic plants have been stored in a mine shaft on the island of Spitsbergen in the Arctic Sea in order to preserve their genetic material for future generations, according to a decision by the Nordic Council of Ministers. The seeds are placed in glass vials and stored in a steel container with a constant temperature of -3.7°C. This will protect the samples from genetic alterations resulting from exposure to radon, gamma radiation and radioactivity.

The Nordic gene bank is said to be the first of its kind to provide this sort of storage of seeds from all the most important varieties of cereals and vegetables. The project started in 1979 when the Council established a joint Nordic institute for that purpose in Alnarp in southern Sweden. By 1985 the gene bank had collected, catalogued and stored about 10,200 species.

Scientists annually request about 2,000 samples from the bank for research purposes. The Nordic gene bank co-operates closely with such counterparts as the Vavilov Institute in Leningrad and similar banks in the German Democratic Republic, the Federal Republic of Germany, Canada and Greece. (Source: SIP, March 1987)

Uganda

Uganda acts to stem epidemic

Uganda is to launch a five-year programme aimed at controlling the spread of AIDS. The Ugandan Ministry of Health drew up details of the programme with a team from the World Health Organization. There have been more than 1,000 cases of full-blown AIDS in Uganda. In Kampala alone, about 10,000 adults are thought to be infected with human immunodeficiency virus (HIV).

Uganda has been one of the few African countries to deal decisively with AIDS, even though it is still reeling from the effects of 15 years of civil war. The Ugandan plan of action could well provide a model for countries such as Tanzania and Kenya, both of which have expressed a wish to establish similar programmes.

Health officials presented their draft plan to the Ugandan national committee for the prevention of AIDS in Kampala in February. The aims are to start screening blood donations throughout the country, step up the health education programme and begin a programme of research into the spread of the virus.

AIDS presents a massive problem in Uganda. In one of the hardest-hit southern districts, Masaka, 30 per cent of adults attending outpatient clinics are infected with the virus. In Kampala, 13 per cent of pregnant women are infected. Tragically, about 5,000 of the babies born each year in Kampala have caught the virus in the womb. At this rate, and without any changes in sexual habits, almost every adult in the capital will have the virus within ten years.

The capital is not Uganda's worst-hit area. Its infection rates are following, with a delay of about two years, those in the south-west of the country, the part of Uganda closest to the world's worst-affected areas: Burundi, Rwanda, eastern Zaire and the Western Lake district of Tanzania. It was in the small Ugandan fishing villages along the shore of Lake Victoria that the prevalence of "slim", as Ugandans call the disease, was first noticed four years ago. The few studies carried out suggest that a third of the people in this part of the country are already infected.

The rest of Uganda is better off. In the northern town of Gulu, 13 per cent of the people have the virus. In the rural West Nile and Mukono districts, fewer than 4 per cent are reacting positively to blood tests. Yet AIDS is being spread to relatively untouched areas by two means.

One is the army. Its soldiers are now mopping up rebel forces in the rural north-east, but most of the soldiers come from the heavily infected southern regions. An ominous epidemic of venereal disease in the northern garrison over the past two years has been reported by doctors working at nearby mission hospitals. A team of Cuban doctors recently completed a two-month survey of AIDS infection in the army: unofficial preliminary results are that one soldier in three is infected.

The virus has also been hitching a lift on the trucks that move along Uganda's main highway, which runs from the stricken areas of Zaire, Rwanda, Burundi and western Uganda eastwards to Kenya and the port of Mombasa. Tests by one large freight company in Kampala found that 30 per cent of its

truck driver were infected. Prostitution is common along the route. In one town in the Rakai district on the main trucking line from the south-west, thin girls can no longer get jobs as barmaids, because it is believed they may have AIDS. Too late: 80 per cent of the barmaids in one town were found to be carriers.

The five-year programme, which will cost $6.8 million, is intended to put blood-testing kits into all 46 government hospitals and to upgrade the once excellent East African Centre for Virus Research.

Uganda has so far had to cope with the epidemic without any local facilities to test for HIV. The authorities have had to send all blood samples by air to the British Public Health Laboratory Service at Porton Down. Now that more funds are available, this situation will improve.

Another difficulty, according to Roy Mugerwa, who is responsible for co-ordinating research into AIDS on the national committee, is that there is a need for more information on the ways in which AIDS presents itself in the African context. "The current definition is too nonspecific. For example, doctors have recently noticed a link between AIDS and tuberculosis. About 40 per cent of patients with tuberculosis in Uganda and Zaire have antibodies against HIV. The incidence of tuberculosis in both countries is rising fast. There is a similar trend in Kenya.

Uganda badly needs funds to finance research into such links. But one of the biggest obstacles facing health authorities is how to get across the health education message. Sadly, in the worst-hit areas of the country, death has proved to be the best instructor. (Source: New Scientist, 19 March 1987 and The Economist, 21 March 1987)

United Kingdom

Programme continues on protein engineering

During December 1986, heads of relevant departments in British universities and polytechnics were notified of the Science and Engineering Research Council's biological initiatives for 1987. These include image interpretation (£600,000 a year allocated for continued support), invertebrate neuroscience (ditto), protein engineering (£400,000 a year will be available through the underpinning programme, in addition to continuing support of the Protein Engineering Club through the SERC Biotechnology Directorate) and membrane function (£200,000 a year allocated to support a preliminary grant round for a new initiative this year).

These sums are for commitment in research grants, and represent funds allocated to biological sciences in addition to the allocation for normal grants. As far as protein engineering is concerned, the underpinning and Club programmes have already committed over £2 million in current grants. (Source: Biotechnology Bulletin, Vol. 5, No. 12, January 1987)

New biotechnology centre

University College London is expected to pair with the University of Birmingham in a separate biotechnology initiative. The two campuses are slated as joint headquarters for a new UK Biochemical Engineering Centre focused on product recovery, advanced bioreactor control techniques and other aspects of bioprocessing. Still evolving, the plan is for the Science and Engineering Research Council (SERC) to provide core funding for work financed in part by contracts with industrial companies. Total funding for the four-year programme is anticipated to be between £2.5 million and £3 million, though all specific projects will have to go through SERC's normal refereeing machinery before being approved. (Extracted from Bio/Technology, Vol. 5, February 1987)

Government studies AIDS vaccine research programme

With an annual budget that would soon be £10 million, it would be possible to organize and direct an effective AIDS vaccine research programme in the United Kingdom.

The claim is that of the Medical Research Council (MRC) which has devised the blueprint of such a plan, currently being studied by government.

The plan outlines a strategy that will give the council extra AIDS funding of £2.5 million in the first year, rising to £4-6 million in the second and then £10 million before the fifth year.

In the written evidence to the committee the MRC had claimed: "We believe that the UK has the scientific capability for making a decisive contribution to the development of an AIDS vaccine provided that a political lead is given and that substantial extra funding, outside the Science Vote, is forthcoming. A number of distinguished scientists in the UK have expressed a wish to take part in a programme of research to develop an AIDS vaccine."

The paper paints a grim picture. To determine the behaviour of the disease, groups of infected individuals need to be studied for another 20 years or more, concludes the MRC. A new British programme to find a vaccine should be mounted and the MRC would speedily allocate the funds through its mechanisms for 'special project grants'.

The MRC, which created a working party on AIDS about four years ago, has since provided eight special grants for AIDS research from its own funds and has diverted resources at its own establishment, the Clinical Research Centre.

The council was recently awarded an extra £1 million a year to pay for further AIDS research. Additional research in Africa, where the MRC already supports projects in the Gambia and Zambia, is now also expected to be financed. (Extracted from Nature, Vol. 325, 19 February 1987)

Shell expands genetic engineering activity

During the coming five years, the London-based Shell International Chemical Co. will spend $20 million on biotechnology research in agrochemicals, seeds, and related areas. Research will cover a wide area, with emphasis on developing genetically modified seeds leading to plant varieties incorporating novel built-in characteristics. Much of the work will be carried out at Shell's Sittingbourne Research Centre near London, where more than $100 million has been spent to date on biotechnology programmes. Additionally, Shell is spending some $20 million annually in the UK and elsewhere in the area of plant genetics. (Extracted from Chemical and Engineering News, 19 January 1987, p. 30)

University news

The University of Reading has merged its departments of horticulture, botany, and agricultural botany to create a new School of Plant Sciences that will embrace crop development, plant breeding, germplasm conservation, and research into

plant diseases. Staffed by 75 scientists and technicians, the School includes a contracts group whose role is to forge strong links with industry.

Meanwhile, in Guildford, the University of Surrey is planning a new cytotechnology laboratory. Funded jointly by the Wolfson Foundation, the University Grants Committee, and Surrey University itself, the project will give Guildford a semi-industrial-scale pilot plant with six 100-litre bioreactors housed in a building suitable for the production of putative therapeutic and prophylactic agents for testing in animals and humans. The laboratory is due for completion in September 1987.

Further north, at the University of Buckingham, the new Clore Laboratory for the Biological Sciences has been opened. Twenty years after the first students arrived at Buckingham University - the only UK college that does not receive direct government funding - it has resolved to expand its coverage of life sciences into physiological biochemistry. Directing both research and teaching will be Professor Anne Beloff-Chain, widow of Sir Ernst Chain, who in 1945 shared a Nobel Prize with Alexander Fleming and Howard Florey for the development of penicillin. She will continue the work on diabetes, obesity and related topics that she pursued at Imperial College, London. (Source: Bio/Technology, Vol. 5, January 1987)

United States of America

NSF promotes team work in biotechnology

Stimulation of multidisciplinary research in biotechnology is the goal of an $8 million Biological Centers Program established by the US National Science Foundation. Two types of centres are planned. The first type, Biological Facilities Centers, will provide university departments with high-cost instruments that can be shared for bioscience research. The second type, Biological Research Centers, will support large-scale multidisciplinary research, possibly including instrumentation development. Facilities Center awards generally will average $500,000, while the more complex Research Center awards will typically be $2-4 million. (Source: Chemical Week, 7-14 January 1987)

'Ice-minus' field trial

The US Environmental Protection Agency (EPA) reinstated two experimental-use permits to Advanced Genetic Sciences (AGS), Oakland, Calif., to field-test ice-minus bacteria - genetically engineered strains of Pseudomonas syringae and Pseudomonas fluorescens bacteria that lack the ice-nucleating protein of the natural species. If the company can get State and local approvals, it may conduct outdoor tests in California at two sites in San Benito County and at one site in Contra Costa County to see whether the ice-minus bacteria protect strawberries from frost damage. The organisms are being treated as microbial pesticides and if the tests go forward, they will be the first officially sanctioned releases of genetically engineered bacteria into the atmosphere. Permits granted AGS in November 1985 were suspended when EPA discovered that the company had tested the bacteria outdoors without permission. (Source: Chemical Week, 25 February 1987)

EPA given first data on bioengineered bacteria

A company seeking to field-test genetically engineered micro-organisms has submitted a premanufacture notification (PMN) to the US Environmental Protection Agency, as is now required under the Toxic Substances Control Act. This is the first PMN for genetically altered bacteria under the toxics law to be subject to EPA's new biotechnology policy. The policy requires a PMN because the organisms are considered to be new, and being developed for commercial purposes, and are to be released to the environment.

A Cambridge, Mass., biotechnology company, BioTechnica International, intends to field test three genetically engineered strains of Rhizobium meliloti at its Chippewa Agricultural Station in Pein County, Wisconsin. The naturally occurring soil organism enhances nitrogen fixation in alfalfa. The firm believes its altered strains have better nitrogen-fixing properties and can enhance alfalfa yields as much as 15 per cent. (Extracted from Chemical and Engineering News, 23 February 1987, p. 24)

Guayule demonstration plant

Engineering has begun on a 150 ton-per-year demonstration plant to extract natural rubber from the guayule shrub. Engineering and construction of the plant is being carried out by Dravo Engineering under a contract awarded by Firestone Tire & Rubber. The project, supported by USDA and the Department of Defense, is intended to spur development of a domestic natural rubber industry. To be located at the Gila River Indian Community just south of Phoenix in Sacaton, Ariz., the plant will employ proprietary process technology developed at Firestone's central research laboratories. Construction is scheduled to begin in March. (Source: Chemical and Engineering News, 9 February 1987, p. 22)

FDA panel urges sales of anti-AIDS drug

An FDA advisory committee has voted 10 to 1 to recommend that the experimental drug azidothymidine (AZT) be allowed to enter the market as the first medication available by prescription for acquired immune deficiency syndrome (AIDS). The committee's recommendation is expected to carry heavy influence with FDA. However, the manufacturer of the antiviral, Burroughs Wellcome Co. of North Carolina, is planning to restrict sales to patients with those types of AIDS cases in which AZT has been shown to be safe and effective. In a clinical trial completed last summer, AZT was shown to bolster the immune system and prolong the short-term survival of AIDS patients with Pneumocystis carinii pneumonia. The drug also improved the condition of patients with AIDS related complex (ARC), a less severe condition. AZT is not considered a cure. However, in another promising development this month, researchers Robert Yarchoan and Samuel Broder of the National Cancer Institute found that AZT may reverse - at least temporarily - some of the dementia and other neurological disorders associated with AIDS. (Source: Chemical and Engineering News, 26 January 1987, p. 17)

Biological centres programme set up

In keeping with its effort to expand interdisciplinary research, the US National Science Foundation (NSF) is setting up an $8 million biological centres programme for research in areas important to biotechnology development. The programme will consist of biological facilities for interdepartmental research funded at about $500,000, and biological research centres for larger-scale efforts that will be eligible for awards of up to $2 million. First awards will be made in 1988. The deadline for proposals for the smaller facilities was 1 April; for the larger research centres the deadline is 1 August. Applicants are urged to contact NSF before submitting proposals. (Source: Chemical and Engineering News, 12 January 1987, p.19)

Synergen and Du Pont sign agreement

Synergen, Inc. of Boulder, Co., and E.I. du Pont de Nemours & Co. have signed an agreement to jointly develop therapeutic uses of an angiogenesis factor first characterized by Synergen in collaboration with academic researchers. The protein will be investigated for its potential in the treatment of significant cardiovascular conditions and neurological disorders as well as for other human pharmaceutical applications.

The angiogenesis factor, a human protein produced using recombinant DNA techniques, has been shown to induce the formation of new blood vessels and to stimulate the production of certain enzymes.

During the project's initial phase, anticipated to require 18 months, Synergen will continue its investigations of the physiological role of the protein and will develop a commercial process for its production. Du Pont will undertake preclinical studies of the potential therapeutic effect of the protein and will provide $1.5 million of research support to Synergen.

The second phase of the programme will focus on clinical trials and obtaining regulatory approval for the most promising applications of the angiogenesis factor. Should Du Pont believe initial results warrant, the agreement calls for the expenditure of approximately $17 million for development, initial clinical testing and preparation of regulatory submissions. Considerable funding for this phase will be provided by Du Pont.

Upon filing the first New Drug Application with the US Food and Drug Administration, the parties would form a commercial venture with Synergen retaining manufacturing rights and Du Pont responsible for marketing activities. Profits, as well as additional expenditures, would be shared equally by Synergen and Du Pont.

Synergen retains all rights to topical application of the angiogenesis factor to promote wound healing. Evaluation of the protein in animal models for the treatment of surgical incisions, skin ulcers, burns and bed sores has already begun. (Source: Company News Release, 3 February 1987)

Union of Soviet Socialist Republics

Cattle fodder

Straw can be converted to cattle food by cooking it under pressure according to L. Ernst of the All Union Lenin Academy of Agricultural Sciences (Moscow). This converts indigestible polysaccharides to simple sugars. Conventional grinding and steaming softens the stems, but does not improve nutritional value. The processed straw can be stored for up to one week in summer without going mouldy. Animals fed the sugared straw gained weight faster, and dairy cattle gave 12 per cent more milk. The cost of installing the needed autoclave could be paid back in one year. Peat waste can also be converted to feed by drying the peat and using the left over pulp and liquid to make a feed supplement by heating under pressure. (Extracted from New Scientist, 1 January 1987)

C. RESEARCH

Research on human genes

Mitomycins crosslink DNA to fight cancer

Chemists at two New York City universities have found that anticancer drugs called mitomycins act by crosslinking adjacent strands of deoxyribonucleic acid. Confirmation of this long-suspected mode of action may lead to design of similarly acting synthetic agents. The investigators' prediction that oxygen blocks the crosslinking mechanism is consistent with the known greatest effectiveness of mitomycins in such oxygen-poor environments as solid tumor cells.

The work was done by chemistry professor Maria Tomasz at Hunter College of the City University of New York, with senior research assistant Roselyn Lipman and graduate student Dondapati Chowdary, and by organic chemistry professor Koji Nakanishi at Columbia University, with graduate student Gregory L. Verdine and postdoctoral fellow Jan Pawlak. They were supported by the National Institute of Health.

The collaborators showed that activated mitomycin C forms crosslinks between adjacent strands both of a double-stranded, synthetic, alternating copolymer of deoxyguanylate and -cytidylate [poly (dG-dC)] and of DNA from the soil bacterium Micrococcus luteus. They further demonstrated that mitomycin crosslinks DNA by reaction at two parts of the drug molecule with the 2-amino groups of different guanine residues.

In addition, the researchers isolated the same crosslinked units from liver cell DNA of rats that were injected with the drug. This last finding indicates that the crosslinking mechanism functions in living mammals as well as in the test tube.

One key to the Hunter/Columbia success was use of sodium dithionite to activate mitomycin C. In the past, workers in the field had used catalytic hydrogenation or enzymic reduction to mimic metabolic activation. Activation is probably enzymic in the body, but test-tube experiments failed to turn up products derived from crosslinking.

Tomasz and Nakanishi suggest that the difficulty was kinetics. Residual oxidized form of the drug may have deactivated the reduced form after the reduced form had reacted with only one DNA strand. Dithionite reduces mitomycin C rapidly and completely, leaving no residual oxidized form.

One indication of the adduct structure came from its ultraviolet spectrum, which looked like a superposition of separate spectra of guanosine and the mitosene nucleus of the drug. Ratios of peak intensities indicated one mitosene and two guanosine moieties. A Cotton effect at one guanosine peak location in the circular dichroic spectrum suggested that the two guanosine groups were close to one another.

The Hunter/Columbia team used computer-assisted modelling of the complete crosslink of DNA by the drug. For this, they used a molecular mechanics programme developed by organic chemistry professor W. Clark Still of Columbia.

The chemists entered data from Brookhaven National Laboratory for the x-ray crystal structure of a known double-stranded polynucleotide with 10 nucleotides in each strand. Then they simulated a crosslink by mitomycin between guanine groups in adjacent strands. The resulting model showed that the mitomycine molecule fits neatly into what is called the minor groove of the DNA double helix with minimal distortion of DNA bonds and bond angles. (Abstracted with permission from Chemical and Engineering News, 16 March 1987. Copyright 1987, American Chemical Society)

Chemotherapy resistance

Cancer cells develop resistance to cancer drugs by some genetic changes and a specific cell protein. All cancers have the potential to develop

resistance, according to P.V. Wolley III of Georgetown University, Washington D.C. Some cancer cells are inherently resistant to drugs. Colon cells, for instance, are regularly exposed to toxins in digested food and are therefore more resistant than other normal cells to chemotherapeutic agents. The cancers that arise from colon cells tend to maintain that property. Cancer cells can also acquire immunity, generally through gene amplification, according to R.T. Schimke of Stanford University. For example, methotrexate acts by inhibiting the enzyme dihydrofolate reductase (DHFR) needed in DNA synthesis. Multiple copies of the DHFR gene have been found in tumors resistant to methotrexate. So resistant cells are always able to make enough DHFR to function. Other processes that block DNA synthesis can amplify genes spontaneously. The extra genetic material may come from dying cells, unequal distribution of genetic material at cell division, or overreplication of a DNA segment.

Another resistance mechanism involves p-glycoprotein, whose function is unproven, but which may carry lethal drugs out of cells before they are harmed. High levels of sorcin and epidermal growth factor have also been observed in cancer cells. Some cancer cells may also become resistant by producing higher levels of a DNA-repair enzyme to overcome damage done by DNA-damaging cancer drugs. Streptozotocin, isolated from fungi, may block the repair enzyme, according to L.C. Erickson of Loyola Medical Center. Further advances in chemotherapy depend on much better understanding of the nature of cancer cells.

A drug used to treat cardiac disorders can also reverse acquired drug resistance, a problem common in patients with cancer of the lymph nodes, according to a report by two researchers at Colorado State University (Fort Collins): Dennis W. Macy, a professor of veterinary medicine, and Stephen J. Withrow, a professor of oncology. The drug, verapamil, is a calcium-blocking agent used to treat angina. Tests in dogs have shown that the drug, when administered late in the course of treatment, renders cancer cells susceptible to drugs to which they had become immune. The Colorado researchers are currently administering verapamil at the onset of treatment, hoping to prevent drug resistance from occurring at all. Drug resistance is said to be the major reason why many cancer patients succumb to the disease after going into remission for several months. (Extracted from Science News, Vol. 131, 3 January 1987 and Chemical Week, 18 February 1987)

Computers graphics used in testing for carcinogeneity

Computer graphics could make redundant many of the tests that scientists carry out on animals to see if chemicals cause cancer. A new method of modelling compounds on computer will make it possible to screen new drugs, for example to check whether they can disrupt a cell's genetic material.

In many cases, a chemical becomes carcinogenic only after biological activation in the cell. Researchers at the University of Surrey have developed a technique that allows them to predict whether such activation will occur. They have shown that a molecule's ability to fit the active site of an enzyme found in all animal cells can predict whether the molecule can cause cancer.

The team, led by Dennis Parke, professor of biochemistry, has used the new method to test nearly 200 compounds. They found that they could divide the chemicals accurately into carcinogens and noncarcinogens with 95 per cent accuracy. Chemicals that were difficult to classify were those known to be weak carcinogens.

The enzymes that Parke's team has been studying are the cytochromes p448, closely related to another family of enzymes, the cytochromes p450. Both families are found in all animal cells.

The role of the cytochromes p450 is to help to eliminate chemical carcinogens from the cell. A process of oxygenation, catalysed by cytochromes p450, converts the carcinogen into a product which then reacts, or conjugates, with other molecules in the cell, ending up in a harmless, soluble form which can be excreted via the kidneys.

If the chemical carcinogen comes into contact with cytochromes p448, however, a different chain of events begins. Cytochromes p448 again catalyse an oxygenation reaction. But this time, an active product results. This form, instead of conjugating with other molecules, remains in the body where it can interact with DNA, so causing cancer.

There is evidence that genetic, dietary and environmental factors may be important in raising levels of cytochromes p448.

American studies have shown, for example, that some strains of mice have a greater ability to convert carcinogenic chemicals into toxic intermediates, by inducing higher levels of cytochromes p448. Diet is also important. People who eat plenty of fresh fruit and vegetables tend to have lower levels of cytochromes p448. Smoking is another factor, as shown by work on pregnant women. Normally, neither cytochromes p450 nor cytochromes p448 are present in the placenta. But if the woman smokes, cytochromes p448 develop in the placenta. Further in the future, this work may have implications for the prevention of cancer. It may be possible to design molecules that will fit in the active sites of cytochromes p448 and block them. This would mean that these enzymes would no longer be available to activate chemicals into their carcinogenic form.

In the meantime pharmaceuticals companies that are developing new drugs will be able to screen out compounds likely to be carcinogenic, greatly cutting the number of drugs that go on to be tested in animals. (Extracted from New Scientist, 26 February 1987)

Research links cancer and hormone receptor

Two groups of researchers, have independently found a link between cancer and the receptor for thyroid hormones. The researchers find that the protein product of a normal gene closely related to a cancer-causing gene called erb-A seems to be a thyroid hormone receptor.

The group at the European Molecular Biology Laboratory in Heidelberg, and at the Pasteur Institute in Lille, France, studied the system in chickens. The US team included scientists at the Howard Hughes Medical Institute in San Diego, the Salk Institute in San Diego, and at the San Francisco and San Diego campuses of the University of California. These researchers studied the human gene.

Both groups studied the gene product of a proto-oncogene called c-erb-A which is closely related to a cancer-causing gene, or oncogene, found in viruses and called v-erb-A. This oncogene does not by itself cause tumors in animals, but it enhances the ability of other viral oncogenes, such as v-erb-B, to transform a type of bone marrow cell - an erythroblast - into a cancerous cell.

Both groups cloned and sequenced the c-erb-A gene and its protein product. This protein product resembles, but is not identical to, certain steroid hormone receptors. Since thyroid hormones are thought to interact with cells in a way similar to the way steroid hormones do, the similarity led the California researchers to suspect that their protein was a receptor for thyroid hormone. The European scientists reached the same conclusion by noting the wide distribution of the protein in different types of cells (also true of the thyroid hormone receptor) as well as the similarity in molecular weight of the gene product and the thyroid hormone receptor. Both groups confirmed their hypothesis by showing that the thyroid hormone triodothereonine (T_3) preferentially binds to the c-erb-A gene product.

The finding has a number of interesting implications for understanding the role of oncogenes in cancer. (Abstracted with permission from Chemical and Engineering News, 5 January 1987. Copyright 1987, American Chemical Society)

Cancer reversal hormones

Teams of Dr. Don Metcalf at Melbourne's Walter and Eliza Hall Institute and of Professor Leo Sachs of the Weizmann Institute in Israel isolated a group of hormones with the ability to transform myeloid leukaemia cells in mice into normal mature cells. Researchers in the US and Japan had cloned the gene for the similar human hormone, and trials on animals and people will begin soon. The hormones are part of a family called colony stimulation factors (CSF) which control white blood cell formation and function. They might also be applied to regenerate bone marrow damaged by cancer treatment. (Source: Journal No. 2, Biotechnics '87, Hannover)

Turning antibodies into catalysts

Using a new biotechnology tool, two research groups have recently endowed one type of protein, antibodies ("abs"), with the chemical properties of another, enzymes. The resulting "abzyme" process is now being studied for commercialisation by IGEN in Rockville, Md., and could result in a simple and efficient new method of designing and producing proteins for cancer treatment, genetic engineering and chemical processing.

Enzymes are catalysts that act as a sort of stage on which chemicals come together to form new products. About 2,000 natural enzymes are known, and many of them are vital to the chemical, food-processing and pharmaceutical industries.

Antibodies are generated by the immune system in response to an antigen (a foreign cell or chemical), and work by a similar mechanism. That is, a portion of the molecule precisely fits the pattern of molecules jutting from a specific antigen and in the process signals other immune-system cells to destroy the antigen.

These similar modes of action have led many researchers to wonder if antibodies (which assume a virtually unlimited number of shapes, depending on the antigenic "template") could serve as catalysts. All one would have to do is inject a laboratory animal with a specific transition-state molecule and let the creature's immune system manufacture an antibody moulded to fit that molecule. The resulting abzyme would thus be able to catalyze the corresponding reaction. That approach, however, has only recently become feasible with monoclonal antibody technology, in which the cell generating an antibody against a specific antigen is isolated from millions of other similar cells and then cultured to produce large volumes of the antibody.

At least one potentially useful abzyme has been developed at the Research Institute of Scripps Clinic (La Jolla, Cal.). Molecular biologists Alfonso Tramontano, Kim D. Janda and Richard A. Lerner injected mice with a phosphonate ester that is similar in shape to, but more stable than, a transition-state molecule in a reaction called ester hydrolysis. As expected, the phosphonate prompted production of antibodies in the mice. The researchers isolated the antibodies and found one that speeded up the hydrolysis by 1,000 times - rather slow compared to the million-fold capabilities of enzymes like carbonic anhydrase, but exciting nevertheless.

Results were even more dramatic at the University of California (Berkeley), where chemists Peter G. Schultz, Scott J. Pollack, and Jeffrey W. Jacobs used an antiphosphonate antibody to speed ester hydrolysis some 15,000-fold. The group has since made other antibodies that provide similar results in other reactions.

One of the first commercial uses for abzymes will probably be to alter other proteins that, like abzymes themselves, consist of chains of amino acids. For example, it may be possible to design antibodies that mimic proteases which cut proteins at specific amino-acid sequences. Today's proteases often lack the required specificity and cut proteins at unpredictable sites.

Healthcare offers several potential uses for new proteases. One designed to cut the protein fibrin (the major component of blood clots) may be useful in treating heart disease by dissolving the clots, as some enzymes are known to do, others could treat cancer by homing in on the proteins that protrude from malignant cells, a process that might fatally damage the cell membrane and an abzyme that recognizes and breaks a specific amino-acid segment in viruses might prevent them from binding to target cells.

At this stage it is doubtful whether the abzyme technique will completely replace such methods as fermentation and chemical synthesis, which already produce large numbers of enzymes efficiently; but the process could complement those methods by providing new antibodies to speed up reactions that are now uncatalyzed. (Extracted from High Technology, March 1987)

Cetus clones map enzyme

Cetus Corp scientists have successfully cloned and expressed the *E. coli* methionine aminopeptidase (MAP) enzyme which is responsible for amino-terminal processing of proteins produced by genetic engineering in prokaryotic and eukaryotic micro-organisms. Many recombinant proteins still contain amino-terminal methionine, which can now be removed *in vivo* using the MAP enzyme - which is unique among other known aminopeptidases in that it has the absolute specificity for the amino-terminal methionine.

The method is particularly useful for those proteins that partially retain the methionine residue, because the MAP enzyme can 'polish' the frayed amino-terminal sequence and generate more homogeneous protein products. Cetus was the first to discover and clone the enzyme, and has filed for US and foreign patents. It is now considering licensing the technology. (Source: Biotechnology Bulletin, Vol. 6, No. 6, March 1987)

EPO in clinical trials

Erythropoietin (EPO), a hormone that is produced mainly by the kidneys, acts on precursor

cells in the bone marrow to stimulate the production of red blood cells. The clinical trials now in progress are to treat the anemia associated with end-stage renal disease. Not only do patients suffering from this disease require dialysis to remove impurities from their blood, but many of them also require frequent transfusions to increase the percentage of red cells in their blood.

About 175,000 patients require dialysis.

Amgen's (Thousand Oaks, CA) recombinant human EPO is already in Phase III clinical trials; the company expects to file with the Food and Drug Administration (FDA) no later than the end of 1987, and approval should follow within 6-12 months.

The results of combined Phase I and II clinical trials have recently appeared in The Lancet and The New England Journal of Medicine. In small trials, both groups found the same thing: EPO, administered three times weekly following dialysis, corrected the anemia. Red-cell build-up was dose-dependent and occurred in a month or less. Previously transfusion-dependent patients no longer are so. Moreover, to date there have been no severe adverse effects such as anti-EPO antibodies, loss of efficacy, or direct toxicity. Some patients develop iron deficiency; the increased red cell production - and demand for hemoglobin synthesis - depletes iron stores. EPO therapy makes patients feel better and increases their appetites: the drawback here involves the need to modify dietary restrictions and increase dialysis times - to cleanse the blood of additional metabolic by-products and impurities.

The Phase III trials will eventually target about 300 patients on dialysis in the US.

Although it is too early to tell whether other hematological diseases will benefit directly from therapy with recombinant EPO, its most extensive use may be for autologous blood donations for patients undergoing elective surgery. Other potential uses of EPO include treating the anemias associated with liver disease and rheumatoid arthritis, as well as use in conjunction with colony stimulating factors in bone marrow suppressed states.

Amgen is scaling-up EPO production at its new mammalian cell culture facility, but the total amount of recombinant hormone needed for the therapeutic applications will be modest. The maximum dose used in the clinical trials is equivalent to 500 micrograms of 98 per cent-pure protein, and a pound of EPO would be enough to supply the world's kidney dialysis needs for five years. (Extracted from Bio/Technology, Vol. 5, March 1987)

Gene link found for two major mental disorders

The genetic underpinnings of two major and quite different mental disorders - manic-depressive illness and Alzheimer's disease - have been established in recent weeks. In both cases, teams of researchers have used sophisticated techniques in molecular biology coupled with long-term inheritance studies to locate the exact genetic region - and in one case, perhaps the exact gene - that predispose certain people to develop the disorder.

Manic-depressive illness is a psychiatric illness which can lead to fatal consequences, including suicide. There is no cure, but it is among the most treatable of psychiatric disorders, often responding to drug therapy that utilises lithium carbonate in combination with tricyclic antidepressants of monoamine oxidase inhibitors.

Alzheimer's disease is a degenerative disease affecting the brain and leads to progressive memory loss, confusion and bizarre behavior. Like manic-depressive illness, it is incurable and frequently causes death within five to 10 years of the onset of the disease.

In a 10-year effort, researchers have shown that in at least one large family, inheritance of a small segment of chromosome 11 located near two marker genes predisposes someone to develop manic-depressive illness. The work was led by Janice A. Egeland, a psychiatry professor at the University of Miami, David E. Housman, a biology professor at Massachusetts Institute of Technology; and Kenneth K. Kidd, professor of human genetics, psychiatry and biology at Yale University's school of medicine.

The manic-depressive study is based on examination of the distribution of the disease among extended families of Older Order Amish in eastern Pennsylvania. A number of social and psychological factors that may play a role in the development of manic-depressive illness are not found among members of this religious sect, including criminal behavior, violence, marital separation and divorce, alcoholism and differences in either socio-economic status or level of formal education. Despite their cultural differences, the Amish have the same incidence, symptoms and development of the illness as the general North American population.

By focusing on this group, the researchers were able to identify a particular family of 81 members in which the tendency to develop manic-depressive illness was clearly passed from one generation to the next as a dominant genetic trait. Blood samples from all 81 members of the family were used as the source of DNA, which was then analyzed to see if a particular piece of that DNA could be pinpointed as the fragment that carried the genetic predisposition to the disease.

Using restriction fragment length polymorphism, Housman at MIT and Daniels S. Gerhard, assistant professor of genetics at Washington University, St. Louis, showed that the critical piece of DNA is located near the tip of the shorter arm of chromosome 11. This technique uses a whole array of restriction enzymes to cut DNA at specific places in its sequence. The technique has been applied successfully to several genetically determined illnesses, including Huntington's disease and cystic fibrosis.

Another gene known to be located on the key fragment of chromosome 11 may be involved in a predisposition to manic-depressive illness, Housman says. That gene determines the structure of an enzyme called tyrosine hydroxylase which catalyzes an important step in the synthesis of dopamine. Finding a gene important in dopamine synthesis on that chromosome segment suggests a biochemical link. Experience with other genetic diseases suggests that overproduction or underproduction of a key enzyme or production defective enzyme could be the biochemical basis of illness.

Promising as the finding of the Amish study are, researchers already know that a defect on chromosome 11 is not the whole answer to their quest for a link between genetics and development of manic-depressive illness. Investigators have long predicted that there would be more than one possible genetic defect that could predispose a person to develop the illness. Such is thought to be the case for most major diseases that have a genetic component, and it greatly complicates the problem of finding such genetic links.

In publications that were simultaneous with that of the Amish study, researchers in London and Iceland and at the National Institute of Mental Health in Maryland reported that for other populations where manic-depressive illness is inherited, the inheritance does not come by means of a fragment of chromosome 11. Many studies are proceeding now to determine just how common the chromosome-11 linked form of manic-depressive illness is in the general population.

Alzheimer's disease, too, has this heterogeneous genetic character. In some cases, a genetic link is clear, it is possible in others, and may not exist for some fraction of cases. The new work, which has taken place in many laboratories, focused on the relatively uncommon form of Alzheimer's in which the genetic component of the disease is most easily seen - a form called familial Alzheimer's disease.

James F. Gusella and Peter St. George-Hyslop, both researchers at Massachusetts General Hospital and Harvard medical school, led an international team of researchers who found in a study of four extended families that, like manic-depressive illness in the Amish study, familial Alzheimer's disease is inherited as a dominant trait and that the particular piece of DNA that is crucial for the inheritance is located on chromosome 21. Like the manic-depressive illness work, the researchers used restriction fragment length polymorphism techniques to pinpoint the critical region of DNA associated with the disease.

Unlike in the manic-depressive study, researchers had reason to expect the key genetic region for Alzheimer's to be on chromosome 21 and focused their effort on that particular chromosome. In its latest stages, another genetic disease, Down's syndrome, shows many of the same symptoms as Alzheimer's disease. Down's syndrome patients have an extra copy of chromosome 21.

One characteristic of the brain cells of patients with Alzheimer's disease is the accumulation of clumps of an abnormal protein called *amyloid*. Several new studies, some of which study the same population studied by Gusella and St. George-Hyslop, find that the gene responsible for production of the amyloid protein is located on the fragment of chromosome 21 that is linked with inheritance of the disease. This location could be coincidental, but it does suggest a possible biochemical basis for development of the disease.

The plausibility of this biochemical basis is somewhat strengthened by recent work by yet another group of researchers - Dennis J. Selkoe at Harvard medical school and Brigham & Women's Hospital (Boston), Donald L. Price at Johns Hopkins University's school of medicine, and their colleagues. These workers find amyloid protein accumulates in the brains of several species of mammals as they age. They conclude that the protein is highly conserved during evolution and thus probably serves a useful, but as yet unidentified, function. These other animals, which include dogs, polar bears, and monkeys, do not necessarily get Alzheimer's disease, but they may, however, serve as "biochemically relevant models for principal features of Alzheimer's disease," the researchers suggest. (Abstracted with permission from Chemical and Engineering News, 9 March 1987. Copyright 1987, American Chemical Society)

Gene synthesis aids study of cytochrome

In an effort to better understand characteristics of the heme protein cytochrome b_5, including how amino acid side chains determine the properties of the heme iron, researchers have synthesized the gene that encodes the protein and have expressed it in bacteria.

A number of features make cytochrome b_5 an ideal target for site-directed mutagenesis experiments, according to Stephen G. Sligar, biochemistry professor at the University of Illinois, Urbana. It plays an important role in electron transfer reactions, including reduction of cytochrome P-450 in the liver and regeneration of ferrous hemoglobin in red blood cells. The protein's amino acid sequence is highly conserved among species, and a high-resolution crystal structure has been determined for bovine cytochrome b_5.

The problem, however, is that efforts to express native mammalian cytochromes at high levels in a bacterial system have not been successful.

To circumvent this problem and develop a method for producing native and mutant cytochrome b_5 in the large quantities needed for biophysical characterization, Sligar, postdoctoral fellow Susanne Beck von Bodman, and Illinois professor of plant biology Mary A. Schuler synthesized the gene. This strategy gives the researchers a number of advantages over standard cloning techniques.

The synthetic gene is expressed efficiently in transformed Escherichia coli. For soluble cytochrome b_5, about 8 per cent of the total protein expressed by the bacteria is cytochrome b_5. Extensive characterization of this protein indicates that it is identical to soluble mammalian cytochrome b_5. The complete cytochrome b_5 gene encodes a protein with an additional hydrophobic domain that interacts with cell membranes. The synthetic gene for the complete protein is expressed in E. coli, and the resultant protein is found in the plasma membrane.

Efforts are under way to use the synthetic gene strategy to better understand the properties of cytochrome b_5 and its interaction with other proteins. The researchers also have produced mutant cytochrome b_5 proteins with altered surface charges to investigate "docking" interactions between cytochrome b_5 and its electron transfer partners. (Abstracted with permission from Chemical and Engineering News, 5 January 1987. Copyright 1987, American Chemical Society)

Muscular dystrophy

A recent description of the gene that causes Duchenne muscular dystrophy (DMD) has intensified the search for a protein for which that gene codes - possibly a muscle protein absent or defective in the muscle-wasting disease. Identifying the gene product could lead to replacement therapy and a halt to muscle loss. A report in the October Biochemistry and Cell Biology from scientists at the University of Windsor in Ontario suggests the sought-after gene product may indeed be a defective protein - more specifically, an inhibitor that fails to inhibit tissue destruction by enzymes called proteases.

Increased protease activity in skeletal muscle, along with loss of muscle proteins and mass, is characteristic of muscular dystrophy in both humans and animals. From mice with a non-DMD form of dystrophy, the researchers have purified an abnormal protease inhibitor that is unable to stop muscle destruction by some classes of proteases. Theoretically, if a defective inhibitor is pinpointed as the cause of the disease, researchers could replace it with a specific, normal inhibitor.

In experiments that may answer some of these questions, the Ontario group is cloning the mouse MD gene, as well as assaying for abnormal inhibitor in tissue from humans with a non-Duchenne, slow-onset type of muscular dystrophy. (Extracted from Science News, Vol. 131, 17 January 1987)

Blood vessel protein leads to a partnership

A new team will investigate the use of angiogenesis factor - a protein that induces formation of new blood vessels - in organ regeneration and cardiovascular and neurological disorders. Du Pont and Synergen (Boulder, Colo.) will jointly fund an 18-month research programme to develop a manufacturing process for the genetically engineered protein. If the product is approved by the US Food and Drug Administration, the companies would jointly commercialize it. Du Pont would get exclusive worldwide marketing rights; Synergen, manufacturing rights. (Source: Chemical Week, 11 February 1987)

Ferrying drugs across the blood-brain barrier

The blood-brain barrier - the brain capillaries that act as watchful, militant keepers of the gate between blood and brain - has been recognized for nearly 100 years. Yet until recently, the barrier has remained largely a mystery. Even now, its tendency to prevent most drugs from entering the brain is regarded almost as a fact of life.

That perception may soon change, however. Pharmatec (Alachua, Fla.) has developed a carrier system that could transport drugs across the barrier to treat just about all brain disorders.

Three of the five organizations that have licensed the Pharmatec technology could enter carrier-drug combinations in clinical trials this year.

The blood-brain barrier insulates the brain from bacteria and toxins in the blood and isolates the brain from transient changes in blood composition. After meals or exercise, blood concentration of hormones, amino acids and ions, like potassium, fluctuates. Exposure of the brain to such changes could result in uncontrolled nervous activity, since some amino acids and hormones are neurotransmitters and the potassium ion effects the firing of nerve cells.

The barrier is a feature of the unique structure of the capillaries that supply blood to the brain. The cells of those capillaries are unusual in that they are joined with impermeable junctions so that they form a continuous wall. Capillary cells elsewhere in the body are more loosely joined, allowing molecules to pass through. Also, ordinary capillaries have pores through which compounds pass; brain capillaries have such pores only in specific regions.

Some molecules do pass through the blood-brain barrier. Essential nutrients like glucose traverse it easily, helped across by transport systems that specifically recognize them. And because the capillary cell membranes are largely lipid, lipid-soluble molecules that are electrically neutral enter the brain with relative ease. For instance, heroin, being more lipid-soluble than morphine, goes into the brain more readily and consequently exerts a greater effect.

That solubility and the electrical characteristics of brain capillary membranes provide the key to the Pharmatec carrier. The system uses a dihydropyridine-pyridinium salt carrier that exists in interconvertible states, either as lipid-soluble dihydrophyridine or as water-soluble pyridinium salt. Those states are induced by reduction and oxidation reactions respectively.

A water-soluble drug is coupled to reduced dihydropyridine by an ester linkage. The combination, electrically neutral and lipid soluble, can thus cross the blood-brain barrier. Once inside the brain, the complex is oxidized by the ubiquitous nicotinamide adenine dinucleotide-nicotinamide adenine dinucleotide phosphate (NAD-NaDP) system, the oxidation-reduction system that generates energy. The oxidized complex, positively charged and water soluble, cannot recross the blood-brain barrier and is trapped in the brain.

Nonspecific esterases then cleave the drug from the pyridinium salt, effectively producing a sustained delivery of the drug. The salt, because of its small size, says Stern, is eliminated from the brain through the blood-brain barrier. Any drug-carrier complex that is oxidized by the body before reaching the brain is eliminated, because the kidneys rapidly remove charged molecules. As a result, drug concentration does not build up outside the brain.

The carrier could help drugs that enter the brain but cause toxicity in other parts of the body. L-Dopa, for instance, used to treat Parkinson's disease, can cause such effects as nausea and vomiting. With the carrier, toxicity could be reduced, because drug availability in the brain would increase "dramatically," compared with that in the blood. (Source: Chemical Week, 18 February 1987)

Scientists outmaneuver a parasite

French scientists have used gene cloning to outmaneuver schistosomiasis, a parasitic disease that afflicts at least 200 million people around the world. The research was led by Dr. André Capron of the Pasteur Institute of Lille collaborating with scientists of the French biotechnology company, Transgene. Until now the disease has been a difficult target for vaccination. Natural immunity to the parasite develops slowly and is not very effective. In a recent issue of Nature, the scientists report success in growing an important protein of the adult schistosome in laboratory bacteria and using this substance to immunize rats, hamsters and primates. (Source: International Herald Tribune, 26 March 1987)

Research into dental cavity vaccine

Several universities are attempting to develop vaccines against dental cavities. The market for such vaccines, when they are available, would be enormous, since over 95 per cent of the world's population suffers from cavities, according to RE Green of OTC America. Major research programmes involving cavity vaccines are under way at Washington University, Forsyth Dental Center, Emory University and the University of Alabama. Burroughs Wellcome is also developing a vaccine against cavities. The National Institute of Dental Research provides about $1 million/year for research.

Most of the researchers are studying the secretory immune system to develop a vaccine against Streptococcus mutans, the bacterium that is the major cause of cavities. Antibodies against the pathogens are produced in mucous membranes of the mouth, lungs, gut and genitourinary tracts. Washington University researchers have developed a vaccine that provides immunity against S. mutans and virulent strains of Salmonella. Vaccination should enable an individual to be immunised against any bacterium, fungus, protozoan or virus that attacks

through the mucosal membrane. Emory University and the University of Alabama have tested vaccines based on killed S. mutans bacteria. (Extracted from Chemical Week, 14 January 1987)

Human genome project

The effort to map and ultimately sequence the human genome has captured the attention of the White House. The cabinet level Domestic Policy Council (DPC) has asked its working group on biotechnology to prepare a report on the human genome project. A first instalment of the report, due next month, will detail present US activities. Future instalments could include a framework for co-ordinating federal activities on the project.

The first report will be primarily to educate DPC members on the costs and benefits of pursuing the genome project. The notion that such an endeavour could cost $3,000 million attracted White House attention. No federal agency is contemplating such a large project, but several are already working on parts of a sequencing and mapping project.

The plans of the Department of Energy (DoE) for the human genome project are the best defined. It is supporting the development of a set of DNA libraries specific to individual chromosomes. Work is under way at Los Alamos National Laboratory on chromosome 16 and at Lawrence Livermore National Laboratory on chromosome 19. A consortium headed by Cassandra Smith at Columbia University is working on chromosomes 21 and X. As well as the DNA libraries, DoE will focus on new sequencing technology and computational activities.

NIH, which supports several projects that will be relevant to any mapping and sequencing effort, has not yet decided exactly what its role in the human genome project will be.

Other reports on the human genome project are in the offing. The National Academy of Sciences Board on Basic Biology plans to complete an evaluation of the project by June. For Congress, the Office of Technology Assessment is also evaluating the genome project. A draft of that report may be available this summer, although it is not officially due until the end of the year. (Source: Nature, Vol. 325, 19 February 1987)

Three new reports on AIDS

The variability of the AIDS virus - from its genes to its effect on people - sometimes seems matched only by the diversity of approaches that can be taken toward its study. Three new reports suggest a variety of actions for the virus or for the body's reaction to it; each of the three could lead to new therapeutic tacks.

The reports detail a newfound importance for immune system suppressor cells in controlling human immunodeficiency virus (HIV), a suggestion that the virus sparks an autoimmune attack, and the discovery of a small protein that blocks the virus's binding site on its target cells.

Jay A. Levy and his colleagues at the University of California at San Francisco come up with what is perhaps the most paradoxical finding of the three - that suppressor immune cells, rather than effector cells that initiate and direct immunity, are key factors towards fighting off HIV infection. Boosting suppressor cells could prevent or help counter infection, they suggest. Levy says he would like to try growing suppressor cells from AIDS patients's blood samples and giving them back to the patients in higher doses, after he first determines the desired levels of suppressor cells. Too many suppressor cells could have a damaging effect.

Meanwhile, other San Francisco researchers have come up with a theory for how the virus wreaks its havoc. According to John L. Ziegler of the Veterans Administration Medical Center and Daniel P. Stites, HIV may cause the body to attack itself. While the idea of AIDS as an autoimmune disease has been proposed before, these researchers suggest a precise mechanism for how the virus could induce the attack.

The problem could result from a similarity between the "hook" the virus uses to grab its target - immune effector cells called CD4 or T4 cells - and an unrelated protein on other white blood cell types that tells the immune system that these cells are "self" and shouldn't be rejected.

According to Ziegler and Stites's hypothesis, when an infected person makes antibodies to the HIV hook, these antibodies would also attach to the "self" areas of white blood cells, blocking their function or leading to their demise. The scientists' conclusion explains why, as observed in AIDS patients, the virus can infect only 0.01 to 0.1 per cent of its CD4 cells yet still devastate the immune system. The hypothesis also implies that immune system suppressants like cyclosporine could prevent the deadly white blood cell loss. Cyclosporine has been tried by French researchers in AIDS patients but the researchers have not yet published their results. There may be nothing left to restore by the time a person has AIDS, Ziegler says, but he and his colleagues are beginning a preliminary trial of cyclosporine in humans. They are also looking for the hypothesized antibody that reacts with HIV and with white blood cells.

The third study, like the other two, has treatment implications. Using a paradigm set up for studying brain neuropeptides and their receptors, researchers found a short peptide on the HIV envelope protein that binds to brain cells in HIV infection. By adding just the peptide to a cell culture line, Candace B. Pert and Joanna M. Hill of the National Institute of Mental Health and several other government researchers were able to block entry of the whole virus. Pert's group plan to try injecting a long-lasting analog of the peptide in humans with AIDS in early 1987. For people already infected, says Hill, the peptide could block infection of new cells. (Extracted from Science News, Vol. 130, 20-27 December 1986)

Colon nurtures the AIDS virus

Researchers in the US have found a protein produced by cells in the colon and rectum that appears to help the AIDS virus inject the human body.

Experiments at the National Institute for Allergy and Infectious Diseases suggest that the virus may take up residence in the colon and rectum before moving on to the rest of the body. Until now, researchers thought that only cells of the immune system and the central nervous system could be infected with the AIDS virus.

Malcolm Martin, chief of molecular microbiology at the institute, led a team of scientists who tried to infect 13 varieties of human cell in a test tube. All resisted cultures of the virus, except three types of cell from the colon and rectum. They accepted the virus and sustained it for a period of up to 10 weeks.

The AIDS virus is attracted to immune cells by the receptor molecule known as CD4 on their surface. Martin's team suspected that cells from the colon and rectum might suppress the same marker. They found no CD4 in the cells, instead they found a type of ribonucleic acid (RNA) that codes for CD4. Cells that resisted infection with the AIDS virus did not produce that variety of RNA.

The team suggests that the AIDS virus may chronically infect the rectum or colon, ultimately spreading to the immune system where the virus actually causes the disease associated with AIDS. (Source: New Scientist, 25 December 1986/ 1 January 1987)

AIDS drug approved, vaccine tested

In the first reported experimental trial of an AIDS vaccine in humans, a French scientist has injected himself with a vaccine made by inserting a gene for the AIDS virus envelope into vaccinia virus. Daniel Zagury of the Pierre and Marie Curie Institute in Paris and his co-workers say in a letter in the 19 March edition of Nature that after the injection, they combined a sample of Zagury's blood in vitro with the AIDS virus and found that the vaccine had activated his immune system against AIDS. His immune response (both antibody production and cell-mediated immunity) was measured for nine weeks following the primary immunization. The scientists detected not only antibodies against the strain of AIDS virus used, but also heightened blood lymphocyte responses when using Zagury's blood in subsequent tests. The cellular response also was mounted against a very different strain of AIDS virus - an important aspect, given the virus's ability to mutate rapidly. No adverse affects, such as body temperature changes, were observed after injection, say the scientists.

According to the report, booster shots of the vaccine have been given to Zagury and some of a "small group" of volunteers immunized in Zaire, where the work is being done. The results of this study do not show that the vaccine could actually prevent AIDS, but they do suggest that the two-pronged immune system may be enticed to subdue the lethal virus. (Extracted from Science News, Vol. 131, 28 March 1987)

Recombinant backbone fragment of HTLV-III virus triggers immune system

Scientists at Repligen Corp. Centocor Inc., Duke University Medical School and the US National Cancer Institute have demonstrated that a single protein from the HTLV-III virus implicated in the transmission of AIDS can trigger the formation of neutralising antibodies. The protein, gp 120, is part of the surface coat of the virus. The fragment used is a segment of the 'backbone' of the naturally occurring protein, produced by Repligen's genetically engineered bacteria. Details from: Dr. Thomas D. Fraser, executive vice president and the chief technical officer, Repligen Corp, One Kendall Square, Building 700, Cambridge, MA 02139, USA or on (617) 225 6000. (Source: Biotechnology Bulletin, Vol. 5, No. 12, January 1987)

AIDS antibodies found in plasma

Scientists have found that blood plasma of some persons infected with the AIDS virus has large quantities of antibodies that inactivate the virus in the test tube.

The New York Blood Center is seeking plasma donations from people infected with the virus to collect more of these antibodies for further research. It has long been known that AIDS victims usually have detectable antibodies against the virus, but in most cases these appear to give the patient no protection against the deadly acquired immune deficiency syndrome.

If some people do have antibodies that actually protect against the virus, it might be possible to purify these antibodies so that they could be administered under special circumstances for temporary protection of persons such as dentists, surgeons and other hospital workers who may often encounter AIDS patients' blood. Recent studies at the center showed that blood samples from about 50 of 500 infected people had large quantities of the antibodies. The ability to kill the virus in the test tube does not necessarily prove that an agent will protect against infection. (Source: International Herald Tribune, 15 January 1987)

Research on animal genes

Gene therapy cures mice of shivering by restoring myelin sequence

Mice born to parents lacking a vital central-nervous-system gene are alive and well, after receiving the missing DNA via genetic engineering. Biologists at California Institute of Technology at Pasadena, California microinjected the gene sequence coding for myelin basic protein (MBP) into the fertilized eggs of 'shiver mice' - congenital mutants that grow up shaking themselves to an early death because their genome lacks the MBP sequence. Those progeny in which the gene transplant 'took' matured free of the lethal tremors, and lived a normal life-span.

Myelin basic protein is a key component of the sheath that wraps around nerve-cell axons in mature mammals. Superficially, myelin suggests the plastic insulation around electric wires, but its actual function is to increase the velocity of nerve impulses. Its absence is associated with multiple sclerosis (MS). A grant from the Multiple Sclerosis Society partly funded the CalTech research. (Extracted from McGraw-Hill's Biotechnology Newswatch, 2 March 1987)

Gene therapy restores mouse fertility

A gene deletion causing infertility in mice has been pinpointed and corrected in recent work, illustrating some curious facts about how genes can express themselves in specific tissues. Using a special breed of hypogonadal (hpg) mice, researchers have found that the hereditary form of infertility found in these mice is caused by a deletional mutation of about half of the gene coding for the precursor of gonadotropin-releasing hormone (GnRH) and GnRH-associated peptide (GAP). The peptide pair stimulates the release of key reproductive hormones.

Scientists at Genentech, Inc., in south San Francisco produced fertile hpg homozygotes by introducing DNA fragments containing the mouse GnRH gene into normal eggs later implanted into surrogate mothers. Subsequent mating of the progeny with hpg mice yielded fertile hpg homozygotes. Hormonal levels and tissue development in these mice were comparable to those in normal mice.

Others have found similar tissue-specific expression elsewhere. For example, a group at the University of Warwick in Coventry, England, reports that muscle protein genes injected into fertilized eggs of the clawed toad Xenopus borealis are expressed almost wholly in muscles.

Earlier this year, the Genentech team reported the isolation of the gene for precursors of GnRH and prolactin-release-inhibiting factor in humans and rats. No mutation such as that described in the hpg mouse was found, although there are forms of hypogonadism found in humans. However, there is no direct clinical application of the newly described gene therapy to treating human infertility problems. The technique, called germline gene transplantation, is unacceptable in humans under current biotechnology guidelines. (Extracted from Science News, 13 December 1986)

Metal-binding protein studied

New rDNA techniques let marine scientists take advantage of the ocean's chemical mechanisms in a new way. D. Bonar of the University of Maryland and D. Powers of Johns Hopkins University are studying metallothionein, a metal-binding protein that allows some marine organisms to concentrate enormous amounts of metal in their tissues. The organisms may sequester the metals they have concentrated or cleanse themselves of the protein-metal complex by dumping them. Ideally, a metal-binding protein could be constructed from a synthetic gene designed to selectively pull out the desired metal. Bonar asserts that it is possible there is a bacterium from a marine organism that produces a metallothionein that concentrates the specific metal. (Extracted from Industrial Chemical News, December 1986)

Feline AIDS virus identified

A virus that causes a fatal disease in cats that is very similar to human acquired immune deficiency syndrome (AIDS) has been isolated from cats living in a cattery in the northern California city of Petaluma. Although the newly discovered virus is distinct from human immunodeficiency virus (HIV), the virus that causes AIDS, it and the feline disease it causes may provide a badly needed animal model for AIDS research.

The virus has tentatively been designated FTLV for feline T-lymphotropic lentivirus. It was discovered by Niels C. Pedersen, professor of veterinary medicine at the University of California, Davis; Davis co-workers Esther W. Ho and Janet K. Yamamoto; and Marlo L. Brown, a veterinarian at Petaluma Veterinary Hospital.

The researchers point out that domestic cats are susceptible to infection by a number of retroviruses, which are viruses that contain RNA rather than DNA as their genetic material. The most common of these is feline leukemia virus (FeLV), which causes, among other symptoms, immune suppression somewhat similar to AIDS. Thus far, studies indicate that FTLV cannot infect human T-lymphocytes. The researchers note that three humans who had regular, close contact with the cats do not have antibodies to HIV or to FTLV. FTLV does not appear to be antigenically related to HIV.

The discovery of FTLV has important implications both for the domestic cat population and the study of human AIDS. A limited survey of cats at Davis' school of veterinary medicine suggests that the virus is already widespread among cats in northern California. Although clearly different from human AIDS, feline AIDS caused by FTLV provides researchers with a potential model system to test new ideas for dealing with HIV infection. (Abstracted with permission from Chemical and Engineering News, 2 March 1987. Copyright 1987, American Chemical Society)

Research on plant genes

Breakthrough in genetic engineering of cotton

In the first reported successful genetic engineering of cotton plants, Agracetus has incorporated a foreign gene into cotton and achieved expression of the new trait in whole plants. The foreign gene added to cotton was a bacterial gene encoding for resistance to the antibiotic kanamycin. Kanamycin resistance is not a commercially important trait in itself, but provides an essential first step in incorporating new useful genes into cotton. The gene enables scientists to separate the cells which have incorporated new genes from those which have not during early stages of cell growth.

The worldwide cotton crop covers more than 80 million acres. A major cost input in cotton production is in the purchase of insecticides, field or aerial insecticide spraying and field scouting to control insect infestations. Annual US expenditures alone for these controls exceed $300 million. One study found that cotton producers in the Mississippi Delta area were typically spending about $60 per acre on insecticides. Insect resistance is therefore likely to be a key target at Agracetus, a joint venture between Cetus Corp and W.R. Grace & Co., based in Middleton, Wisconsin. (Source: Biotechnology Bulletin, Vol. 5, No. 12, January 1987)

A gene to break down a herbicide cloned

A gene coding for an enzyme that breaks down the herbicide bromoxynil, which controls broadleaf weeds in corn and various small-grain crops, has been cloned by Calgene (Davis, Calif.). The company has expressed the gene - isolated from the soil bacterium Klebsiella ozaenae - in tomato and tobacco plantlets and is beginning tests for bromoxynil tolerance at the whole-plant level. Calgene's aim is to introduce the cloned gene into selected broadleaf crops. In that way, bromoxynil could be safely applied to the crops. (Source: Chemical Week, 4 March 1987)

Rice research

Foreign genes have now been transplanted into cells of monocotyledenous plants such as rice and maize. Researchers at the University of Nottingham have made major advances in generating rice plants from single protoplasts. Removing the cell wall to form a protoplast greatly facilitates introduction of foreign genes, but until now it has not been possible to regenerate whole cereal plants from protoplasts. (Extracted from New York Times, 13 January 1987)

Herbicide-resistant commercial tobacco

The gene that imparts resistance to sulfonylurea herbicides has been introduced successfully into commercial tobacco plants by researchers at Du Pont. Sulfonylureas are a class of herbicides developed by Du Pont that can be used at extremely low application rates and have very low mammalian toxicity. The gene that imparts resistance to the herbicides was first isolated by researchers at Advanced Genetics Systems, an Oakland, Calif., genetic engineering company that has a five-year research agreement with Du Pont. The tobacco varieties come from Northrup King Co., a Minneapolis seed company. Du Pont and Northrup King are now evaluating the commercial potential of the new plants. The two companies predict that if these tests are successful, seeds for sulfonylurea-resistant tobacco could be on the market in four to six years. (Reprinted with permission from Chemical and Engineering News, 2 February 1987, p. 2a. Copyright 1987, American Chemical Society)

Belgians succeed in herbicide resistance

Researchers at Plant Genetic Systems have developed strains of three plants that are resistant to Hoechst's broad-spectrum herbicide Basta. Using Agrobacterium tumefaciens as a vector for transferring genetic information, scientists at Plant Genetic Systems have conferred resistance to tomato, potato and tobacco.

These plants have a gene that codes for an enzyme that inactivates phosphinotricin, the active ingredient in Basta, inserted into their own genetic complement which is inheritable. The company chose to develop resistance to Basta, as the herbicide which kills all plant life can be metabolized in the soil and thus reduces residue fears.

This kind of research will allow farmers to use the herbicide all year round without killing off important crops. Plant Genetic Systems confirms that it now has plans to investigate other herbicides and other crops particularly sugar beet and cereals. The company will, however, have to overcome the barriers associated with the transference of genes to monocotyledons such as the cereals.

Other agrochemical majors are also seeking to confer herbicide resistance on commercially important crops. Monsanto has conferred resistance to its glyphosate herbicide Roundup on tobacco, tomato and petunia so far. Ciba-Geigy and American Cyanamid are also researching. (Extracted from European Chemical News, 2 February 1987)

Pine regenerated via somatic embryogenesis

The loblolly pine can now be added to the very short list of gymnosperms (or conifers) that can be regenerated in culture via somatic embryogenesis. Conifers represent major sources of softwood and fibre and reforestation efforts with clones or selected lines propagated via organogenesis are highly labour-intensive. Somatic embryogenesis (polyembryogenesis) offers forestry the welcome prospect of large numbers combined with cost-efficiency.

P. Gupta and D. Durzan of the University of California demonstrated that the techniques of freeze-preservation and encapsulation, just now being developed for somatic embryos of flowering plants, are also applicable to conifers. Both are methods for short- and long-term storage; encapsulation has the added potential of providing a method of dissemination.

Of special interest is the use of various staining regimes to identify specific cell masses that have embryogenic potential. Plant cells, whether grown in agitated or stationary cultures, are typically composed of mixed populations. In some instances, cells and cell masses may look different under the microscope, varying in size, shape, or degree of vacuolation. When these cells are plated out or individually isolated, the inconsistencies often foretell differences in developmental potential. In other instances, cells may appear similar but behave differently.

In almost all cases, however, only a certain percentage of cells goes on to regenerate plants. The task, then, is to identify embryogenic cells in the population of any one culture or among replicate cultures, avoid their loss during subculture, and then enrich their number, particularly prior to embryo maturation and plantlet formation. Identifying and selecting the proper cells or callus segments, for example, has proved essential in demonstrating and using somatic embryogenesis in cereals. And it is critically important in commercial operations where regeneration efficiencies, numbers of cultures and plants, and operating costs are critical. Researchers are now considering a number of "high-tech" strategies, such as using molecular probes targeted to embryo-specific RNA, or antibodies directed to embryo-specific proteins. Gupta and Durzan's use of standard stains (acetocarmine, Feulgen, and Evan's blue) offers an inexpensive and readily available tool for screening, selecting, and studying embryogenic populations. (Source: Bio/Technology, Vol. 5, February 1987)

Marker found for gene transfer to monocots

The Ti plasmid of agrobacteria is an important and widely used vector for carrying foreign genes into plant tissues. Its use has been expanded to monocotyledonous plants (which include corn, wheat, rice and many other important food crops) in the work of Barbara Hohn, Nigel Grimsley, and colleagues at the Friedrich Miescher-Institut in Basel, Switzerland, and at the John Innes Institute, Norwich, England. The researchers inserted cloned genes for the maize streak virus (MSV) into the Ti plasmid, inserted this into bacteria and infected maize plants with the recombinant using conventional techniques. They find that the maize plants develop signs of MSV infection, indicating that the gene has been transferred to the plant's genome. Thus the virus may be used as a sensitive assay to determine whether foreign DNA has been taken up by the plants. Earlier efforts to transfer genes to monocotyledonous plants may actually have worked but have gone undetected because the assays being used were not appropriate to this type of plant, the researchers say. (Reprinted with permission from Chemical and Engineering News, 12 January 1987, p. 20. Copyright 1987, American Chemical Society)

Whole monocot plant with altered genes grown

The race to grow a whole monocot plant with altered genes has been won by a simple new method. The idea is to send in new genes at the times when plant cells are more hospitable. A team led by Dr. Alica de la Pena at Complutense University in Madrid (Spain) noticed that at one stage in the process of cell division that produces the pollen in the flowers of rye plants, the dividing cells are not surrounded by a cell wall. The genetic factories inside these cells are thus especially receptive to injected chemicals. This suggested that they might even be open to a visit from a new bit of DNA.

Dr. de la Pena and two scientists from the Max Planck Institute for plant-breeding research in Cologne (FRG), Dr. Horst Lörz and Dr. Jozef Schell, then tested this promising suggestion. They injected DNA containing a gene for antibiotic resistance into the side shoots of 98 rye plants, allowed them to cross-pollinate and then collected more than 3,000 seeds. Resistance to antibiotics is not something farmers need in a crop, but it is an easily detectable trait and thus a useful test of the method. Seven of the seeds grew into thriving plants, despite the presence of an antibiotic in their diet. By testing for the enzyme which it moulds, the team showed that two of the seeds had, indeed, received the new gene. The beauty of the method is that it co-operates with a plant's natural reproductive cycle to produce genetically changed seeds.

A success rate of just two in over 3,000 leaves plenty of room for improvement. It remains to be seen whether the technique can be used to transfer the genes that biotechnologists are interested in - and not just marker genes such as the one for antibiotic resistance. This may be hard to do because injecting DNA often jumbles up the genes it contains. The germ cells of other cereals develop similarly to those of rye and the glimmerings of success with this new tool should give genetic engineers better access to the genetic works inside monocot plants. (Extracted from The Economist, 7 March 1987)

Research on bacterial genes

Product of Hg-resistance gene identified

Chemists Thomas V. O'Halloran and Christopher T. Walsh of Northwestern University and Massachusetts Institute of Technology, respectively, have isolated and characterized the protein that controls mercury resistance in certain bacteria. The protein, produced by a specific gene called merR, is considered a prototype for other metal-responsive switches found in cells. These switches sense and translate inorganic signals into changes in metabolism. The protein is a dimer of molecular weight 16,000. The chemists have identified the site on DNA to which it binds, and find that it does so in the presence or absence of mercury. This protein-DNA system "is now set for quantitative and high-resolution probes of specific metal-protein and protein-DNA interactions," the researchers say. (Reprinted with permission from Chemical and Engineering News, 12 January 1987, p. 20. Copyright 1987, American Chemical Society)

Research instrumentation

New silver stain kit

A silver stain kit for the detection of proteins, nucleic acids and lipopolysaccharides is now available from Amersham International under the trademark 'Quick-Silver'. Quick-Silver is claimed to be 50-100 times more sensitive than Coomassie brilliant blue for many proteins and 10-20 times more sensitive than ethidium bromide for nucleic acids. (Source: Biotechnology Bulletin, Vol. 5, No. 12, January 1987)

Optical probes for biomolecule detection

Existing immunodiagnostic techniques often involve sophisticated instrumentation and methods, expensive chemicals and highly trained personnel. Now, the Ares-Serono Group, a pharmaceutical and diagnostic company based in Boston, USA, and Switzerland, is developing a new, inexpensive diagnostic technology that physicians can use in their own offices. Scenarios like the one above could be possible by 1990. Ares-Serono is developing the technique in collaboration with FA Technology, a British Scientific consulting firm. Company scientists are using a physical phenomenon called surface plasmon resonance for directly detecting specific infectious viruses and bacteria in samples of blood or other body fluids. Plastic or glass strips are coated with a thin film of silver followed by a layer of monoclonal antibodies that recognize only specific infectious agents. When light is beamed onto the test strip's surface, the silver's electrons undergo a collective motion known as a surface plasmon.

Since this motion draws off energy from the light beam, reflections from the surface are significantly lower in intensity. If present, antigens - the infectious agents - bind to the antibodies, and the properties of the test strip surface are altered, resulting in changes in reflection angle and intensity. From these differences doctors will be able to determine what infectious agents are present in patients. (Extracted from Science News, Vol. 130, 13 December 1986)

Urease conjugated antibodies offered

Sera-Lab offers a comprehensive range of Urease conjugated anti-human, mouse, sheep and rabbit antibodies suitable for ELISA testing and hybridoma screening. A new service recently introduced by the company is a custom conjugation service, whereby customers' own antibodies can be Urease conjugated. Details from: Chris Lear, Sera-Lab Ltd., Crawley Down, Sussex RH10 4FF. (Source: Biotechnology Bulletin, Vol. 6, No. 2, March 1987)

Toxicological testing and drug screening with the aid of ECM

International Biotechnologies (IBT) Ltd. of Jerusalem, Israel, are offering tissue culture dishes coated with ECM - extracellular matrix - for use in toxicological testing and drug screening. ECM, a naturally produced basement-like membrane, closely resembles the basement membranes which exist in vivo. Because cells cultured on ECM grow in a manner similar to that in vivo, it is possible to more accurately extrapolate results regarding in vitro toxicity to human conditions.

ECM offers an improved, cheaper alternative to laboratory animals. The use of cells grown on ECM may reduce the cost and simplify the procedure of studying the effect on cells of single drugs, drug metabolisms, drug combinations, various chemicals and hormones. This ability to grow primary cells in vitro for drug screening and toxicological testing may offer an alternative to the use of whole-animal tests which are both costly and time consuming.

ECM in combination with serum-free media provide a superior primary cell culture for drug screening studies. ECM increases plating and cloning efficiency, induces differentiation and enables the growth of epithelial cells in serum-free media. The serum-free media in turn inhibit the proliferation of stromal fibroblasts, resulting in an almost pure epithelial cell culture. This improved cell culture facilitates the assessment of the effect of drugs without interference by serum components. For further information please contact Rosanna Milstein, Director of Marketing, IBT, P.O. Box 15149U, Jerusalem 93469 Israel. (Source: Company News Release, March 1987)

Microporous membranes

Pall's Biosupport division will be marketing high quality microporous plastic membranes for transfer and immobilisation of biologically active molecules. A range of surface chemistries make the membranes suitable for nucleic acid or protein transfer, immobilisation and specific absorption purposes. Details from S.R. Osborn, Pall Process Filtration Ltd., Europa House, Havant Street, Portsmouth, Hants PO1 3PD or on 0705 753545. (Source: Biotechnology Bulletin, Vol. 6, No. 2, March 1987)

FTIR in fermentation process control

A type of photometer that can measure radiation absorbed by an organic molecule may be useful in analyzing the raw materials used in biotechnology products made during fermentation, according to a Lehigh University scientist.

Dr. Janice Phillips, associate professor of chemical engineering at the university, says that knowing the concentrations of raw materials and products during the fermentation process could increase production and lower operating costs. She is evaluating the potential of Fourier transform infrared analysis, or FTIR, for use in fermentation monitoring and control.

Current methods for controlling what occurs during fermentation are limited to measurements of temperature, relative acidity, dissolved oxygen and gas composition.

FTIR, traditionally used in analytical chemistry but new to biotechnology, can measure concentrations as low as one gram per litre and as high as a few hundred grams per litre by identifying and quantifying an organic molecule by the type and amount of infrared radiation it absorbs.

The Lehigh researcher has used FTIR to track glucose and ethanol concentrations during a bioreaction and says results are "encouraging". However, to measure raw materials and products during fermentation she says a sampling system must be designed to deliver samples to the FTIR spectrometer. Fibre optics could further enhance analysis by connecting the spectrometer to the fermenter so measurements could be made without removing samples, she says.

One drawback of FTIR is that it cannot detect very low concentrations of raw materials, although there are a limited number of applications where such low-concentration detection is necessary. (Extracted from Chemical Marketing Reporter, 16 February 1987)

Digital imaging aids chromosome analysis

A small but growing number of genetics researchers have a new tool for studying chromosomes: digital imaging systems that not only display the chromosomes but also permit the images to be sorted, enhanced and manipulated for faster and more accurate study of genetic disorders. The imagers could also aid in prenatal diagnosis, determination of exposure to drugs and environmental toxins, and monitoring the effects of radiation.

Several such imagers are now on the market, with prices as high as a quarter of a million dollars. A relatively low-priced system, however, has recently been developed by Houston's Perceptive Systems Inc. (PSI).

To study the 23 pairs of chromosomes contained in every human cell, researchers often prepare a karyotype - a photo in which the 46 chromosomes are paired and arranged according to size. A missing or extra chromosome - or one that is too big, too small, or rearranged - is often sufficient to confirm a diagnosis.

Using traditional manual methods, the procedure often takes hours or even days; in contrast, the imagers perform the task in minutes.

PSI's Genetiscan imager consists of a microscope-mounted video camera, key-board, computer, and two video display terminals. The stained chromosomes are displayed on one of the screens, with the images digitized so that the banding patterns are more clearly visible than on the original slide - an important diagnostic factor, since some genetic disorders are associated with just a single missing band.

The system features two karyotyping modes: automatic and interactive. With the first (which adds $10,000 to the $65,000 base price), the chromosomes under study are compared with others previously entered by the user, then automatically arranged into sized pairs and displayed.

Genetiscan is one of several PSI digital imagers, and software is available for a variety of studies - counting cells and distinguishing different cell types to diagnose blood disorders, for example. PSI is now working with Du Pont to develop an imager to scan brain tissue and produce 3-D images of selected areas. (Extracted from High Technology, January 1987)

General

Modified enzyme communicates directly with metal electrodes

Chemists have modified the enzyme glucose oxidase in such a way that direct electrical communication can occur between the enzyme and metal electrodes. This is the first time that direct electron transfer between an enzyme that catalyzes oxidation-reduction reactions and a metal electrode has been demonstrated.

The successful research effort opens up a new route to development of electrochemical and bioelectronic sensors. Specifically, the work on glucose oxidase may open a path to a biocompatible glucose sensor. Such a device could be used for continuous monitoring of the blood glucose level of diabetics.

The research was performed by Adam Heller, head of the electronic materials research department at AT&T Bell Laboratories, Murray Hill, N.J., and Yinon Degani, a post-doctoral member of the staff at Bell Labs. Essentially, the scientists introduce electron relays into glucose oxidase that shuttle electrons from the reduced redox center of the enzyme to the metal electrode.

Redox enzymes naturally accept electrons from and transfer electrons to small ions or molecules in solution. For instance, glucose oxidase, as its name implies, oxidizes glucose to gluconolactone. In the process, glucose transfers two electrons to the oxidized flavine adenine dinucleotide (FAD) redox centre of the enzyme, thereby reducing it to reduced flavine adenine dinucleotide ($FADH_2$).

The enzyme does not, however, directly exchange electrons with metal electrodes. Therefore, the current flowing through a gold or platinum electrode in an electrolytic solution containing glucose oxidase does not increase with the concentration of glucose even though the enzyme is reduced by glucose and the reduced enzyme diffuses to the surface of the electrode. Although the electrode is maintained at a sufficiently oxidizing potential, the reduced enzyme is not reoxidized and the oxidation of glucose by the enzyme stops.

Enzymes are notoriously delicate in terms of structural changes that will be tolerated without significant loss of activity. At high enough concentrations, urea denatures enzymes. Although they have not yet proved it, the scientists believe that, in 3M urea, the two subunits of glucose oxidase separate to some extent, but the globular structure of each subunit remains essentially intact. Therefore, only amine groups on those portions of the subunits that are in contact with each other in the intact enzyme are acylated. In other words, in the modified enzyme, the electron relays are restricted to the interface between the two subunits. This limits the structural changes in the subunits themselves and allows retention of greater than 50 per cent of the enzyme's catalytic activity. Repeated gel filtration steps do not change the properties of the modified enzyme.

Such an electrode could monitor directly and continously a diabetic's blood sugar level. The output from the electrode could be fed into a microprocessor that controls a source of insulin. Such a device could deliver insulin through a syringe in response to changes in blood glucose level in much the same way that the pancreas of a non-diabetic delivers insulin. Such an insulin delivery system could alleviate or eliminate many of the severe physical problems, such as damage to the kidneys and eyes, resulting from glucose

fluctuations in diabetics. Such fluctuations are associated with the most prevalent method of administering insulin, which is subcutaneous injection.

The modified enzymes also open the way to the possible use of biocompatible electrodes incorporating modified enzymes to control through direct electrochemical oxidations or reduction reactions the concentration of compounds in a tissue. The establishment of direct electrical communication between enzymes and metal electrodes is not limited to glucose oxidase, Degani says, but is feasible in other dimeric enzymes such as D-amino acid oxidase. Research on other enzymes and other electron relays is being pursued in Heller's laboratory. (Abstracted with permission from Chemical and Engineering News, 16 March 1987. Copyright 1987, American Chemical Society)

D. APPLICATIONS

Pharmaceutical and medical applications

New cell technology technique

A new technique of mimicking cell membranes lies at the heart of a new British company just formed with £1 million of venture capital. The technology could have commercial applications in many branches of health care - from artificial organs to artificial blood.

The company, Biocompatibles, hopes to exploit some of the scientific research already carried out at the Royal Free Hospital School of Medicine by a team headed by Dennis Chapman, Professor of Biophysical Chemistry.

The company will develop, manufacture and market products based on artificial membranes. One product will be a preparation that mimics the outer surface of red blood cells. Plastics and other artificial substances introduced into the body normally cause the blood to clot. But if the surfaces of artificial substances are coated with this preparation, the body fails to recognize the substance as foreign.

The product could have many different applications in medicine. Attempts to give people artificial hearts, for example, have failed not because the organ did not work, but because the patient suffered strokes as a result of blood clots. Sprayed with this preparation, artificial implants - cardiac and intravenous catheters for diagnosis or treatment, and artificial arteries - would all survive longer in the body or perform better. On a more mundane level, contact lenses coated with this kind of preparation would be far more comfortable to wear.

Another area of research that the company hopes to exploit is the manufacture of liposomes which could eventually allow doctors to administer drugs directly to particular organs of the body.

Liposomes may also prove useful in the development of artificial blood. Liposomes containing haemoglobin can be freeze-dried and then reconstituted by adding water. This work presents the possibility of having easily stored artificial blood freely available for emergencies. (Extracted from New Scientist, 19 March 1987)

Novel glycoproteinase

A novel glycoproteinase can be used to modify the cell surfaces of living cells for the purpose of defeating cell/cell recognition or as a tool for the specific cleavage of biological molecules in structural studies. The enzyme from the bacterium Pasteurella [illegible]ytica, while it does not kill or burst animal [illegible]s, can remove some important labels from the cell surface. Further information available from C.M Ostrovski, Technology Development Officer, University of Guelph, Office of Research, Guelph, Ontario N1G 2W1, Canada.

Alpha-thalassaemia screening test

Alpha-thalassaemia is probably the single most common human genetic disorder worldwide, resulting from the deletion or inactivation of one or more of the four genes coding for the haemoglobin 'a' chains. The subsequent decrease in 'a' chain production can be rapidly detected in newborn infants by measuring the level of Hb Bart's (γ_4), formed when the extra gamma chains of Hb F ($\alpha_2\gamma_2$) combine in tetramers-γ_4. The Isolab screening kit offered by Advanced Laboratory Techniques of Tonbridge Wells, UK provides rapid quantitation of Hb Bart's. (Source: Biotechnology Bulletin, Vol. 5, No. 12, January 1987)

Better treatment for thalassaemia?

Scientists and doctors at Essex University and University College, London, have developed a promising new technique for removing excess iron from the bodies of patients being treated for thalassaemia. The blood transfusions which are an essential treatment for severe thalassaemia inevitably lead to surplus iron accumulating in the body, with increasingly harmful and eventually fatal results unless the iron is removed with an appropriate pharmaceutical agent.

At present the drug used is desferrioxamine which, while being effective, is expensive and has to be given intravenously by infusion. The new drugs, being developed at Essex University by Dr. Bob Hider and tested at University College Hospital by Professor Ernie Huehns, so far on animals, can be administered orally and would be much cheaper to produce than desferrioxamine. They also have a potential for treating other serious conditions besides thalassaemia.

Thalassaemia, anaemia caused by genetic defects, affects several million people in North Africa, the Middle East, across India and Pakistan and especially in Thailand. The name comes from the Greek thalassa, meaning the sea, because of the frequency of the condition in countries bordering the Mediterranean.

Beta thalassaemia

Among the most severe and common forms of the disease is beta thalassaemia (in which the defect distorts the beta chain of the haemoglobin molecule, which is made of two parts called the alpha and beta chains). Infants who inherit the beta thalassaemia defect from both parents seldom live to one year old unless they are treated with regular transfusions of normal blood to restore oxygen-carrying capacity.

Unhappily this, too, brings increasingly severe problems in the long term. The haemoglobin in the transfusions carries oxygen around the body normally but it adds enormously to the total amount of iron in the patient's body. Every molecule of the abnormal thalassaemic haemoglobin, as well as of the haemoglobin in transfused blood, has four atoms of iron at its centre. Normally, the body tends to be chronically short of iron, a metal which is essential for making enzymes, our natural catalysts, as well as in haemoglobin, so mechanisms have evolved for storing iron rather than excreting it.

Our bodies lose iron only in cells sloughed off in dead skin and dead cells from the constant turnover in the lining of the gut.

The body keeps a day-to-day y of iron inside big, hollow-shaped protein molecules of ferritin. Each single ferritin molecule is able to store up to 4,000 atoms of iron. Normally the ferritin stores are only partially full of iron atoms. But if continuing iron overload, through repeated intake in blood transfusions, fills up the ferritin molecules, iron begins to be deposited in the tissues - especially the cells of the heart and liver, where it is extremely toxic. And, because bacteria feed on free iron, the deposits encourage infections. Moreover, the presence of free iron generates free radicals, hydroxyl chemical groups which are so reactive that they literally tear living material to pieces.

Without treatment to remove iron overload, victims of severe thalassaemia given blood transfusions become increasingly ill from early adolescence on, and may not reach puberty. Desferrioxamine, when it can be made available, can penetrate into cells containing iron and bind on to it, making a chemical complex which is then excreted from the body.

But desferrioxamine has two severe limitations. It is expensive: a course of treatment costs £4,000 per year and has to be continued, along with blood transfusions, for life. And it cannot be taken orally, but has to be taken continually because it is rapidly excreted from the body. So it has to be given by slow infusion, which requires expensive infusion pump equipment and is unpleasant for the patient.

Now, animal tests imply that a drug that Dr. Hider has produced can provide a cheap alternative to desferrioxamine; and it could be taken orally. Dr. Hider's breakthrough came from looking into the way in which fungi and bacteria obtain the iron they need in their diet. They dissolve it out of iron-containing complexes in the environment by means of biological solvents called siderophores. These solvents are very efficient at scavenging iron but they need special receptors through which they bring their cargo of iron into the fungi that need it. Hider has redesigned siderophore molecules so that they retain their ability to scavenge iron but have been given an ability to enter cells by simple diffusion through the membranes of the cells.

Animal trials carried out by Professor Ernie Huehns of University College Hospital in London, over the last few years, have shown that hydroxy pyridones, the chemical name for the modified siderophores created by Bob Hider, are as effective as desferrioxamine at getting iron out of cells in which it has been deposited through overloading of tissues. Pyridones are, too, as iron-selective as desferrioxamine. They do not remove other vital elements such as copper, calcium and zinc, are cheap to produce and can be taken orally. They appear to have no toxic side effects.

Long trials

The stage seems set for trials of pyridones in human victims of thalassaemia. But because such people might have to take pyridones regularly for life, along with their regular blood transfusions, pyridones will have to undergo exceptionally long, stringent and expensive toxicity trials in animals before being licensed for clinical testing. Such toxicity trials are beyond the resources of Essex University, UCH or the British Technology Group (BTG), which has been supporting the work so far.

So Dr. Hider is now hoping that a pharmaceutical company or international agency will come forward to take the work through the next stage. The outcome could be a treatment which would make a normal life and life-span possible, without discomfort and at moderate cost, for many thousands of thalassaemic people.

It could have spin-offs in several other clinical areas. Other siderophores could be developed to remove aluminium from the bodies of those patients on dialysis machines who suffer from aluminium overload. The iron-scavenging siderophores could be used to preserve organs such as kidneys for longer periods outside the body before they are used in transplants: one limit on the life of isolated organs is tissue damage from free radicals liberated by iron.

Radioactive isotopes are often injected into the body to image, and even to treat, cancer tumours. Appropriate siderophores could be used to remove such potentially harmful substances from the body after their period of usefulness came to an end. They might even be used to remove absorbed plutonium. (Article written by Stanifortb Webb for SPECTRUM/a, No. 205/1987)

Two companies collaborate to study nervous system

California Biotechnology Inc. has signed an agreement with Organon International, BV, of the Netherlands, to collaborate on research and development of products resulting from Cal Bio's neurobiology programme.

Under the agreement, Organon will fund and collaborate in the development of products for Alzheimer's disease and other degenerative diseases of the central and peripheral nervous system. Following research, California Biotechnology and Organon anticipate entering into a further agreement granting worldwide clinical development and marketing rights to Organon for all products resulting from this collaboration.

The therapeutic research programme is based on human proteins called neurotrophic factors (which principally affect development and maintenance of cells in the brain and peripheral nervous system) developed at California Biotechnology.

These factors include the company's genetically-engineered fibroblast growth factor (FGF), which has been shown to stimulate the function of key nerve cells. California Biotechnology researchers claim they were the first to clone and express FGF, which is also being developed for various wound healing applications.

The programme includes several neurotrophic factors exclusively licensed from the laboratory of Dr. Stanley H. Appel at the Baylor College of Medicine, Houston. (Source: Chemical Marketing Reporter, 16 March 1987)

Lilly gets approval for growth hormone

Eli Lilly & Co. has received FDA approval to market its natural-sequence human growth hormone, called Humatrope.

The company says its hormone, made by recombinant DNA technology, is identical in chemistry and structure to the growth hormone produced by the human body. The newly approved product will compete with Genentech's human growth hormone, marketed under the tradename Protropin, which was approved for marketing in late 1985.

Like Protropin, Humatrope is indicated only for long-term treatment of children whose pituitary gland does not secrete adequate normal endogenous growth hormone. Lilly says that among actions mediated by Humatrope and human growth hormone are skeletal growth, cell growth and improved metabolism of proteins, carbohydrates, lipids and minerals.

The human growth hormone business is currently in the midst of a patent quandary as Hoffmann-La Roche has sued Genentech for patent infringement. Hoffmann-La Roche's 1974 patent on synthetic production of human growth hormone, the company claims, extends to recombinant DNA methods of production. Also, the "composition of matter" argument comes into play when the patent is on the substance, no matter how produced. How this will apply to the Lilly product, which is somewhat different in composition, is not yet known. (Extracted from Chemical & Engineering News, 16 March 1987 pp. 5 and 6)

Sumitomo develops exotoxin Mab

Sumitomo Chemical and its drug affiliate Sumitomo Pharmaceuticals have developed the technology to mass produce a human monoclonal antibody capable of attacking the Pseudomonas aeruginosa blue pus toxin. The two companies have succeeded in cloning the genes for the toxin antibody. These genes have been transplanted into mice myeloma cells.

Both partners have succeeded in propagating the manipulated mouse cells and are planning to commercialize the process to produce the antibodies as a drug to treat various diseases. The blue pus toxin prevents human protein synthesis and poses a danger for people with reduced immune functions. At present a number of antibiotics can be used to treat the blue pus but there are no effective methods to attack the toxin. (Source: European Chemical News, 19 January 1987)

New DNA probes

The applications of DNA probe technology seem to be limited only by the imagination. DNA probes may be used as anti-counterfeiting devices. The UK's Department of Trade and Industry recently awarded a prize to BioTechnics Ltd. for its Bio-Tab invention. Today, the security measures taken to protect documents, bank bonds and other sensitive items are largely electronic; tomorrow they could be biological. BioTechnics says that it will be possible to use DNA markers as covert or overt labelling devices of very high specificity. One merely couples DNA probes to small stretches of identifying DNA covalently bound to paper, or, for example, to the canvas of a priceless work of art. This security device might be especially valuable to large organizations such as the FBI where it is important to know that paper from outside sources has not somehow slipped into in-house documents.

DNA probe technology is also being used to create a new type of fingerprint for forensic identification of potential criminals. Lifecodes applies its DNA-Print™ technology to samples of blood, semen and tissue - the company predicts that the tests should increase conviction rates for rape, murder and other violent crimes.

Probe tests are being developed for field uses as well. Enzo Biochem recently received a contract from the US Army to develop rapid identification and diagnostic systems, suited to use at the scene of infection. Based on monoclonal antibodies as well as the company's probes, the technology "is ideally suited to ... the environmental stability requirements for military detection systems," Enzo says.

In addition, scientists from the Harvard School of Public Health, Brazil and Thailand have devised a field assay using DNA probes to detect the malarial parasite in blood samples taken from fingerpricks. Not only can the samples be collected in the field, but they can also be lysed and the DNA immobilized there - using a manifold that can be operated under the vacuum supplied by a hand pump. The samples are then taken back to the laboratory to hybridize with ^{32}P-labelled probes. The results can be read off an exposed X-ray film. Field trials have shown that populations can be tested rapidly. Once this probe is commercialized, each test should cost no more than five to ten cents (after necessary equipment has been purchased). (Source: Bio/Technology, Vol. 5, March 1987)

Q-fever antigen available

An enzyme-linked immune absorbent assay (ELISA) antigen is available for the detection of antibodies to Coxiella burnetii, the agent of Q-fever in humans. Unlike other ELISA antigens for C. burnetii, this test fills a gap in the technology of veterinary diagnostic procedures by detecting infected animals, verifying vaccination results and monitoring the establishment of coxiella-free stock. Further information available from C.H. Ostrovski, Technology Department Officer, University of Guelph, Industrial and Innovation Services, Guelph, Ontario, Canada N1G 2W1.

BTD launches gene-probe test

A gene-probe test that can detect periodontal (gum) disease at an early stage has been launched by US biotechnology company, BioTechnics Diagnostics (BTD). The company's first commercial product is designed to detect the presence or three different gram-negative bacteria involved in causing the disease.

Because of the complexity of DNA probe techniques, BTD has established a clinical reference laboratory at its headquarters in Cambridge, Massachusetts, to test samples received from dentists in New England and further afield. The laboratory can handle hundreds of samples and will be expanded as required.

The company is hoping to develop a simplified test for dentists to use in their surgeries.

BTD's president Bill Coll reckons that the periodontal disease detection market has "huge" commercial potential. The condition affects some 23 million Americans who spend over $4 billion/year on surgical and other treatment. (Source: European Chemical News, 9 February 1987)

Tumour necrosis factor as obesity-curbing agent

Weight-control with a two-way switch is the role proposed for tumour necrosis factor (TNF) in a patent pending at Cetus Corp., Emeryville, Calif. TNF genetically engineered by Cetus is in early clinical trials as a tumour-killing drug at Fox Chase Cancer Centre, Philadelphia. Other biotechnology companies in the USA and Japan are also trying recombinant versions of the tumour-wasting molecule in chemotherapy studies.

Cetus' patent application, "Use of Tumour Necrosis Factors as a Weight Regulator", was published last November in Europe by the World Intellectual Property Organization. The text describes in vitro tests of TNF that suggest it may some day be administered to obese persons to suppress production of excess body fat and that this lipid-depleting effect can be turned off by monoclonal or polyclonal antibodies that neutralize the necrosis factor.

TNF, a 157-amino-acid peptide, has been identified as identical with a molecule called cachectin, which mediates cachexia - body-wasting - in animals or humans reacting to malignancy, infection or bacterial endotoxin. Both apparently prevent the expression of genes responsible for producing enzymes important in storing adipose tissue.

Stanford University scientists working with Cetus and biochemist Anthony Cerami at The Rockefeller University, New York City, each discovered the molecular and metabolic identity between TNF and cachectin. Rockerfeller has also filed for patents on using the peptide's fat-deleting properties for weight control and licensed their approach to Chiron Corp., Emeryville. (Extracted from McGraw-Hill's Biotechnology Newswatch, 2 March 1987)

Cancer drug deal

The US pharmaceuticals major, Merck, which is strong in two of the fastest growing areas of the pharmaceutical market, cardiovasculars and antiarthritics, has entered into agreements with Biogen to develop and market a recombinant protein currently being investigated as a treatment for cancers of the female reproductive system. Merck is also believed to be in negotiations with Yamanouchi Pharmaceutical for a US licence for Smancs, a cancer drug in Phase III trials in Japan.

In the agreement with Biogen, Merck will make payments for the achievement of specified research goals and additional research to be conducted in collaboration with the Massachusetts General Hospital in Boston. All three partners will conduct basic research and development work on the protein, recombinant Mullerian inhibiting substance (Mis), but Merck will be responsible for clinical trials and regulatory procedures.

Merck is believed to be one of the leading candidates to win US rights to Yamanouchi's anti-cancer therapy, Smancs, a neo-carzinostatin conjugated with partiallly esterified poly(styrene-co-maleic anhydride). The drug is an analogue of Yamanouchi's other experimental anti-cancer agent, currently in Japanese trials, neo-carzinostatin. (Source: European Chemical News, 9 March 1987)

Treatment for septic shock

Pfizer has signed a letter of intent with Xoma Corporation to develop and commercialise the latter's monoclonal antibody-based products for treatment of septic shock - a disease which kills about 80,000 people annually in the US. One product is already in Phase II clinical trials with others in preclinical testing. (Source: European Chemical News, 2 February 1987)

Growth factors might speed healing

Selected peptide growth factors might be useful in helping injuries that extend only partway through the skin heal more quickly. That prospect has been suggested by Gregory S. Schultz of the University of Louisville School of Medicine and George J. Todaro of Oncogen. Topical application of epidermal growth factor (EGF) had been shown earlier to accelerate epidermal regeneration of mid-dermal skin injuries. Transforming growth factor-α (TGF-α) and vaccinia virus growth factor (VGF), the researchers note, have substantial sequence homology to EGF, and all three growth factors appear to bind to and activate a common tyrosine kinase receptor. The researchers applied chemically synthesized rat or human TGF-α and VGF to middermal wounds - in this case second-degree burns - on the dorsal thorax of anaesthetized adult pigs. The growth factors were applied in a water-miscible antibiotic cream. A comparison of the three growth factors at 0.1 μg per mL showed that VGF and TGF-α produced a more rapid growth of epithelial cells in the wound area than did other forms of treatment tested. (Reprinted with permission from Chemical & Engineering News, 19 January 1987, p. 30. Copyright 1987 American Chemical Society)

Merck brings recombinant hepatitis B vaccine to market

Merck Sharp & Dohme Research Laboratories announced the marketing launch of Recombivax HB®, a recombinant vaccine against hepatitis B infection. It was approved last July by the US Food and Drug Administration, and will now be offered to high-risk groups in the USA, alongside Merck's blood-plasma-based hepatitis B vaccine.

Both products have produced substantially the same high levels of immunity in clinical trials, but the blood-derived version excited anxiety that it might contain hepatitis or AIDS contamination.

Chronic-disease carriers number at least 150 million worldwide, 700,000 in the USA, according to World Health Organization estimates. Merck perceives the "global market in the USA as 8 to 12 million persons at risk, of whom 1.5 million have already been vaccinated," states a company spokesman. Immunization with either Merck vaccine involves three injections over a six-month period, at a cost of $113 to $120. (Extracted from McGraw-Hill's Biotechnology Newswatch, 16 February 1987)

Drug monitor

Using micellar chromatography, a new separation technique can handle untreated blood, urine and saliva samples. In addition to spotting drug abuse, the method could insure patients receive therapeutic amounts but not overdoses of prescribed medicines. Drugs monitored thus far include acetaminophen, phenytoin, procainamide, quinidine, theophylline, LSD, cocaine, and THC. Further information available from W. Stevenson Bacon, Research Corp., 6840 East Broadway Boulevard, Tucson, Arizona 85710-2815.

New insulin process

Novo Industri, the Danish biotechnology concern, has started production of human insulin using genetically engineered baker's yeast.

The company claims that the new technique offers two advantages over conventional technology involving the use of the gut bacterium Escherichia coli. The yeast produces a precursor insulin molecule which already possesses the essential disulphide bridges for correct 3-D folding and only requires a one-step enzymatic conversion.

The other advantage, says Novo, is that the gene-spliced yeast is able to secrete the precursor into the fermentation broth. This simplifies isolation and purification. The yeasts can be sterilised and sold for animal feedstocks and Novo has started to investigate this potential market and plans to use the technology to produce other important proteins.

Conventional production of insulin using recombinant E. coli yields a protein that must be further treated. Furthermore the bacteria need to

be broken up to isolate the therapeutic protein from other proteins. (Source: European Chemical News, 26 January 1987)

Immunex starts Gmcsf trials

Immunex Corporation, the US biotechnology company, has started Phase I clinical trials of a gene-spliced immune system protein against cancer. The drug, granulocyte-macrophage colony stimulating factor (Gmcsf), is being developed by the company in collaboration with the Hoechst drug subsidiary, Behringwerke.

The trials are being conducted in hospitals in Texas and across the US, as well as in the Federal Republic of Germany. Immunex says that it has produced enough of the drug for Phase I and II testing. The protein acts by stimulating the bone marrow to produce disease-fighting white blood cells. It is one of several colony stimulating factors that the two companies are looking at.

Animal tests with Gmcsf have shown that the drug boosts white blood cell counts and triggers some cells to directly kill tumour cells. Chemotherapy and radiation treatment frequently depress white blood cell production in cancer patients, reducing their bodies' ability to fight opportunistic infections. (Source: European Chemical News, 9 February 1987)

Biogen licenses IFN

Biogen has licensed its gene-spliced gamma interferon for use in cancer therapy to Baxter Travenol Laboratories for all markets except the Federal Republic of Germany and the Far East. The biotechnology company says it is retaining the rights for other indications, including rheumatoid arthritis and viral diseases.

Biogen currently has its gamma interferon in Phase III trials in the US and Europe against renal cancer and Phase II studies for a number of other cancers, including ovarian carcinoma, chronic myelogenous leukaemia and malignant melanoma.

Following regulatory approval, Baxter Travenol will market the gamma interferon through its Travenol Chemotherapy Services arm, which distributes premixed anti-cancer drugs to oncologists. (Source: European Chemical News, 5/12 January 1987)

Promising schizophrenia drug developed

Glaxo is developing a new drug for the treatment of schizophrenia, anxiety and nausea. The drug, codenamed GR38032, is likely to find its first commercial application in the control of nausea and vomiting in patients receiving chemotherapy. First launch could be around three years hence, estimates a company spokesman.

Details of animal studies with the new drug were presented at a meeting of the British Pharmacological Society in London last December. Early clinical trials with humans have subsequently begun. The animal experiments indicate that GR38032 seems to act against schizophrenia by controlling the dopaminergic overactivity in the brain, which is thought to cause the symptoms of the disease, without affecting normal behaviour.

The animal tests also suggest that the drug could be a non-sedative, non-addictive treatment for anxiety. (Extracted from European Chemical News, 5/12 January 1987)

Genetically engineered protein A available

Using gene-spliced E. coli, researchers at the UK Centre for Applied Microbiological Research, Porton Down, have developed a protein A which is now available from Porton Products. The protein A produced represents over 20 per cent of the total cell mass and is free from the toxins associated with production from Staphylococcus aureus. Protein A has applications in cytochemistry, immunochemistry and the purification of monoclonal antibodies. (Source: European Chemical News, 26 January 1987)

Gene-spliced factor VIII products

Genetics Institute, in collaboration with Baxter Travenol Laboratories, is poised to push its gene-spliced factor VIII into clinical trials in the near future. The biotechnology company has isolated the gene for factor VIII:C and expressed it in mammalian cells and is planning an expansion of its pilot and clinical production facilities. The company is going to shift its production activities to Andover, Massachusetts where a facility will be built on a recently purchased site. Construction of this new facility is expected to be completed by the end of the year.

Genetics Institute is expected to select a site for its joint venture company with Burroughs Wellcome, Wellcen Manufacturing, in the very near future.

Preclinical tests indicate that the product is efficacious in treating dogs with haemophilia A. Genetics Institute is currently focusing its efforts on the development of a commercial-scale process.

Close behind, Genentech, in collaboration with Bayer subsidiary, Cutter Biological, has entered preclinical trials and may be in a position to launch full human trials by the end of the year.

Biogen and Kabi-Vitrum are expected to be in a similar position by the year-end with their product, which is believed to be factor VIII:C analogue. Chiron, in collaboration with Denmark's Nordisk will probably enter trials early next year.

With current therapy using concentrates of factor VIII:C from donated blood, the risk of exposure to infectious diseases is high. Tragically as many as two thirds of haemophiliacs in developed nations may have been exposed to the AIDS virus. It is for this reason that projections for the gene-spliced product are high. (Extracted from European Chemical News, 30 March 1987)

Joint R&D angiogenesis venture

Synergen Inc. of Boulder, Colo. has joined with E.I. du Pont de Nemours & Co., Wilmington, Del., to research the uses of angiogenesis factor (AF), a protein that induces formation of new blood vessels. The two companies will jointly finance the next 18 months of preclinical animal testing of recombinant AF's utility in cardiovascular and neurological disorders, as well as tissue-regeneration.

Synergen will focus on developing a manufacturing process that meets FDA regulations. Under the agreement, the firm retains manufacturing rights to AF; Dupont gets worldwide rights to market any applications developed, except topical wound healing.

California Biotechnology, Inc., Mountain View, is researching the related fibroblast growth

factor. Amgen, Inc., Thousand Oaks, Calif., and Chiron Corp., Emeryville, Calif. are also pursuing potential wound-healing products.

Synergen's initial source of AF was human placenta, but now they produce it in bacterial hosts. Synergen, in collaboration with a group at New York University, identified, characterized and initially purified the protein. It also did all the cloning and gene-expression. Synergen has a US patent pending, and late last year applied for European patents. At the end of animal screening trials, the two companies will, if the research results warrant, conduct the clinical studies necessary to obtain FDA approval of any products. Dupont would assume a major financing commitment during this phase. (Extracted from McGraw-Hill's Biotechnology Newswatch, 2 March 1987)

Human and animal hormones agreement

A new team has been formed to use an amidation process that could more efficiently produce a large class of hormones for use in human and animal medicine. Italy's Farmitalia Carlo Erba and Unigene Laboratories (Fairfield, N.J.) will further develop Unigene's patented process that uses genetically engineered bacteria to produce a precursor of a hormone. An amidating enzyme then converts the precursor to the fully active hormone. Farmitalia will retain exclusive worldwide marketing rights to certain hormones for use in human and animal health care and animal nutrition. For its part, Unigene will retain rights to other hormones in those areas. (Source: Chemical Week, 4 March 1987)

Blood protein agreement

Behringwerke, a wholly-owned drug subsidiary of Hoechst, has entered into a deal with Integrated Genetics to develop and market genetically engineered blood protein erythropoietin. Integrated Genetics will manufacture and supply the product while Behringwerke will conduct the clinical trials. No date has yet been set for the trials although they are expected to be later this year.

The partners are expected to test the protein for the prevention of organ transplant rejection but it may also be tested for its efficacy in reducing anaemia. Erythropoietin, in an unrelated study, has been shown to be effective in ameliorating anaemia in chronic kidney failure. Clinical trials using genetically engineered erythropoietin produced by Amgen are currently under way in the US and UK while Genetics Institute in the US plans to have trials under way in the near future. (Source: European Chemical News, 2 February 1987)

Bacterial antigen kit

Soluble bacterial antigens can be detected in body fluids using the Wellcogen bacterial antigen detection kit. This contains reagents capable of detecting, in as little as 15 minutes, the soluble antigens of group B streptococci, H. influenzae b, S. pneumoniae N. meningitidis ACTW135, and N. meningitis B/E.coli K1. Details from: John Twycross, Wellcome Diagnostics, Temple Hill, Dartford DA1 5AH or on 0322 77711. (Source: Biotechnology Bulletin, Vol. 6, No. 1, February 1987)

Treatment for sickle cell anaemia

A new composition offers a safe and effective treatment for sickle cell anaemia. Phlorizin benzylaside at therapeutic concentrations in the bloodstream interacts with the red blood cell membrane, allowing salt and water to enter the cell. The additional salt and water swell the red blood cells to a spheroid shape and reduce the concentration of haemoglobin S below a critical concentration. Upon deoxygenation, sickling does not occur. Further information available from Mr. D. Keach, University of Kentucky Research Foundation, Room 312, Kinkead Hall, Lexington, KY 40506-0057. (11584)

Products that detect arthritis and cancer

Development of autoimmune disease and cancer diagnostic products is the aim of a three-year, $3.7 million agreement between T Cell Sciences (Cambridge, Mass.) and Yamanouchi Pharmaceutical (Tokyo). Yamanouchi will provide funding to develop products that use genetically engineered T cell antigen receptors to diagnose rheumatoid arthritis and lung cancer. T cell's surfaces have antigen receptors that detect antigens, or foreign substances, in the body. Such detection activates the immune system, which starts producing antibodies against the antigen. (Source: Chemical Week, 7-14 January 1987)

Bright market outlook seen for monoclonal antibodies in diagnostic imaging agents

Besides harnessing monoclonal antibodies (MAbs) to deliver immunotoxins and chemotherapy drugs, a number of companies that gave presentations at the Hambrecht and Quist, Inc. (H&Q) Healthcare Conference in San Francisco last January are also developing MAbs as high-precision diagnostic-imaging agents.

Analysts expect this approach to be rapidly accepted, because of the superior diagnostic capability and reduced toxicity of MAb systems over existing methods. The incremental costs associated with MAb imaging are expected to be far less than the ultimate saving from improved therapy.

Market potential is conservatively estimated at $135 to $225 million, based on 900,000 new medical cases yearly. The number of imaging procedures per patient is in the range of 1.5 to 2.5, but subjects who survive beyond the first year will require constant monitoring and frequent re-scanning.

What follows rounds up the development status of monoclonal diagnostics on their way to market, as reported at the Conference.

Centocor, Inc., Malvern, Pa., considered by H&Q analysts to be the leading company in the development of monoclonal agents for imaging, has a colorectal-cancer scanning test in early clinical trials. Tracers for ovarian, breast, lung and prostate cancers are slated for mid-1987.

For MAb imaging of cardiac disease, two Centocor products are deemed to have no significant competition: Myoscint is a myosin-specific monoclonal package that pinpoints dead heart muscle, distinguishing it from temporarily damaged or ischemic tissue. It is on the market in Italy, Austria and the Netherlands, all of which have limited regulatory hurdles for in vivo imaging. In the USA, it is in Phase II/III clinical trials.

Centocor's second cardiac product is an anti-clot (anti-fibrin/anti-platelet) MAb, capable of locating blood thrombi throughout the body. It has potential for tracking the effects of tissue plasminogen activator, and is diagnostic for pulmonary embolisms, deep-vein thrombosis, peripheral arterial occlusion and strokes - as the blood-brain barrier is breached by the antibody fragment.

Cytogen Corp., Princeton, N.J., has developed a proprietary technology to bind substances only to an antibody's constant region, leaving intact the MAb's ability to recognize and bind to the antigen. This yields a 10- to 100-fold increase in the amount of payload that can be attached. In early clinical trials, no immunological problems have been seen.

Cytogen is currently using whole murine antibodies, licensed from academic researchers, as well as six for which it has US patents pending. The firm received a Canadian patent in 1986 covering all 83 claims for which it had filed. Phase I clinical trials have begun on renal-cell cancer at Memorial Sloan-Kettering Institute, New York City. Cytogen is also working on imaging systems for lung, colorectal, and breast cancer with Eastman Kodak Co., Rochester, N.Y., which has exclusive rights for those three applications.

The company has tested 22 antibody/isotope systems in nude mice, including seven types of human tumours, six different sites, 10 different antibodies. All have yielded successful results without significant uptake of the imaging agent by the liver. Some tumours were as small as 200 mg - one-tenth the size of a normal mouse lymph node.

The firm has patents on antibody linker composition, and will be able to patent MAb/linker/-payload complexes, allowing it to establish proprietary drugs that cannot be directly copied, say the analysts. E.F. Hutton has reported that if the advantage in linker technology in mice translates into similar benefits for humans, Cytogen will be a contender for leadership in the field.

Hybritech, Inc., San Diego, Calif., is initially using murine MAbs to image breast and colon cancers. It has in early clinical studies what it says is the first all-human breast-cancer tracer, and murine-based MAbs for imaging prostate cancer and melanoma under early development.

Immunomedics, Inc., Newark, N.J. did not present at the H&Q conference, but holds the most (seven), and earliest patents, granted - the first in 1982 - for production and use of monoclonals. Its imaging agents are being developed for colorectal, lung and ovarian cancers.

NeoRx Corp., Seattle, Wash., a privately held company, is in advanced clinical trials with a melanoma-imaging agent. It expects to follow this year with systems for colon cancer, adult T-cell leukaemia, breast cancer, melanoma and ovarian cancer. Eastman Kodak is funding some of these clinical studies.

Oncogene Science, Inc., Mineola, N.Y., is taking a slightly different approach, using MAb payloads designed to detect and localise activated oncogenes. These sequences yield products, including cell-surface antigens, detectable by the imaging agents.

Xoma Corp., Berkeley, Calif., employs murine antibodies produced in ascites fluid, as well as developing chimeric mouse-human and human antibodies, and monoclonal cocktails, as varied strategies for increasing sensitivity and avoiding immune responses. Xomaseam-Mel, an ^{111}Indium-linked therapeutic, as well as imaging agent, for metastatic melanoma, is in Phase II trials, and has been granted Orphan Drug status. (Source: McGraw-Hill's Biotechnology Newswatch, 16 February 1987)

AIDS: neither prevention nor cure

A characteristic of AIDS is that years can elapse between exposure to the virus and onset of the disease. If the drug ribavirin lives up to its first results, it may prolong the delay and so buy time for those infected.

This hope comes from a trial conducted at four big American medical centres. In it, volunteers took the drug or a look-alike placebo without their doctors or themselves knowing who was getting which. To enter the trial, the volunteers had to have antibodies to the AIDS virus in their blood and to have had two of the early symptoms that their immune system was in trouble: swollen lymph nodes in at least two places in their bodies for six months or more, and a low level of T-cells, the white blood cells that the virus kills.

At the end of the 28-week study, 10 of the 56 volunteers on placebo had gone down with AIDS. So had six of the 55 who got 600 milligrams of ribavirin a day, but none of the 52 who had received 800 milligrams a day has so far got AIDS. The probability of getting such a result by chance was less than 1 per cent.

Ribavirin - also known as Virazole - is an anti-viral agent made by ICN Pharmaceuticals and a subsidiary, Viratek of Costa Mesa, California. It is licensed in Europe for the treatment of herpes and influenza A and B. In the USA, the Food and Drug Administration (FDA) has approved its use only in the form of an aerosol spray for babies with respiratory syncytial virus disease. According to Dr. Frank Young, the head of the regulatory agency, it is not possible to derive enough drug from the spray to achieve an 800 milligram-a-day oral dose.

Dr. Young is non-committal about the future of the drug in combating AIDS because the FDA received a summary of the trial only four days before its manufacturers held a press conference to announce its results. The agency has yet to receive all the data it needs properly to analyse the findings.

If further studies confirm the results, ribavirin may, indeed, be the first drug that heads off AIDS, just as azidothymidine (AZT) is the first to prolong the lives of some already stricken with the disease. (Extracted from The Economist, 17 January 1987)

The search for an AIDS therapy

The search for an effective AIDS treatment is considerably more pressing than for diagnostics. However, the process will almost certainly be slower and less dramatic, largely because of the difficulty of treating viral diseases.

There are now two separate categories of anti-AIDS drugs: antivirals, which seek to destroy the virus by interfering with its reproductive cycle, and immunostimulants. It is possible, though, that treatment will hinge on combinations of drugs rather than on any single agent, according to Anthony Fauci, director of the National Institute of Allergy and Infectious Diseases; one or more antivirals will probably be used to fight off the virus, while immunostimulants may be called upon to restore the ability of the immune system to ward off infection. Such an approach is commonly and often successfully used in cancer therapy.

However, antivirals are often limited by their inability to cross the blood-brain barrier. The

problem arises from the different chemical natures of the two systems; drugs that are soluble in blood are usually insoluble in spinal fluid, and vice-versa. Immunostimulants are compromised by the fact that they need a reasonably intact immune system to stimulate, a requirement that is usually lacking in advanced AIDS cases. Patients who can best utilize the therapy, in other words, are usually those who need it the least.

In the antiviral category, ICN/Viratek (Costa Mesa, Cal.) and Burroughs Wellcome (Research Triangle Park, N.C.) were the first to enter their products in multicentre clinical trials approved by the Food and Drug Administration - a distinction that usually (but not always) carries a clear marketing advantage. Among the companies pursuing immunostimulant research, leadership positions are occupied by Schering-Plough (Madison, N.J.) and Hoffmann-La Roche (Nutley, N.J.), both of which produce the recently approved alpha-interferon. Meanwhile, Immunex, Cetus and several other companies produce an immune-system stimulant called interleukin-2 (IL-2), which is also used in the experimental treatment of some forms of cancer.

The National Institutes of Health (NIH) in Bethesda, Md., has screened over 200 compounds (mostly commercial drugs) for in vitro activity against the AIDS virus, and last autumn - considering such criteria as past use, animal safety studies and experience outside the US - NIH selected five drugs for further study. It then launched a programme to conduct US clinical studies on ribaviria, alpha-interferon, azidothymidine (AZT), foscarnet and HPA-23.

Meanwhile, other compounds being developed and tested by NIH and other agencies will most certainly be added to the list. One example is difluorodeoxycytodine, a drug similar to AZT that was originally developed by the National Cancer Institute.

Burroughs Wellcome's AZT recently received limited approval for patients with PCP (a rare form of pneumonia); recent trials suggest that the drug significantly improves the survival of this group of AIDS patients (although it carries serious side effects, including anaemia and severe nausea).

Meanwhile, Burroughs Wellcome claims to have improved AZT's ability to penetrate the blood-brain barrier by teaming with Pharmatec (Alachua, Fla.), which has developed a process for enhancing blood-brain barrier permeability 10- to 20-fold in animals.

Predictably, a number of immunostimulant producers hope to find applications for their compounds in the treatment of AIDS. Examples include IL-2, as well as Ampligen - an antiviral immunostimulant, produced by Hemo Research, that appears to be active against AIDS - and Serono's thymostimulin; the latter is currently in clinical trials and is already available in Italy and the Federal Republic of Germany.

The urgency of the situation has not been lost on the Food and Drug Administration (FDA). While the agency is unlikely to soften its demand for hard data on potential new anti-AIDS drugs, officials have taken the unprecendented step of inviting representatives of every involved drug company to Washington to clearly specify the conditions and methods of the clinical trials, thus minimizing time lost due to misunderstanding of FDA requirements.

While researchers hold out little hope for an AIDS "cure" in the near future, several drugs seem to either fight the virus or partially relieve certain symptoms. Below, a brief look at eight of these drugs:

Drug	Action	Manufacturer	Status and outlook
Ribaviria	Antiviral	Viratek/ICN	In clinical trials. Canada has approved for some AIDS patients.
AZT	Antiviral	Burroughs Wellcome	Toxic at higher doses. Approved for limited use in the US.
Foscarnet	Antiviral	Astra (Sweden)	Little data available. US trials just beginning.
HPA-23	Antiviral	Rhône-Poulenc (France)	Little data available. US trials still being planned.
Alpha-interferon	Antiviral	Hoffmann-La Roche Schering-Plough	Is effective on some cancers. Now being tested on AIDS.
AL-721	Antiviral	Praxis	Works by weakening virus membrane. US trials just beginning.
Interleukin-2	Immune-system stimulator	Cetus, Amgen, Biogen, Immunex, Hoffmann-La Roche, Ajinomoto (Japan)	Boosts immune-system function. Could be used with antiviral.
Isoprinosine	Immune-system stimulator; weak antiviral	Newport Pharmaceuticals	Is approved outside US for other disorders. Clinical data in AIDS patients now being reviewed by FDA.

(Extracted from High Technology, January 1987)

AIDS drug trials start in Europe

Clinical trials have started in Europe on Wellcome's AIDS drug AZT with 300 sufferers. Recent clinical trials demonstrated that AIDS patients given the antiviral drug showed more resistance to the opportunistic infections which are fatal to sufferers than a control group given a placebo. Zidovidine, like other promising compounds, is thought to be able to knock out a key viral enzyme, reverse transcriptase. It is thought that the enzyme mistakes the drug for thymidine triphosphate, an essential nucleotide building block in DNA.

ICN Pharmaceuticals is also expected to apply for approval to use its drug Ribaviria for the

treatment of an early form of infection by the AIDS virus. ICN recently released the results from clinical trials indicating that the drug was effective in preventing the development of AIDS in some patients suffering from an early form of the disease involving inflammation of the lymph nodes.

Researchers at the Institut Pasteur have demonstrated that small concentrations of benzalkonium chloride - a widely used spermicide in France - neutralized the AIDS virus. Researchers from Zaire and France are currently conducting human tests with an AIDS vaccine in the African State. (Source: European Chemical News, 19 January 1987)

AIDS therapy gets FDA approval

Officials at the US Food and Drug Administration have followed the UK's lead and granted marketing approval to Wellcome's AIDS therapy Retrovir. The drug is now available for treating AIDS and related complications such as severe AIDS-related complex (Arc). Burroughs Wellcome, the US unit of the UK-based company, estimates that the initial market will be 30,000 patients.

Regulatory approval has been granted within 20 months of it first being tested on human patients. But with an estimated $80 million worth of research and development costs to recover, the drug, which is also quite expensive to make, will have a price tag of $10,000 for a year's treatment.

Switzerland's Hoffmann-La Roche which recently successfully bid for the licence to develop, test and possibly market dideoxycytidine (DDC), an analogue of Wellcome's drug, has been found to be as potent as Retrovir, if not more so, by scientists at the US National Institutes of Health. (Extracted from European Chemical News, 30 April 1987)

Two new AIDS virus detection kits

Two American companies have each developed diagnostic kits for detecting the AIDS virus itself rather than the antibodies raised by infected people. The kits, developed by Du Pont and by Abbott Diagnostics, detect the p24 protein located in the core of the virus.

In theory, the kits can reveal with absolute certainty when people are infected. This is not possible with the existing antibody-detecting kits, because there is a time lag before infected people begin to raise antibodies. This means that infected blood donors screened for the antibodies may slip through the net and supply blood infected with the virus.

The drawback with both of the new kits is that they are cumbersome and take several hours to yield results. (Extracted from New Scientist, 26 February 1987)

Variant AIDS kit to French market

Pasteur Diagnostique, Paris, a commercial arm of France's Pasteur Institute, won approval to market a novel AIDS detection kit, specific for the second viral variant of its Human Immune-Deficiency Virus (HIV-2). This form of the syndrome, recently identified among Africans, has not yet spread widely beyond that continent. Meanwhile, Pasteur has arranged for the first detection kit, directed at HIV-1 (formerly LAV), and trade-marked ELAVIA, to be distributed in Japan by the Tokyo Institute of Immunology, acting for the French subsidiary, Sanofi-Japon. Prospective users of the kit in Japan are blood-banks, potential customers for nine million kits, and pathology laboratories, for three million. The second AIDS diagnostic target differs from the original virus by only a single antigen, say Pasteur experts. ELAVIA-1 is now a compulsory test in France for all blood donations; no position has yet been taken as to requiring ELAVIA-2. (Source: McGraw-Hill's Biotechnology Newswatch, 2 March 1987)

Livestock applications

Animal vaccines

Applied biotechnology (ABI) of Cambridge, Ma, using recombinant DNA techniques, has produced two types of vaccines. One is based on live, genetically engineered viruses and subunit vaccines, in which non-infectious particles found on the surface of the virus often elicit an immune response against the live organism. The other is made using a proprietary technology called CRESP (Coding Region Expression Selection Plasmid), which identifies the viral genes responsible for the non-infectious particles and thus allows researchers to manufacture the particles themselves. ABI's major efforts in vaccine development thus far include vaccines against canine parvovirus and against pseudorabies virus of swine (a highly contagious and often fatal disease that also infects cattle and sheep). (Extrated from High Technology, February 1987)

Vaccine against equine colic

A vaccine against bacteria that cause colic in horses has been developed by researchers at the University of Missouri (Colombia). Colic and similar diseases are caused by endotoxins released when bacteria in the gut die. The bacteria normally aid in digestion, but when conditions are upset, the bacteria die and release the endotoxins. The vaccine will be licensed to Schering-Plough. Vaccination in horses should be at six and six and a half months, with yearly boosters thereafter. (Extracted from New York Times, 6 January 1987)

New African swine fever test

Restriction enzyme analysis has solved the previously intractable problem of how to differentiate between strains of highly contagious and invariably fatal African swine fever (ASF). Studies at the Institute for Animal Disease Research's Pirbright Station indicate that the technique will be useful in identifying the source of virus strains and thus preventing or stifling outbreaks at an early stage - the only possible control strategy in the absence of effective vaccines.

ASF is endemic to many parts of Africa south of the Sahara, where the virus is maintained through a transmission cycle between warthogs and soft ticks, from which it will probably never be eliminated. The virus also occurs in Portugal, the Iberian Peninsula, and Sardinia, where it poses a constant threat to Europe's pig industry. (Extracted from Bio/Technology, Vol. 5, February 1987)

Monoclonal dipstick for feline virus

Millions of cats are potential beneficiaries of a monoclonal dipstick test, just launched by Synbiotics Corp. of San Diego, Calif., to detect feline leukaemia virus. The firm's president, Edward T. Maggio, describes the product, Virastat/FeLV™, as "the first saliva test" for confirming the viral infection in cats.

FeLV is a retrovirus, as is the human AIDS virus. Like AIDS, it depresses the immune system, but the Synbiotics dipstick cannot readily be adapted to screen AIDS carriers.

Veterinarians will use the test as a pre-screening or differential diagnosis to determine

whether a pet is a carrier, and so spreading the disease. Only felines free of infection can benefit by vaccination against the virus. The test will be distributed by Norden Laboratories, a SmithKline-Beckman company based in Lincoln, Neb. Norden also markets the only available vaccine against the disease.

Of the $4.5 billion veterinary market in the USA, $995 million are spent on the country's 50 million household cats. Between three and five million of these pets are FeLV carriers, but the risk rises to 33 per cent in multi-cat households.

Norden will market the test nationwide to the 30,000 US veterinarians "at a price close to $5 or $6 per test". (Extracted from McGraw-Hill's Biotechnology Newswatch, 16 February 1987)

New growth-promoting agent being tested

A new breed of growth-promoting agents called beta-agonists is now undergoing trials in Ireland. The agents look to be more potent than the hormones they may replace.

One of the beta-agonists, Cimaterol, is being tested by Ireland's Agricultural Research Institute on behalf of Böhringer Ingelheim, the FRG company which developed it.

Early results indicate that lean meat is laid down at the expense of fat and that growth rates are accelerated.

The agonists work by binding to beta-adrenic cell membrane receptors blocking the deposition of fat. They also encourage cells to take up protein. In animals treated with Cimaterol, growth rates rose from 0.82 kilograms per day to 1.06 kilograms per day, an improvement of almost 30 per cent.

The improvement in meat quality was even more dramatic, say the researchers. Waste internal fat levels fell by 40 per cent while the percentage of lean meat in the carcas rose by 10 per cent to 70 per cent.

The researchers believe that by producing lean meat at the expense of fat, Britain's farmers could save the £100 million that they spend each year to dispose of 300,000 tons of waste fat, while with the improvement in livestock growth rates, farmers could produce 20 per cent more meat without spending any extra money, the researchers say. (Extracted from New Scientist, 8 January 1987)

Agricultural applications

Pilot plant to produce nematodes

Production of marketable quantities of nematodes as a competitive alternative to chemical pesticides is the objective of an agreement between the Alberta Research Council in Edmonton and Biosis, a biological pest control company headquartered in Palo Alto, Calif. Under the three-year contract, the Alberta Research Council's pilot plant will be used to scale up Biosis' technology for producing the microscopic, wormlike, insect-killing organisms. Biosis points out that although the nematodes occur naturally and already destroy many below-ground insects that cause crop and plant damage, they are not plentiful enough to constitute a method of insect control at a level required in many applications. The firm has identified specific insect-killing nematodes and has developed a liquid culture that acts as a breeding medium. (Source: Chemical & Engineering News, 26 January 1987, p.17)

Plant growth regulators slow to make impact

Plant growth regulators (PGRs) are likely to capture 6.5 per cent of the total agrochemicals market by 1990, according to Hans Geissbuehler of Ciba-Geigy. With a market value of $900 million, however, this still falls far short of the optimistic forecasts of the 1970s. Research and development costs - products cost about $50 million to develop - and the inherent complexity of modes of action have been the two major stumbling blocks to faster development.

Only the cereal and rice markets are likely to exceed $150 million, estimates Geissbuehler. Other major target crops include cotton ($100 million to 150 million), tobacco, vegetables and deciduous trees ($50 million to 100 million). Geissbuehler estimates that the turf market will not top $50 million which surprised some observers who believe that the market already exceeds this and will grow much further with shifting emphasis in land use from agricultural production to amenity use.

However, firms will have to drop their current "spray-and-pray" approach and adopt a more rational outlook to PGR research and development, Geissbuehler argues. Companies have tended to develop products that have been shown to exhibit regulatory effects on plants by accident. Many of the leading PGRs are triazoles which were probably first developed as fungicides. Triazoles not only inhibit fungal sterol biosynthesis but can affect the synthesis of giberellins, which are endogenous plant growth stimulators.

A major drawback, however, is the lack of knowledge concerning the mode of action. Moreover, by focusing on potential biochemical and molecular targets the search for PGRs will be more successful particularly in the field of growth stimulants. All products so far developed are growth retardants.

Biotechnology, however, may offer some important opportunities particularly where the target is the expression and regulation of specific genes. Already biotechnology firms have tabled some important breakthroughs. Using gene-splicing techniques researchers at UMAF have improved the quantity of solids in tomatoes. In maize, molecular genetics has improved the quantity of the amino acid tryptophan in kernels and developed plants resistant to imidazolinone herbicides.

Global market for plant protection products ($ billion)

	PGR	Total agrochemicals
1975	0.20	6.0
1980	0.35	10.0
1985	0.50	12.5
1990	0.90	14.0

(Source: European Chemical News, 19 January 1987)

Insect resistance to pesticides is growing problem

"Resistance management" is a concept relating to pesticide and antibiotic use that seems likely to gain more importance soon. Scientific efforts are increasingly being focused in this direction, as the development of insect and microbial resistance accelerates.

According to Brian A. Croft, Professor of Entomology at Oregon State University and

Robert L. Metcalf, Professor of Entomology and Biology at the University of Illinois and the discoverer of carbamate insecticides, problems with insect resistance to pesticides are rapidly getting worse. Resistance poses an increasing threat to agriculture, world food supplies and human health.

Because of shortsighted and irresponsible use of pesticides and antibiotics some strains of insects and microbes have appeared that are resistant to nearly everything in our chemical arsenal. Most alarming is the accelerating rate at which insects and microbes develop resistance to new chemical weaponry.

Croft and Metcalf were among a panel of scientists examining the status of pesticide and antibiotic resistance and efforts to deal with it in a symposium at the annual meeting of the American Association for the Advancement of Science, held during February in Chicago. Noting that the problem is widespread with antibiotics as well as with pesticides, Richard T. Roush, Assistant Professor of Entomology at Cornell University, argued that planning be started for a couple of decades from now.

Examples of resistance are widespread. More than 500 species of insects have formed some type of immunity to insecticides, Croft notes. An example cited by Metcalf is the extremely destructive Colorado potato beetle. Since 1950, he says, 15 insecticides have been introduced to control it. Thirty-seven years of chemical control, he points out, has now produced a super-beetle immune to everything thrown at it.

Croft notes that research on resistance to synthetic organic pesticides began soon after it was first discovered among pests of agriculture and public health in the late 1940s and 1950s. The emergence and spread of the concept of integrated pest management (IPM) by the 1970s represented an important major response to resistance problems. IPM emphasized a more thorough study of the ecology of pests, the greater use of beneficial biological control agents, a wider array of other non-chemical tactics of pest control and better pesticide management. Research followed on a greater diversity of factors influencing resistance - physiologic, genetic, ecological and operational.

Most recently, Croft notes, a study by the National Research Council summarized what he terms the "new renaissance in resistance research". Published last year as "Pesticide Resistance: Strategies and Tactics for Management", the study brought together scientists from a wide range of disciplines - from cellular biology to population genetics; from many organismal perspectives such as arthropods, nematodes, plant and medical pathogens, mammals, and others; and from diverse fields such as agriculture, medical entomology, and veterinary medicine.

Croft notes that though his own focus is on arthropod species, the principles may be applicable to many other pest groups. Pesticide resistance in arthropod pests, Croft explains, is a complex evolutionary phenomenon. It arises from selection of a population having traits that confer resistance to pesticides. And it can develop over relatively short time periods with devastating consequences to pest control.

Pesticide resistance management is the implementation of a strategy that includes a variety of tactics or measures to contain or suppress resistance. Among the more important basic science issues limiting greater development and implementation of resistance management is the study of the underlying mechanisms of resistance at the cellular or organismal biological level, including the genetics, biochemistry and toxicology of resistance. Such research underpins the understanding of resistance, including ways of overcoming it. For example, the genetic basis of resistance is a critical subcomponent of the population genetics of pesticide resistance.

In the area of applied science, Croft says, greater progress has been achieved in some respects than it has in basic resistance research. An example is detection and monitoring of resistance, where techniques such as classical bioassay, biochemical enzyme tests, immunological techniques and biotechnological probes using appropriate DNA or RNA segments are all being intensively researched.

A variety of old and new tactics for management of resistance to pesticides has been proposed in recent years. Integrating them into an overall strategy of resistance management requires an organized system of implementation. Such a system usually includes personnel at several levels of decision making and monitoring and management application. Programmes may vary greatly in their objectives and temporal and spatial scales of operation.

Beyond technical knowledge and implementation, resistance management requires a diverse range of policies governing pesticide development, registration, marketing, regulation, and education. Such policies often are more of a constraint to resistance management than are technical limitations. But if resistance management is to be practised more effectively in the future, policy improvements must be integrated with technical advances in new ways. (Abstracted with permission from Chemical & Engineering News, 2 March 1987. Copyright 1987 American Chemical Society)

Microbes to tackle plant disease by
Dr. Annabel Renwick, Margareta Lennartsson and Dr. Richard Campbell, Department of Botany, Bristol University

Biological control of disease in plants, setting one organism against another, continues to gain favour economically and environmentally. Pests have a remarkable ability to develop resistance to chemicals, so the cost of keeping one jump ahead of them rises inevitably, while many people are worried about chemicals in soil and food; today's intensive farming depends largely on them to control diseases formerly kept at bay by rotation of crops. One promising example of the new approach is the selection of organisms to deal with Take-all, a serious fungal disease in the chief cereal-growing regions of the world.

In its simplest sense biological control of diseases in crops means the reduction of a disease-causing organism, the pathogen, by another organism, the antagonist. At present, the emphasis in research is on trying to find and isolate antagonistic micro-organisms that can be used against specific diseases. Such work has been fostered by many biotechnology companies, who foresee the potential sales value of formulations containing micro-organisms. Interest has been encouraged, too, by research in genetic manipulation, which has accelerated greatly during the past 10 years and holds out possibilities of improving the performance of antagonists. So far there have been only a few commercial successes but, considering how little time and money has been spent so far on this research, it is hardly surprising that few micro-organisms are sold. Enormous resources have been invested in developing chemical pesticides over the past 40 years, but biological control is still in its very early days.

In a wider sense, biological control also includes manipulating the plants' soil environment by cultural practices. For example, Dr. Richard Smiley at Cornell University reported in 1977 that the disease known as Take-all was more severe when nitrogenous fertilizer was applied as nitrate instead of in the form of ammonium salts. Some of his investigations showed that the nitrogen source may have had an indirect effect by altering the proportion of micro-organisms antagonistic to Take-all: it seemed that with ammonium salts more antagonists were present, so Take-all was less, and that with the nitrate there were fewer antagonists and therefore more Take-all.

No other controls

Take-all is a serious fungal disease of wheat and barley throughout the chief cereal-growing regions of the world. Yet there are no effective chemical controls nor any disease-resistant varieties on the market; farmers can control the disease only through careful cultural practices. One possibility is to use micro-organisms naturally present in the environment to compete with and reduce the effect of the pathogenic fungus. So Take-all is an excellent candidate for the study of biological control; the challenge is to find micro-organisms that can be applied to the crop to control the disease. This is the aim of our work.

When the Take-all fungus invades the roots of wheat and barley, it causes black lesions and, in more severe cases, blackens the base of the stem. The infection interferes with the uptake of nutrients and water by the plant, and early infection can lead to poor establishment of the crop; later infections may harm the formation of the grain, resulting in prematurely ripened ears called "whiteheads". The fungus survives between susceptible host crops by "overwintering" on infected plant debris in the soil.

Loss of flexibility

When cereals are grown year after year the disease may become less severe after four to five years. Earliest reports of this phenomenon came in 1935 from the Rothamsted Experimental Station, just north of London. This type of reduction in Take-all has now been observed throughout Europe, Australia and the USA, and the term that has been coined for it is Take-all decline. Nevertheless, a farmer loses flexibility if he uses a cropping system which allows him to grow only certain cereals. If, for economic reasons, he wishes to grow a non-cereal crop for one year, he breaks his "decline" and Take-all will once again be a problem when he returns to growing wheat or barley. The opposite approach is to adopt a traditional and diverse cropping system, with a wide variety of crops grown in rotation so that wheat or barley is grown on the same ground only at long intervals. That allows enough time for the fungus to be eliminated from the soil, simply by starvation.

The research team here at Bristol, led by Dr. Richard Campbell, is searching for soil micro-organisms that are natural enemies of the fungus. The aim is to select antagonists that can be formulated as biological control products, so-called microbial inoculants. Early research has shown that when samples of certain soils are heated, the specific reduction of Take-all is lost. Moreover, the cause of reduction can be transferred from one soil to another. This is good evidence to show that at least one of the mechanisms of suppression in a Take-all decline soil is of a microbial nature. Such soils were therefore obvious targets in collecting microbial antagonists. Already we have looked at 1,800 micro-organisms to assess their ability to control Take-all. Those showing good control in early tests have been further investigated in different soils and under field conditions in collaboration with staff from Imperial Chemical Industries (ICI) based at Bracknell, near London, headed by Dr. Keith Powell.

One big problem with micro-organisms used to control soil-borne diseases is that they are not very reliable: a 30 to 40 per cent failure rate is not acceptable when selling a product, even if the other 60 per cent of the time results are good. It should be remembered that microbial inoculants are not inorganic chemicals: they consist of living organisms which respond to environmental factors such as soil temperature, pH, water aeration and, of course, the quality and quantity of nutrients available in the soil or on the root. This means that the response of a pathogen to a microbial inoculant in one soil may be quite different from that in another. All these factors must be considered when developing a microbial inoculant. We expect a great deal from our micro-organisms when we apply them to a crop without understanding the mechanisms by which they control Take-all in the field. So it is important early on to try to understand as much as possible about the selected organisms, their mechanisms of disease control and the environmental conditions under which they show greatest activity. This is an important part of our work.

Colonizing the roots

In our opinion, one of the most important characteristics that we test for is the micro-organism's ability to colonize the roots so that it will be present and active at the site of infection. Micro-organisms reintroduced into the soil as inoculants must be able to compete against the pathogen and indigenous microflora for available nutrients and for space on the root surface. Several of our selected bacteria have been tested for their colonizing ability under field conditions. They can be recovered from the soil by giving them resistance to antibiotics and then growing them in the laboratory, using the antibiotics: only resistant organisms grow, while the natural ones in the soil do not, so we have a means of identifying organisms against indigenous soil populations.

We have found that certain of our selected strains of bacteria colonize the roots early and their numbers are high very soon after sowing and inoculating the wheat. They also persist for a considerable time on the roots of the crop. Many researchers, including Dr. D.W. Deacon from Edinburgh University, Dr. Lemaire and colleagues from France and Dr. P.T. Wong in Australia, have successfully used fungi closely related to the Take-all pathogen as inoculants. These antagonists actively compete for the same sites on the root surface and in doing so exclude the pathogen.

In the competition for nutrients, one good example is the ability of certain micro-organisms to produce extra-cellular chemicals called siderophores, which bind or associate specifically with iron. When the amount of iron available in the environment is limited, these microbes have a competitive advantage over other micro flora, including the pathogen, so they effectively starve the pathogen of this essential element. Not many of our selected organisms do produce detectable quantities of siderophores in culture and we do not consider it to be an important mechanism operating against Take-all. A research team in the Netherlands led by Dr. B. Schippers has reported successful biological control of a disease in potato crops, under field conditions, using bacteria specifically selected for production of siderophores.

Antibiotic substances

Another way in which our micro-organisms may work is by producing antibiotics that kill or inhibit the growth of the pathogen. We can observe this effect in culture, but it is very difficult to quantify in the field. About one quarter of our selected micro-organisms that show good control of Take-all also inhibit the growth of the pathogen in culture; some of them produce volatile antibiotic substances. We are now investigating the part that these antagonists play under conditions more representative of those in the field. Dr. R.J. Cook and colleagues at the United States Department of Agriculture at Washington State University have selected antagonistic bacteria that control Take-all in the field and have found that the same bacteria produce a potent antibiotic in culture. The inference is that the bacteria control Take-all through this antibiotic.

Micro-organisms are also able to prey on the Take-all fungus. Dr. Alan Feest in our Department of Botany has investigated the populations of protozoa from samples of wheat field soils in the south of England. Those with less serious Take-all had more amoebae than those with serious Take-all. Work in the USA has shown that such amoebae perforate and destroy filaments of the Take-all fungus; small holes can be observed in the walls of the fungi with the electron microscope. The technology for producing inoculants made from amoebae is not very advanced and such micro-organisms do not yet offer a practical solution to the problem of controlling Take-all.

We have found that certain of our micro-organisms are able to break down the cell walls of the Take-all fungus. This can be brought about by toxins or enzymes. About 60 per cent of our selected microbes have produced detectable quantities of such substances in culture. It may be an important and interesting mechanism in the laboratory, but our main aim is to find out what microbial activity there is under natural conditions in the field for that knowledge should help us design a microbial inoculant which can be applied in such a way that it works most effectively on crops.

Cultural practices

Another line of research here is the study of how different cultural practices affect the incidence of Take-all. First, we are investigating what effects incorporating organic matter into the soil have on the severity of disease. In greenhouse trials we have found that incorporating lucerne and trefoil as fresh plant material, a practice known as green manuring, reduces the infection. What the mechanisms are behind these reductions we do not yet know, but we do know that during the initial stages of the decomposition of the incorporated material the soil microflora is changed; some groups of micro-organisms increase in numbers. It may be that such a change of the microflora creates a condition unfavourable to the pathogen; the activity of natural antagonists may also have been encouraged. Second, we have looked at the effects on Take-all of growing wheat with a companion crop, so-called mixed species cropping. Here, too, there was a reduction in disease levels when wheat was grown with a legume under greenhouse conditions.

Our research on cultural practices is still in its infancy and a lot more work needs to be done to evaluate how relevant our observations are under field conditions. Mixed species cropping and green-manuring are often adopted by farmers wishing to reduce the use of chemical fertilizers and pesticides. We hope that this kind of research will be beneficial to them when planning cropping systems in the future. (This article has been reprinted from Spectrum, No. 205, 1987/2)

Deliberate release proposal

Biotechnica International (Cambridge, MA) has notified the US Environmental Protection Agency and the Department of Agriculture about its plan to field-test genetically engineered strains of Rhizobium meliloti to increase alfalfa yields in Arkansas, Wisconsin. The company reports that conventional strains of this bacterium are now used as a source of nitrogen fertilizer for about 60 per cent of the US alfalfa production acreage. In the greenhouse, strains engineered to supply additional quantities of nitrogen have been 15 per cent more effective than non-modified bacteria. (Source: Bio/Technology, Vol. 5, March 1987)

New grass breeding technique

A new technique has been developed for the accelerated cultivation of complete generations of perennial ryegrass, Italian ryegrass, Fescue grass, Orchard grass and a hybrid material for the cross-breeding of Lolium multiflorum Lam and Festuca arundinacea. A complete generation from the sowing to the harvesting of seeds is possible in six to eight months, depending upon the type of grass. Further information available from The Academy of Agricultural Sciences of the GDR, Institute for Feed Production, Paulinenaue, DDR-1551, German Democratic Republic.

Food production and processing

Milk concentration by osmosis

Mr. Steward Marshall of CSIRO's Division of Food Research in Melbourne has developed a superior method of concentrating milk while maintaining palatability. The process, known as reverse osmosis, uses technology from the water desalination industry. The main advantage of this process is reduction of energy and transport cost and ease of cheese production. Further information available from CSIRO, 314 Albert Street, East Melbourne, Australia. (Source: Biotechnica '87, Hannover, Journal No. 2)

Customizing lipases for industrial processing

Biotechnologists have not been slow to notice the trend away from chemical additives in food. The lipases developed by Biocatalysts, a subsidiary of Grand Metropolitan Innovation Ltd., are a case in point. Short to medium length fatty acids are potent flavour compounds, found naturally in many foods. They can be produced synthetically by the acid hydrolysis of fat. Alternatively, the use of natural enzymes (such as lipases) to catalyze the hydrolysis can result in fewer side reactions - which might otherwise damage essential fatty acids.

In the food industry, lipases are now used in a variety of processes, including flavour production and fat hydrolysis. Trade-named LIPOMOD, the customized lipase blends developed by Biocatalysts can be used for the modification and processing of a full spectrum of animal fats, including short and long chain fatty acids. The enzymes used come from both animal and microbial sources, and the blends are formulated on the basis of the target substrate, required characteristics and processing methods. For the speciality chemicals industry, natural enzymes have some significant advantages over chemical catalysts. These include high potency and specificity, which cuts side reactions and can result in higher yields. (Extracted from Biotechnology Bulletin, Vol. 6, No. 1, February 1987)

Salmonella detection

A new immunoassay method for the rapid detection of Salmonella in food samples is based on the immobilisation of Salmonella on a solid substrate -

titanous hydroxide. Features: the method detects Salmonella in a food product within a period of 24 to 36 hours, compared to 4-5 days required for conventional methods. Further information available from Barry Rosenberg, Unisearch Ltd., University of New South Wales, 221-227 Anzac Parade, P.O. Box 1, Kensington, NSW, Australia 2033.

Improved cheese ripening process developed

A new method for reducing the length of time to ripen cheese has been developed. Using microencapsulated enzymes in cheese curd ensures an even distribution of enzymes in the milk and curd and cuts enzyme losses to some 10 per cent against 95 per cent by adding solid enzyme to the curd after the whey has been run off. The Institute of Food Research has developed this method and hopes to apply it to controlling the addition of flavour compounds and additives during processing. (Extracted from Chemistry and Industry, 15 December 1986)

Energy and environmental applications

Natural cleaners

Brulin (Indianapolis) has unveiled a line of industrial cleaning agents that are said to be 100 per cent biodegradable and to contain no ingredients that the US Environmental Protection Agency defines as hazardous. The six WorkSafe heavy-duty cleaners are free of chlorinated hydrocarbons, petroleum distillates, butyl ethers and phosphates. Still, Brulin say its products, based on naturally occurring citrus oils, are as effective as "the harshest cleaning solvent". In addition the company says WorkSafe products reduce hazardous waste disposal costs and avoid exposing employees to toxic cleaning agents. (Source: Chemical Week, 11 March 1987)

Bacteria engineered to degrade organic pollutant

Researchers at Geneva University's Medical Centre have genetically engineered a bacterial catabolic pathway to enable a bacterium to degrade a formerly non-biodegradable synthetic compound.

The TOL pathway of Pseudomonas degrades natural alkylbenzoates, but not 4-ethylbenzoate, a related compound. The researchers found that the compound did not induce crucial enzymes and that one important enzyme, which cleaves the aromatic ring, was inactivated by one of the metabolic products. By extracting genes from mutant bacteria and inserting them into normal bacteria, they managed to produce a strain which can degrade 4-ethylbenzoate - with degradation of natural alkylbenzoates proceeding unimpaired. (Source: Biotechnology Bulletin, Vol. 6, No. 1, February 1987)

Waste water treatment

The TAHAN process of anaerobic waste water treatment in use at Tampella's paper mill in Aanjala, Finland, has been expanded after 12 months of successful tests to treat all waste water from the mill's pulp and paper manufacture which means 11,000 m^3/day. Trials have shown that it can achieve over 95 per cent reduction in biological oxygen consumption (BOD). Further information available from Tampella Ltd., P.O. Box 250, SF-33101 Tampere 10. (Source: Biotechnics '87, Hannover, Journal No. 2)

A better fungus to remove heavy metals

A Tel Aviv University botanist has developed a method of using fungi to remove heavy metals from industrial waste water. Professor Margalit Galun says that many other micro-organisms are able to absorb metals from aqueous solutions, but the fungus used is much more efficient because it has higher absorptive capacity and is more economical. Galun says that the mass of fungus can be stored between production and use and that its absorptive capacity does not deteriorate in cool storage. The process has been shown to work on a laboratory scale. Ramot, the Tel Aviv University authority for development, is looking for funds to scale up the project. (Source: Chemical Week, 25 February 1987)

Microbes melt Japan's snow

The Japanese are experimenting with a novel way of getting rid of snow - melting it with microbes. Toyama, a city in northwestern Japan, has installed a network of pipes underneath a 120-metre stretch of pavement in front of its municipal baseball ground. Water is heated to 90°C by micro-organisms before circulating through the pipes, keeping the pavement's surface above freezing point.

The microbes are produced by fermenting a mixture of rice bran, chaff and sawdust in a tank. One batch of the mixture continues to produce heat for about two weeks.

The system, known as Bioheat, was developed by a local private research organization, the Taisei Institute of Physical and Chemical Research. Its initial purpose was to grow asparagus. Subsequently, the institute installed it under a car park, which it managed to keep clear during an overnight snowfall more than two metres deep.

Such snowfalls are common in Toyama. The city is on the coast of the Japan Sea, which in winter is exposed to cold north-westerly winds sweeping in from Siberia. A ridge of mountains behind the coast blocks the winds, resulting in the heaviest snowfalls in Japan.

Toyama says Bioheat is cheaper than other methods of getting rid of snow. The system also works for 24 hours a day.

At £190 per square metre, the system is quite expensive to install. But once in place, Bioheat's running costs are very low.

If this winter's experiment proves successful, the city plans to install the system under some of its other pavements, too. (Source: New Scientist, 22 January 1987)

Microbial waste rubber digester

A microbe that digests natural rubber wastes has been discovered by the Agency of Industrial Science & Technology's Fermentation Research Institution. The Nocardia organism, a member of the Actinomycetes family, was isolated from soil samples three years ago. During experiments it was placed in a liquid culture containing only inorganic nutrients. Strips of rubber cut from gloves and other products were added 0.1 g at a time. Soft rubber was degraded completely in three weeks, but only 3-6 per cent of hard rubber products like bicycle tyres decomposed after eight weeks due to the presence of carbon, sulphur and other additives. (Extracted from Japan Economic Journal, 20 December 1986)

Industrial microbiology

New industrial enzymes

Koki Horikoshi, leader of the Japanese Government's Superbugs Project is convinced that within the next five or six years "hot bugs" will become a source of industrial enzymes. "Thermophilic bacteria can produce many interesting enzymes," he

says, "because they have different metabolisms. So, if we can get some information about them, I'm sure we can apply it to other micro-organisms."

Horikoshi cites an example of an enzyme obtained from a thermophilic bacterium that has potential industrial applications. The enzyme - a recent find - can break down lactose in high concentrations to produce glucose and galactose. This, he claims, is unusual because similar reactions using ordinary enzymes produce other, unwanted, disaccharides and trisaccharides.

The Superbugs Project, now half way through its five-year programme, is intended to provide more information about micro-organisms that live in extreme environments, to find out their capabilities and whether or not these capablities can be put to work. In addition to thermophilic bacteria, the project is interested in micro-organisms from other types of extreme environments such as soda lakes and salt flats; and in microbes that can tolerate toxic chemicals such as industrial solvents. Funding for the project, from the Research Development Corporation of Japan, is around £1.2 million a year.

When they come across an interesting bacterium, Horikoshi's scientists attempt to determine how it tolerates such extreme surroundings and how its metabolism works. An understanding of these mechanisms, Horikoshi hopes, will serve as the basis of a "new biotechnology". This will build on the fact that "superbugs" carry different genes from their less tolerant counterparts. These genes might, perhaps, be engineered to produce cheap catalysts. One of Horikoshi's main aims is to substitute such biological catalysts for the expensive, and often toxic, chemical ones used in the petrochemicals industry. "As far as organic chemistry is concerned," he says, "I think bugs can do anything."

Horikoshi has reason to be confident. He has seen an entire industry grow from his work on alkaliphilic micro-organisms, those that thrive in highly alkaline conditions. In the early 1970s, he and his colleagues at the Institute for Physical and Chemical Research in Tokyo were screening soils for a micro-organism that could produce alkaline amylase, for use in washing-up liquid. During this research, they stumbled across an enzyme that produced cyclodextrin from starch. This proved serendipitous for, at that time, Japanese noodle companies were hunting for a preservative to replace hydrogen peroxide, which the Japanese Government had banned. The best substitute they could come up with was alcohol, but unfortunately alcohol was too volatile.

Cyclodextrin offered a way round this problem because as an "inclusional compound", it could trap ethanol in the molecule so preventing it from evaporating. The trouble was that cyclodextrin made by conventional methods required carcinogenic precipitating reagents to give a big enough yield. Horikoshi's enzyme could produce cyclodextrin without those reagents and with twice the yield.

Companies immediately began to manufacture cyclodextrin with the new enzyme. The market for cyclodextrin, according to Horikoshi, has doubled in size each year and the growth shows no sign of slowing down, as the product is applied in new areas. The Dutch Government has recently permitted its use as a food additive and the manufacturers of perfumes and agro-chemicals have also begun to work with it.

The Superbugs Project is gathering micro-organisms from extreme environments all over the world. Scientists with collections of such micro-organisms have been invited to Japan. The first to come was Bill Grant, of Leicester University. In 1978, Grant systematically sampled micro-organisms from the soda lakes of the East African Rift Valley. In addition, Grant taught the Japanese researchers techniques that he had developed for dealing with halophilic (salt-tolerant) bacteria in particular, how to distinguish between archaebacteria and eubacteria. These techniques immediately came in useful when the project's scientists isolated a triangular archaebacterium from soil at a salt farm in western Japan. The second foreign scientist brought in was Keith Joblin, a New Zealander who is an expert on anaerobic fungi. (Extracted from New Scientist, 19 February 1987)

Fructose from cellulose

Dr. Hans Bisswanger of the Physiological-Chemical Institute of University Tübingen has developed an enzyme reactor which is capable of converting cellulose from residues into fructose by a continuous process. The reactor operates at about 50 centigrades and uses three enzymes for its multi-step synthesis. The final product needs no cleaning. Further information available from the University of Tübingen, Hoppe-Seyler-Str. 1, D-7400 Tübingen, Federal Republic of Germany. (Source: Biotechnica '87, Hannover, Journal No. 4)

Industrial equipment

Swedish company to develop new biosensors

The Swedish company Pharmacia is raising $33 million to finance the development of a new class of biosensors. Researchers at the firm are currently developing sensors that will detect proteins almost instantly. Unlike conventional biosensors these will not have enzymes immobilized on electrode supports and will not require replenishment by reagents.

Currently the project has yielded a number of prototypes. Details of the technology will be revealed once patents have been awarded.

Once developed, Pharmacia plans to focus initially on the medical and analytical sectors to measure proteins associated with allergies and auto-immune disorders. In addition to the healthcare applications, Pharmacia plans at a later date to develop sensors for quality control in the food and process industries. A true commercial impact is expected by 1990. (Extracted from European Chemical News, 17 January 1987)

New literature announcement: improved tissue culture results with ECM

A new eight-page brochure is now available from IBT International Bio-Technologies Ltd., describing the advantages of extracellular matrix (ECM) - coated tissue culture plasticware produced by the company. An improvement over regular tissue culture plastics and isolated matrix components, ECM provides an optimal surface for culturing primary epithelial cells, particularly when combined with serum-free media. Some of the advantages yielded by ECM are expression of differentiated properties; higher plating and cloning efficiency; better plating consistency; lower requirement for serum and added growth factors; improved attachment; flattening and rapid migration of cells; faster proliferation and higher saturation density; and longer life span. The brochure also lists the wide scope of applications for ECM, which is available on a range of tissue culture dishes, flasks, multiwells, membranes and microcarriers, and as a coating service or on a contractual research basis. Readers are provided with a list of the company's specific brochures which are also available on request.

Further information available from IBT, P.O. Box 131490, Jerusalem 93469, Israel. Tel.: (02) 722-959. Telex: 26664 ibt il. (Source: Company News Release, March 1987)

Fermentation plant

The Provesta Corp., subsidiary of Phillips Petroleum (Bartlesville, OK) plans to build a fermentation products plant, featuring a 25,000-litre fermenter. The plant, which will have the capacity to produce several million pounds of yeasts per year, will use the firm's high cell density fermentation technology to make Provesteen® yeast products. These include food flavouring, livestock and aquaculture feed, and "Meals-on-the-go" nutritious food bars. (Source: Bio/Technology, Vol. 5, March 1987)

E. PATENTS AND INTELLECTUAL PROPERTY ISSUES

FRG studies reform of biotechnology patent law

European patent law has thus far been unable to keep pace with the rapid development in biotechnology and its research results which are becoming ripe for application. On national and international levels attempts are now being made to adapt the patent law to this development through appropriate reforms. The Max Planck Institute of Munich is making a considerable contribution to efforts concerning foreign and international patent rights, copyrights and competition rights and patent law researchers in Munich have outlined reform proposals in several studies.

Altogether these reform proposals are aimed at extending and easing patent protection which so far has been restrictively applied to genetic engineering. In the future it will be possible to obtain patent protection in all countries for micro-organisms and similar results of microbiological research (cell lineage, plasmids, monoclonal antibodies) as well as for macrobiological discoveries (new species of plants and animals) if these meet the usual requirements (originality, inventive merit, commercial applicability and sufficient information). The depositions on micro-organisms recognized so far for patent protection in this field should be sufficient to complement production patents. Patent protection should also include the animal breeding field, which has been completely ignored up to now. As far as plant breeding is concerned, it should be possible in the future after the abrogation of the ban on double protection to choose between variety protection or patent protection or to claim both. Finally, the Max Planck Institute of Munich is proposing a novelty grace period of one year which would make it possible for the researcher to give written or verbal reports within this period on the results of his research without excluding future patent protection.

Prof. Friedrich-Karl Beier, director of the Max Planck Institute for Foreign and International Patent Rights, Copyrights and Competition Rights, and Dr. Joseph Strauss, scientific spokesman for the Institute, are supported in their reform proposals by their legal comparison of patent protection for biological discoveries in different countries, primarily in the United States and Japan. (Source: Technologie Nachrichten - Management Informationen, No. 437, 10 August 1986)

Final settlement of patent rights for AIDS diagnostic test

The details of a final settlement to the US-French dispute over the patent rights to a diagnostic test for AIDS (acquired immune deficiency syndrome) have been drafted by the two interested parties and could spawn an international research foundation devoted to the disease.

The final version of the agreement is now expected to be signed during the visit by the Prime Minister of France, Mr. Jacques Chirac, to the United States on 29 March.

Dr. Robert Gallo from the US National Cancer Institute and Professor Luc Montagnier of the Pasteur Institute in Paris have both applied for patents in the United States for the use of antibodies as a basis for testing for infection by human immunodeficiency virus (HIV). This is essentially the test now widely used for assessing the infectious state of people and for deciding whether blood given for transfusion is contaminated.

Under the draft agreement, royalties from the use of HIV antibody tests for AIDS infection will be divided three ways, with one third of the income going to each of the US Public Health Service (which, through the National Institutes of Health, is ultimately responsible for the National Cancer Institute) and the Pasteur Institute. The remaining third of the income will be directed towards a new international foundation, yet to be established, for the support of AIDS research and treatment, especially in Africa.

The main substance of the draft agreement will deal with the apportionment of patent royalties from the application of the antibody tests as they are used at present. The financial importance of the arrangement, and thus the potential of the proposed foundation to make a substantial impact on the problem of AIDS in Africa or elsewhere, will depend on the patents generating income for some substantial time.

At the request of the US parties to the draft agreement, a precondition for the settlement of the dispute has been that there should be an historical statement of the contributions of US and French groups to the discovery and characterization of the AIDS virus. This historical summary takes the form of a chronology going back to the characterization of the virus known as HTLV-I, which is responsible for the adult T-cell leukaemia endemic in southern Japan. (Extracted from Nature, Vol. 326, 26 March 1987)

Hybritech now sues Abbott Laboratories

After Hybritech emerged from a successful battle against Monoclonal Antibodies to defend its patent on sandwich assay diagnostic kits, the San Diego-based company was back in court - this time tackling Abbott Laboratories, who the company claims has infringed its patent with their sandwich assay tests for hepatitis-B, pregnancy, thyroid disorders and several types of cancer. These tests are thought to account for some $50 million of Abbott's annual $750 million revenues from its diagnostics business. (Extracted from Biotechnology Bulletin, Vol. 5, No. 12, January 1987)

Applied Biosystems, University Patents and Biosearch settle differences

Applied Biosystems Inc. and University Patents Inc. (UPI) announce the settlement of patent infringement litigation against Biosearch Inc., a subsidiary of New Brunswick Scientific Co. Inc. and American Biomedics (AMB) Inc. both defendants admitted that their [illegible] products, including cyanoethyl phosphoramidite reagents, infringe the University of Colorado tests exclusively licensed to Applied Biosystems. The patents cover the DNA

synthesis chemistry invented at the University of Colorado and the automated instruments (DNA synthesizers) that use it. (Biotechnology Bulletin, Vol. 5, No. 1, February 1987)

European Patent Office to revoke Biogen's Interferon patent

In December 1986 four patent examiners of the European Patent Office issued an oral decision that the Opposition Division intends to revoke Biogen's European patent relating to the production of recombinant alpha interferons. The examiners held that the Biogen patent described a patentable invention, but objected to the scope of certain claims of the patent. Because EPO rules require either total acceptance of all claims or revocation of the patent, the Opposition Division indicated that it intended to revoke the patent. The patent had been challenged by ten other companies, including F. Hoffman-La Roche & Co.

The company intends to appeal the decision to the EPO Technical Board of Appeals. The oral decision does not affect Biogen's patent protection in the United States and the European patent is not necessary for Biogen's licensee, Schering-Plough Corp., to be able to sell 'Intron A' interferon. Last year Biogen filed a complaint against Boehringer Ingelheim Zentrale, claiming an infringement of this patent. (Source Biotechnology Bulletin, Vol. 5, No. 12, January 1987)

Collaborative Research receives cloned-rennin patent

Five years after filing, the US Patent Office has granted Collaborative Research, Inc. (Bedford, Mass.) the first patent for recombinant rennin, a milk-clotting enzyme usually found in the fourth stomach of calves and used in cheese making. There are at least a half-dozen competitors who are either producing or developing rennin, CEO, who must license the technology from Dow Chemical Co., Midland, Mich., which owns world-wide marketing rights to the Collaborative Research protein. Collaborative Research has already been granted rennin patents in the UK, Spain, New Zealand and Brazil.

Rennin, also called chymosin, is chronically in short supply, as veal production lags behind cheese production. World market predictions range from $50 million to $100 million. Collaborative Research's patented process uses yeast cells as hosts which secrete rennin in a fully active, non-glycosylated form. When the protein is produced recombinantly and intracellularly by bacteria, it is non-oxidized, insoluble, and the yields are low.

Neither Dow nor CRI will scale up rennin commercially. Rather, Dow will most likely license the technology exclusively to a large US manufacturer. A spokesperson from Genencor, Inc., (S. San Francisco, Calif.), claims that the patent does not affect them, as they use filamentous fungi, not yeast, as recombinant hosts for rennin production. (Source: McGraw-Hill's Biotechnology Newswatch, 5 January 1987)

Inventor of all-year edible oyster seeks reversal of Patent Office turn-down

Is a man-made oyster patentable? US patent examiners have said no. If an appeal lodged last month before the Patent Office in Washington, D.C. reverses their rejection, this "could have a salutary effect on the economy of the Pacific Northwest," according to attorney Jeffrey J. Miller of Seed & Berry, a law firm in Seattle. He represents the University of Washington, where a graduate student in the Department of Fisheries, Standish Allen, has produced a variant polyploid Pacific oyster, Crassostrea gigas, which is edible the year-round, as compared to only nine months for the natural form.

His invention produces the polyploid bivalves by controlled hydrostatic pressure applied to fertilized oyster eggs.

While allowing claims to the process, the Patent Office takes the policy position, "that life forms such as humans and other mammals, fish and insects are not patentable subject matter, because the Supreme Court did not specifically address such life forms in its 1980 decision in Diamond vs. Chakrabarty." Moreover, Miller continues, "the Patent Office relies upon a statement by the Court of Customs and Patent Appeals, to the effect that biologically pure cultures and micro-organisms currently given patent protection, are much more akin to inanimate chemical compositions such as reagents and catalysts, than they are to horses and honeybees."

However, the University of Washington cites the Supreme Court decision in Chakrabarty that "Congress intended statutory subject matter to include anything under the sun that is made by man." Moreover, the University emphasizes that a denial of patent protection to its year-round oysters "would simply result in a disincentive for commercial industries to put resources into research and development of products that have a tremendous potential for human benefit," in this case, the oyster industry of the region.

A Seattle seafood company is negotiating to license the invention, Miller notes. He expects the Board of Patent Appeals to soon decide and if it upholds the rejection, the University will carry the case to the Federal District Court of Appeals in Washington, D.C., which decides patent cases. (Source: McGraw-Hill's Biotechnology Newswatch, 16 March 1987)

F. BIO-INFORMATICS

New journal on molecular simulation debuts

A new journal that focuses on applications and techniques of molecular-scale simulation is scheduled to begin publication early this year. Called Molecular Simulation, the journal will publish original research papers as well as regular review articles. Among the topics expected to be covered are applications of simulation to liquid and solid-state chemistry, materials science, interfacial phenomena, macromolecular and biological systems, and intermolecular potential energy functions. Advances in methodology, such as new quantum simulation methods, as well as improvements in computer hardware, graphics processing and languages will also be topics of contributions. The journal will be published by the British science publishers Gordon & Breach. Its editor is Nick Quirke of SP Research Centre, Sunbury-on-Thames, UK. Potential US contributors can get further information from US regional editor James M. Haile, Department of Chemical Engineering, Clemson University, Clemson, S.C. 29631. (Reprinted with permission from Chemical & Engineering News, 19 January 1987, p. 30. Copyright (1987) American Chemical Society.)

European biotechnology equipment market to reach $2.5 billion by 1995

Genetic engineering will not come of age until the late 1990s in Europe, according to a new market study by analysts Frost & Sullivan, but the intervening years will see $2.5 billion in demand for

the equipment needed to keep the microbes breeding. Biotechnology Process Plant Market in Europe (No. E921) suggests that "public acceptability (i.e. regulatory authorities) will delay rapid rise in new products until the later 1990s".

The Federal Republic of Germany, however, is already spending almost $40 million a year (DM 116 million), the UK $31 million (£24 million) and France $29 million (FF 260 million) on bioreactors, fermenters and downstream processing equipment such as mills for rupturing cell walls, membranes for separating process elements and ancillary products such as pumps and heat exchangers. In relation to the total European market, comprising 18 countries, the FRG represents more than a fifth of demand, the UK about 16 per cent and France 14 per cent.

Using constant 1985 dollars, Frost & Sullivan predict that the total annual market for biotechnology equipment in Europe will double between 1986 and 1995: from $180 million in 1986, it will reach $228 million by 1990, representing a 5.8 per cent annual growth over the intervening period. It is predicted to reach $348 million by 1995, showing 8.9 per cent yearly gains after 1990. Spain is picked as the fastest growing national market, though of the largest three countries, the FRG will exceed the market average in yearly volume growth, the UK will parallel it closely, and France will rise more slowly than Europe as a whole.

The study also examines the market by end user industries. Chemical firms are purchasing more than 60 per cent of all products sold - and the finer breakdown shows more than a fifth of this being used to make organic acids, another fifth going to antibiotics production, with enzymes being the next largest use. The food and beverage industry follows chemicals, accounting for nearly a third of the market value, with sweeteners growing rapidly.

By equipment type, the largest component (fermenters and bioreactors) is also one of the fastest growing. This market is a combination of laboratory, pilot plant and production fermenters - with about 20, 40 and 30 per cent shares respectively. A fifth of all equipment dollars go to liquid/solid separation goods, nearly two thirds in filters. Alfa-Laval/Chemap is quoted as perhaps the most important firm covering the whole range of equipment, with AVP Osborne Craig, DeDanske Sukerfabrikker, and New Brunswick also strong contenders. Details of the report, priced at $2,500, from: Frost & Sullivan Ltd., Sullivan House, 4 Grosvenor Gardens, London, SW1W 0DH or on 01-730 3438. (Source: Biotechnology Bulletin, Vol. 5, No. 12, January 1987)

Biotechnology directory with weekly updates

Bio1000 lists over 1,000 biotechnology companies worldwide with contacts, addresses, telephone numbers, and telexes. This directory comes with 24 weekly issues of BioEngineering News, which keeps the directory up to date, as well as with World Bio-Licensing Report, a monthly listing of technology sought or available. Potential end-users of this $247.50 directory package include chemical, food, petro-chemical, medical, agricultural and similar producers and marketers. Further information available from Tony Mysiewicz, Vice Pres., Deborah J. Mysiewicz Publishers, Inc., Dept. CN, PO Box 1210, Port Angeles, Washington 98362-0224 USA. Tele: 650-254-6515.

BCC foresees increased protein drug sales in US by 1990

Since protein drugs first appeared over 60 years ago, with production achieved either through organ extraction or chemical synthesis (with a small contribution from micro-organisms and plants), their medical contributions and sales have climbed steadily. Today, the combined manufacturer-level revenues from protein drug sales amount to some $500 million (2.9 per cent of all pharmaceutical and biological sales) in the United States alone. The emerging trends in this field are already having a significant impact on suppliers of equipment, materials, chemicals and services.

A new report from Business Communications Co., (BCC) Bioengineered Medical Proteins (G-065), forecasts US sales of protein drugs rising to about $763 million by 1990, and to $1.117 billion by 1995 - representing an average annual growth rate of 7.5 per cent. US sales of biotechnology-based protein drugs already account for about $38 million in revenues, and BCC projects that they will increase to about $256 million by 1990, and to over $551 million by 1995.

In terms of the current market, protein hormones represent the largest protein drug category, generating about $420.9 million in manufacturer-level revenues in the US, or about 75 per cent of total protein drug revenues. The two biotechnology-based protein hormones now on the market are human growth hormone and insulin. BCC expects such revenues to increase to $501.0 million by 1990, an average annual growth rate of 4.5 per cent, and to $611.0 million by 1995 - representing an average annual growth rate of 4.3 per cent.

Current sales for clotting and anticlotting (clot dissolving) proteins in the US are about $131.8 million, giving a 23 per cent share of the protein drug market. BCC forecasts a rise to $143.2 million by 1990, and to $165.3 million by 1995, with average annual growth rates of 2.1 per cent and 2.5 per cent respectively. Lymphokines are an entirely new class of drug products, and a product of biotechnology. BCC values 1986 US revenues for alpha interferon, used in the treatment of hairy-cell leukaemia, at about $15.4 million. Based on anticipated product and indication approvals within the US, as well as on health statistics and expected treatment dosages and prices, BCC projects US lymphokine revenues of some $110 million by 1990, rising to $305 million by 1995.

Among the various other proteins being developed for drug use through biotechnology are growth factors, blood-building proteins, lung proteins and neuropeptides. While these products have not yet hit the market, BCC expects sales to materialize soon, projecting revenues of about $8 million in 1990, rising to $33 million in 1995. Details of the report, price $1,950.00, from: Business Communications Co., 25 Van Zant Street, Norwalk, CT 06855, USA or on (203) 853 4266. (Source: Biotechnology Bulletin, Vol. 6, No. 1, February 1987)

Biotechnology: The University-Industrial Complex. By Martin Kenny. Yale University Press: 1986. pp. 300, $23.95, £22.50

In under a decade, a whole new industry, capitalized with many billions of dollars, has come into being. Such is the rate of change in the late twentieth century. The product of 30 years of government support of basic biomedical research, biotechnology emerged from its incubator in the mid-1970s and quickly found its niche in the socio-economic structure of American and multinational industry.

The author chronicles, in intimate detail, the unfolding patterns of this development as determined by the extraordinary constraint that the basic knowledge - the blueprint for the industry - was

almost exclusively to be found in the minds of university faculty. Industry had the production facilities and the marketing skills, but it was barren of the new expertise. The professorial start-up companies, the university-industry contracts, the limited partnerships in research and development, the equity purchases and licensing agreements by the multinational corporations, all stemmed from this unprecedented circumstance. Also described are the subsequent contractual and fiscal interventions of the large chemical and pharmaceutical companies, as well as their successful efforts to purchase, in whole or in part, access to or even sole rights to the output of appropriate university departments, so as to acquire instant expertise and to ensure the economic future of the companies concerned.

Particular attention is paid to agricultural biotechnology, potentially the largest market. Organizational arrangements here were complicated because the land-grant universities, traditionally the source of agricultural research, have not been in the forefront of molecular biology, which is largely funded instead by the National Institutes of Health. Other universities, such as Harvard, MIT, Washington (St. Louis) and Stanford, have consequently become the corporate partners for the development of plant molecular biology.

Biotechnology: The University-Industrial Complex bears upon questions of fundamental importance to science, academia and society, and provides valuable documentation of the magnitude of the actions already taken and the multitude of participants involved. But it is hoped that someone will write the sequel, for which this is only the prologue. (Extracted from Nature, Vol. 325, 19 February 1987)

Biotechnology research in US federal agencies

For two years running, the Resources Community and Economic Development Division of the US General Accounting Office surveyed 11 federal agencies to find out to what extent they were supporting biotechnology-related research. The results, for five of the agencies, are contained in a 41-page document, Biotechnology: Analysis of Federally Funded Research (PB86-247095), available through the US National Technical Information Service (NTIS).

The agencies are: the Department of Agriculture (USDA), the Environmental Protection Agency (EPA), the Food and Drug Administration (FDA), the National Institutes of Health (NIH) and the National Science Foundation (NSF). Each profile includes estimates of the fiscal year 1985 level of support, both in terms of dollars committed and the number of projects funded. Also discussed are programmes on biotechnology risk assessment research. Details from: Gene Amey, Microinfo Ltd., PO Box 3, Alton, Hampshire or on 0420 96848. (Source: Biotechnology Bulletin, Vol. 6, No. 1, February 1987)

US biotechnology regulations

For any but the most resolute followers of Federal biotechnology regulator activities, the documents needed for tracking this process can be as elusive as they are voluminous. "Biotechnology Regulations: Environmental Release Compendium," available for $95 from OMEC International, 727 Fifteenth Street, N.W., Washington, D.C. 20005, compiles this material in a single volume. The loose-leaf compendium, which also contains information about several local ordinances pertaining to biotechnology, will be updated periodically. (Source: Bio/Technology, Vol. 5, March 1987)

Scrip Healthcare Biotechnology Company Profiles

Some 275 companies developing products by recombinant DNA or hybridoma technology are identified in the updated second edition of Healthcare Biotechnology Company Profiles, a 370-page guide containing 1,500 product entries. Details of the publication, priced at £90.00, from: Scrip Bookshop, 18-20 Hill Rise, Richmond, Surrey TW10 6UA or on 01 948 3262. (Source: Biotechnology Bulletin, Vol. 6, No. 1, February 1987)

Free ASTM publications catalogue available

The 1987 ASTM Publications Catalogue describes 66 volumes of the Annual Book of ASTM Standards and several hundred ASTM special technical publications, compilations, data series and standard adjuncts. ASTM standards and its related technical publications are used worldwide to specify materials, assure quality, integrate production processes, promote trade and enhance safety.

The catalogue is available free from Jacqueline Holden, ASTM Marketing & Promotion Services, 1916 Race Street, Philadelphia, Pennsylvania 19103, 215/299-5594. (ASTM News Release 6 February 1987)

Biomass: International Directory of Companies, Products, Processes & Equipment by James Coombs. Macmillan Publishers Ltd., UK (1986), 243 pages, $90.

From Argentina to Zimbabwe, this guidebook lists for 45 countries of East, West and in between commercial firms and public organizations involved in conversion of organic wastes to fuels and chemicals. Its 2,769 annotated entries range from the single University of Mauritius School of Industrial Technology ("Investigating methods of producing fuels, fertilizers and/or chemicals from waste products of the sugar industry ...") to the USA's 551 R&D firms, major corporations, suppliers, universities and government agencies with interests in bioconversion. Aside from minor quirks, such as alphabetizing some entries under "The" rather than their actual names, the listings - complete with telephone and telex numbers - are serviceable. A 48-page "Buyers Guide to Products, Research and Services" cross-indexes company names to their respective specialties.

The author also produces an annual Biotechnology Directory of Products, Companies, Research and Organizations.

The Gene-Splicing Wars: Reflections on the Recombinant DNA Controversy edited by Raymond A. Zilinskas and Burke K. Zimmerman. Macmillan Publishing Co., New York, N.Y. 10023 (1986), 288 pages, $24.95.

A dozen leading bioscientists, ethicists, and one journalist - plus the two editors of this work - all fought the gene-splicing "wars" of the 1970s, as they raged through the halls of national, state and local government, and the screens and pages of the media. Their accounts and analyses of the controversy's history is today a trifle dated and beside the point; yet these documented reminiscences add up to a useful textbook in the proliferating biotechnology course-curricula at high school or junior college level. The volume is one of the American Association for the Advancement of Sciences series on "Issues in Science and Technology".

Biotechnology: Strategies for Life by Elizabeth Antebi and David Fishlock. The MIT Press, Cambridge, Mass., London, UK (1986), 239 pages, (9 1/2 x 12 1/2), $39.95.

For the lay but curious reader in general, and the would-be investor in particular, this volume covers its subject from the ancient Aztec and Egyptian fermenters to tomorrow's protein-engineered enzymes and biochips. In vivid pictures as well as informative text, it wraps up biotechnology in a single, all-encompassing package - its history, science, mode of action, promised benefits commercial prospects, patents, regulation ethics.

Genetic Engineering News lists molecular millionaires

The average value of shares owned by 50 major stockholders in 20 leading biotechnology companies is worth almost $13 million, according to a survey of "molecular millionaires" that appears in the February issue of Genetic Engineering News (GEN).

GEN's Fifty Molecular Millionaires include corporate officials and businessmen such as Genentech's Robert Swanson, Biogen's James Vincent and Amgen's Jack Schuler, and venture capitalists like Moshe Alafi and Isaac and David Blech.

"The companies and individuals on the list were chosen arbitrarily," said Mary Ann Liebert, publisher of Genetic Engineering News. All information was gleaned from public documents. In each instance GEN used its latest information available and multiplied the number of shares attributed to an individual by the closing price of the stock on 31 December, 1986.

This finding reinforces the importance of university/industry ties to the still-evolving biotechnology business.

Although many of the Ph.D. molecular millionaires are full-time officials of biotechnology firms, many are not.

"I think it's wonderful that scientists who, for generations, have been improving the quality of our health and lives should be able to reap financial rewards as well as public recognition," Mrs. Liebert said. "Certainly this should be true in an era when huge salaries are paid to sports figures, newscasters, and quiz show hostesses."

With 2,043,887 shares of Genentech, chief executive officer Robert Swanson tops the list with a value of $173,730,395. Herbert Boyer, Ph.D. is second with 1,037,996 shares of Genentech valued at $88,229,660. (Company News Release, 18 February 1987)

Microbial database

A computer database designed to make microbial culture collections more accessible to industry has been set up at the UK Laboratory of the Government Chemist (LGC). It contains data from the National Collection of Type Cultures, the National Collection of Yeast Cultures, the CAB International Mycological Institute and the National Collections of Industrial and Marine Bacteria.

According to the systems designers, it will eventually contain data from all the UK National Culture collections enabling subscribers to search from over 30,000 strains. The system is housed on LGC's CEC minicomputer and users can access the information either on-line to the computer or by means of a postal telephone inquiry service. (Source: Nature, Vol. 326, 26 March 1987)

TEKTRAN offers preview of ARS research

Over 5,000 brief, easy to read summaries of the latest research on genetic engineering, safeguarding crops and animals from diseases, biological control of pests, human nutrition, and other fields are available on a new computer information service provided by the Agricultural Research Service of the United States Department of Agriculture.

Known as TEKTRAN, for Technology Transfer Automated Retrieval System, it offers notice of research results which have been peer-reviewed and cleared by ARS management. About 300 new findings are entered into the database each month, according to a report in Agricultural Research (Vol. 34, No. 8).

ARS is offering - on a first-come, first-served basis - an opportunity for a limited number of interested organizations with computers and telephone modems to have direct access to TEKTRAN. There is no cost for using the database. However, users are responsible for their own telephone charges.

Each entry on the database includes a brief summary describing the research but does not reveal specific details that would preclude patenting or publication. TEKTRAN also provides the name, address, and phone number of ARS scientists involved in the research.

Computer searches can be made in several categories. Among these are: Keyword, Multiple Keywords, Scientist's Name, and Commodity. The file can be accessed by specific dates in addition to the search categories indicated above. A user could enter the system once a month, for example, to search for new entries on a specific topic without having to look at the entire database each time.

Additional information on the procedure necessary to obtain access to this new database can be obtained by contacting: James T. Mall, National Technology Transfer Co-ordinator, USDA-ARS, Room 403, Building 005, BARC-West, Beltsville, MD 20705. Telephone (301) 344-4045. (Source: Agricultural Information Development Bulletin, March 1987)

Hewlett-Packard's anaerobic library for automated microbial identification system

A new database library containing more than 50 groups of anaerobic bacteria is now available for Hewlett-Packard's HP 5898A Automated Microbial Identification System. The system identified microbes by means of their fatty acid profiles. Applications are likely to be found in clinical and dental laboratories and in the food industry. Details from: Analytical Instrumentation Group, Hewlett-Packard Ltd., Miller House, The Ring, Bracknell, Berkshire RG12 1XN or on 0344 424898. (Source: Biotechnology Bulletin, Vol. 3, No. 12, January 1987)

Electronic networks for biotechnology

More information about the computer-based networks is now available to biotechnologists, by way of a copy of EBTP News 12 (from the European Biotechnology Information Project, The British Library, 9 Keen Street, London WC2B 4AT or on 01-323 7293). Three networks are mentioned:

(1) CODATA (the Committee on Data for Science and Technology), now available on the DIALCOM/British Telecom Gold system. This gives access to CODATA sponsored databases and enables participating scientists to communicate directly

with one another. Details from: Network Administrator, CODATA, 12301 Parklawn Drive, Rockville, MD 20852, USA.

(2) For UK scientists, the SEQNET electronic bulletin board is offered by the University of Cambridge. It covers meetings, software developments, materials and experiment updates. Details from: Martin Bishop, SEQNET, Computer Laboratory, Corn Exchange Street, Cambridge or on 0223 334724. Alternatively, talk to Michael Ashburner, Department of Genetics, Downing Street, Cambridge or on 0223 333969.

(3) In the USA, BIONET offers users the ability to participate in specialist user communities covering such subjects as gene expression or DNA repair. Details from: BIONET, Intelligenetics Inc., 124 University Avenue, Palo Alto, CA 94301, USA. (Source: Biotechnology Bulletin, Vol. 6, No. 1, February 1987)

Computer-aided molecular design and enzyme engineering proceedings

Molecular modelling and computer graphics were exploited first in the pharmaceutical and agrochemical industries, followed by the design of catalysts, both homogeneous and heterogeneous, paralleled by advances in enzyme studies. The latest area to be influenced by molecular design techniques is molecular electronics. The increasing availability of single-user computer workstations means that these techniques are no longer restricted to major companies. The proceedings of the Third European Seminar on Computer-Aided Molecular Design, October 1986, and the International Conference on Enzyme Engineering held in Cambridge in September are now available. Details of these two publications, both priced at £40.00. From: IBC Technical Services Ltd., Bath House, 56 Holborn Viaduct, London EC1A 2EX or on 01 236 4080. (Biotechnology Bulletin, Vol. 6, No. 1, February 1987)

Genetic codes dictionary

The "Gnomic: A Dictionary of Genetic Codes" has been compiled by Weizmann Institute Professor Edward N. Trifonov and his former graduate student Volker Brendel. It brings together relevant definitions of about 800 genetic sequences in a 275-page alphabetical dictionary, complete with indices and some 400 useful references. An updated 1,500-entry edition is now in preparation, and a computer accessible version of these data is currently being considered for inclusion in the US Bionet Database System and a similar service provided by the German Cancer Research Center. (Balaban Publishers, Rehovot, Philadelphia 1986) (Biotechnica '87, Hannover, Journal No. 2)

New database for AIDS research

New gene sequences and information about proteins of the AIDS virus are being reported so quickly that researchers are hard-pressed to keep up. To help streamline the process, scientists at Los Alamos National Laboratory in New Mexico are establishing a computerized data bank for recording and analyzing information about the molecular biology of the rapidly changing virus that causes AIDS. The National Institute of Allergy and Infectious Diseases (NIAID) has just awarded a three-year grant to Gerald Myers, of the Theoretical Division at Los Alamos, who plans to have the database available by March.

Not only does the AIDS virus mutate quickly so that different isolates have different gene sequences, but in recent months researchers have also found that more than one AIDS-like virus exists - some cause disease and others apparently do not. Until now, information about the genetics of the AIDS virus has been fed into the GenBank system, which is already established at Los Alamos. The new compendium will include analytical information that GenBank is not funded to provide, will contain quarterly updates of fresh data and will be available free to qualified investigators in both hard-copy and on floppy discs (that are IBM PC-compatible). The new resource is being established in co-operation with both GenBank and EMBL, the European Molecular Biological Laboratory in Heidelberg, Federal Republic of Germany, but is an independent entity.

The AIDS database will contain DNA, RNA and protein sequences of all the AIDS virus isolates, the sequences that recognize the T4 receptor of lymphocytes, and similar information about animal viruses that are related to the AIDS virus. It will identify regions of the AIDS virus genome that are most variable, and, if known, note how the altered regions affect peptide sequences and protein function. The resource will publish corrections of sequence information and will include references from the literature. (Source: Science, Vol. 235, 6 February 1987)

Communicate quickly with colleagues all over the world

The International Information Center for Plant and Animal Biotechnology has established an electronic mail network for the biotechnology community. You may connect to the system with any personal computer in any city in the US and from over 40 other countries. Electronic mail has already changed the way thousands of researchers communicate. The IICPAB NETWORK is being operated by The University of Georgia through a non-profit co-operative that provides modern communications technologies at a reduced cost.

- Send letters, reports, data, abstracts, preprints to collaborators, associates, or editors, across the world.
- Transfer computer programmes and files to others error-free.
- Schedule or actually conduct meetings on-line.
- Stay in touch with your office when travelling.
- Post jobs, meetings, announcements on bulletin boards.
- Access Telex, OAG, Foundation Center Grants.

Further information from IICPAB NETWORK, International Information Center, Plant and Animal Biotechnology, P.O. Box 2006, University of Georgia, Athens, GA 30612 USA, Telephone (404) 542-0377, Telex 4900006591.

Problems of information management in agriculture by B. Uviss Uruma

This article is adapted and extracted from the quarterly International Association of Agricultural Librarians and Documentalist (IAALD) bulletin, Vol. XXIX, No. 4.

Sophisticated information services in the field of agriculture are now in use all over the world ranging from the use of elaborate abstracting and indexing services to computerized databases. Information processing centres within the technologically advanced nations are too numerous to list.

A similar situation exists at the international level where the International System for the Agricultural Sciences and Technology (AGRIS), the Current Agricultural Research Information System (CARIS) and the International Food Information Science (IFIS), to mention just a few, have grown to gain intergovernmental recognition and support. The situation was remarkably different less than a half a century ago when agricultural documentation strove for international acknowledgement. 1/

It appears that the demand for sophisticated information organization in agriculture started to gain momentum in international circles with the prolific production of agricultural literature. It is believed, however, that agricultural documentation received an initial spur from the documentation of nuclear science literature. The demand for more and better information networks increased with the pioneer success story of INIS (International Nuclear Information System).

The documentation of nuclear information at the international level was seen by many as a massive drive in the wrong direction particularly as nuclear science could not be proved to be the de facto need of the world. As John Woolston later put it in an address he read at a meeting of information scientists, "History would have no respect for governments that would invest millions for an information system in atomic energy and then neglect to make adequate investment for a similar system in agriculture. To do that would show disregard for the real priorities of this world, in which the majority of men and women are suffering the debilitating effects of not having enough to eat." 2/

INIS, according to Buntrock, permitted intergovernmental co-operation on a large scale and it was from here the political impact of information networks grew. 3/ This, therefore, paved the way towards international co-operation for AGRIS and other international information networks for which agricultural documentation is now famous the world over.

Woolston further remarked that "there is an enormous potential for increasing world food production simply by applying existing knowledge". 2/ The emphasis has, therefore, been on increased food production by the application of "existing knowledge" through proper information services.

From the urgent demand for food grew the need for information in agriculture. This problem, however, was not as simple or as straight-forward as it was with the documentation of atomic information. Complications arose from the handling of agricultural literature, the solutions to which have evaded the classic librarian up to the present. Even now the problem of information management still heads the agricultural librarian's long list of concerns.

The three major problems which contribute directly to the existing complications in the management of agricultural information are identified as:

- The two levels of operation in agriculture;
- The multidisciplinary nature of agriculture and;
- The imprecision of the term 'agricultural literature'.

The two levels

There is a well-known dichotomy in agriculture the world over but particularly noticeable in developing countries. This gap has been created and is being widened largely by the vested interest which various governments have shown in agriculture. Government participation in agriculture is easily justified by the argument that agriculture provides the people with the basic essential of life: food.

Related to the provision of food is the contribution which agriculture makes to people's health, economy and independence or self-dependence. This explains why most governments have protectionist restrictions on agricultural practices to ensure that human nutrition and the nation's economy is to a large extent independent of foreign supplies. Such protectionist measures as governmental supervision and financial subsidies for agricultural research make agriculture unique in comparison with most other fields of study.

There is then this two-phased problem arising from national governments' subsidies to institutionalized agricultural research when this is only secondary in terms of production to the unsubsidized traditional practice of agriculture. In general and as Malta 4/ and Brannen 5/ observed "agricultural research is not in the hands of the private agriculturist" but in the institutionalized government-aided research programmes.

Ironically, however, agricultural production is in the hands of the private agriculturist. In practical terms this means that the information services in agriculture are directed towards the research level which is different from the local production level, the level that is traditionally responsible for the major agricultural output.

Generally, agricultural writers produce literature that is suitable for the theoretical and experimental level, i.e., the research level. This means that the agricultural documentalist faces an additional problem in that he is collecting, storing, retrieving and disseminating information for two levels of readership within the same field. This dichotomy creates a problem in agricultural information handling. 4/

The multidisciplinary nature

The second problem in agricultural documentation is the imprecision of the term 'agriculture'. Agriculture before the 20th century was understood to be related rather narrowly to farming. Since then, however, documentalists, agriculturists and agricultural researchers have redefined agriculture so generally as to make it unmanageably vast.

So broad has agriculture become that it now embraces animal sciences, crop husbandry, forestry, fisheries, human food and nutrition, rural development and sociology, biotic resources, environmental sciences and much more. All this is in addition to what is traditionally known as agriculture.

Leatherdale in constructing his agricultural thesauri inferred the need to redefine the scope and scope of what is included in the word 'agriculture'. This might prove very useful to the agricultural documentalist if he is not already too accustomed to some scope definition of an agricultural field that is almost limitless.

Agricultural literature

The third major problem in agricultural information handling today is the definition of the term 'agricultural literature'. Consequent upon the multidisciplinary nature of agriculture the term 'agricultural literature' has taken on an imprecise and vague meaning which contributes to the existing complexities in agricultural documentation.

Summing this situation Leatherdale wrote: "I find it difficult to bring to mind a single subject that may not be implicated (in agriculture). Activities so far removed from each other as the design of fishing boats, the physical chemistry of clay particles, the sociological history of sugar cane harvesting or even the taxonomy of fungi infecting acarine parasites of insects injurious to oranges may all be accommodated." 6/

The situation is further aggravated by the much talked about information explosion. Since it is only being perpetually talked about and not being curbed, the information explosion is forcing researchers to specialize in narrower and narrower fields of study. This is the trend in most fields of research as a means of coping with the ever-growing information explosion problem.

Regrettably, however, the present definitions of agricultural literature lead not towards specialization but to a further broadening which has reached a stage where even the peripheral and marginally related literature are all included and the agricultural documentalist cannot afford this broad definition.

The position as it now stands is one of extensive research at the expense of the intensive. So much effort, time and funds is being put into documenting an unmanageably vast collection, resources which should be profitably invested in an intensive organization of information within a well-defined field.

The ever-broadening definition of what is agriculture and of therefore, what constitutes agricultural literature should be limited. Then food production and productivity should be promoted. In particular, developing countries, which can ill afford the luxury of expensive research, should redefine agriculture so that the site of agricultural research and production coincide approximately.

For their part, international information agents like AGRIS should endeavour to deliver vital research information to the level of agricultural production rather than to a theoretical research level.

National agricultural information centres should be reorganized to liaize with AGRIS to promote governmental awareness of the need to subsidize actual agricultural production and to provide for agricultural experimentation at the site of production.

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2/ Woolston, J. The future for international information systems, pp. 23-24. In: Proceedings of the American Society for Information Science (1972).

3/ Buntrock, H. Some remarks on international co-operation in agricultural documentation and information. Quarterly Bulletin of IAALD 18(r): 301-210 (1973).

4/ Malta, D. J. Information needs in agriculture. Quarterly Bulletin of IAALD 17(4): 170-177 (1972).

5/ Brennan, P. W. Information flow in American agricultural literature. Quarterly Bulletin of IAALD 20(2): 86-93 (1975).

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G. MEETINGS

3 - 7 May 1987	Biomechanisms Regulating Growth, Beltsville Symposium XII. Details from: Agricultural Research Service, US Dept. of Agriculture, Bldg. 200, Rm. 125, BARC - East, Beltsville, MD 20705, USA
4 - 6 May 1987	Third International Conference on Progress in Cancer Research, San Remo, Italy. Details from: M. Grazia Moro, Instituto Nazionale per la Ricerca sul Cancro, Viale Benedetto XV, 10, 16132 Genoa, Italy
5 - 6 May 1987	Biotechnology for Fuels and Chemicals, Boulder, Colorado, USA. Details from: Oak Ridge National Laboratory, Energy Research Division, P.O. Box X, Oak Ridge, Tenn. 37831, USA
11 - 13 May 1987	Therapeutic Applications of Liposomes, Scanticon Conference Center, Princeton, New Jersey. Details from: Conference Co-ordinator, The Third Princeton-Liposome Conference, P.O. Box 9301, Trenton, N.J. 08650-1301, USA
11 - 15 May 1987	1st International Symposium on Post-Translational Modifications of Proteins and Ageing, Lacco Ameno d'Ischia, Bay of Naples, Naples, Italy. Details from: AIM s.r.l. - Via Lattuada 26, 20135 Milano, Italy
13 - 17 May 1987	RNA Processing. Cold Spring Harbor, New York, USA. Details from: Meetings Co-ordinator or Course Registrar, Cold Spring Harbor Laboratory, P.O. Box 100, Cold Spring Harbor, New York 11724, USA
17 - 20 May 1987	Annual Meeting of the Canadian Institute of Food Science and Technology, Hamilton, Ontario, Canada. Details from: Canadian Institute of Food Science and Technology, 111 Churchill Rd. S, Acton, Ontario L7J 2J5, Canada
19 - 20 May 1987	Freezing Quality Control: Cell Culture Hybridomas, Rockville, Md., USA. Details from: ATCC, 12301 Parklawn Drive, Rockville, MD 20852, USA
19 - 24 May 1987	RNA Tumor Viruses, Cold Spring Harbor. Details from: Meetings Co-ordinator or Course Registrar, Cold Spring Harbor Laboratory, P.O. Box 100, Cold Spring Harbor, New York 11724, USA
27 - 31 May 1987	38th Annual Meeting of the Tissue Culture Association, Washington, D.C., USA. Details from: Tissue Culture Association, 19110 Montgomery Village Avenue, Suite 300, Gaithersburg, MD 20879, USA

27 May - 3 June 1987	Symposium on the Evolution of Catalytic Function, Cold Spring Harbor, USA. Details from: Meetings Co-ordinator or Course Registrar, Cold Spring Harbor Laboratory, P.O. Box 100, Cold Spring Harbor, New York 11724, USA
28 - 29 May 1987	Discussion Meeting on Mitochondrial Biogenesis, London, UK. Details from: Miss C.A. Johnson, The Royal Society, 6 Carlton House Terrace, London, SW1Y 5AG, UK
1 - 3 June 1987	IX Meeting of the European Association for Cancer Research, Helsinki, Finland. Details from: EACR-87, Duodecim, Kalevankatu 11, SF-00100 Helsinki, Finland
1 - 4 June 1987	Industrial Bioprocessing Short Course, Estes Park, Colorado, USA. Details from: Office of Conference Services, Colorado State University, Rockwell Hall, Fort Collins, CO 80523, USA
14 - 19 June 1987	4th European Congress on Biotechnology, Amsterdam, The Netherlands. Details from: 4th European Congress on Biotechnology, c/o Organisatie Bureau Amsterdam bv, Europaplein 12, 1078 GZ Amsterdam, The Netherlands
29 June - 2 July 1987	Animal Cell Reactor Engineering (short course), Minneapolis, Minnesota, USA. Details from: Jan Becker, University of Minnesota, Dept. of Professional Development, Continuing Education and Extension, 315 Pillsbury Drive S.E., Minneapolis, MN 55455, USA
2 - 3 July 1987	Plant and Animal Biotechnology, Kensington Town Hall, London, UK. Details from: Janet Mulhall, Macmillan Conferences and Exhibitions, 4 Little Essex St., London WC2R 3LF, UK
5 - 9 July 1987	Second International Symposium on Nitrate Assimilation - Molecular and Genetic Aspects, University of St. Andrews, St. Andrews, Scotland, UK. Details from: J.L. Wray, Plant Molecular Genetics Unit, Sir Harold Mitchell Building, University of St. Andrews, St. Andrews, Fife, KY16 9TH, Scotland, UK
7 - 11 July 1987	Third Annual Meeting on Oncogenes, Hood College, Frederick, Maryland, USA. Details from: Ms. Margaret Fanning, Conference Co-ordinator, PRI, NCI-Frederick Cancer Research Facility, Frederick, Maryland 21701-1013, USA
12 - 16 July 1987	First International Meeting on Marine exchange, Stowe, UK. Details from: Prof. Baker, Dept. of Physiology, King's College, London, The Strand, London, WC2R 2LS, UK
21 - 22 July 1987	Envirochem '87, Robinson College, Cambridge, UK. Details from: Linda Doggett, Philips Analytical, York Street, Cambridge CB1 2PX, UK
30 July - 4 August 1987	12th International Herpes Virus Workshop, Philadelphia, Pennsylvania, USA. Details from: Gary H. Cohen, or Roselyn J. Eisenberg, University of Pennsylvania, 4001 Spruce Street, Philadelphia, Pennsylvania 19104-6003, USA
11 - 16 August 1987	Yeast Cell Biology, Cold Spring Harbor, New York, USA. Details from: Meetings Co-ordinator, Cold Spring Harbor Laboratory, P.O. Box 100, Cold Spring Harbor, New York 11724, USA
18 - 23 August 1987	Prokaryotic Gene Regulation, Cold Spring Harbor, New York, USA. Details from: Meetings Co-ordinator, Cold Spring Harbor Laboratory, P.O. Box 100, Cold Spring Harbor, New York 11724, USA
25 - 30 August 1987	Molecular Biology of Mitochondria and Chloroplasts, Cold Spring Harbor, New York, USA. Details from: Meetings Co-ordinator, Cold Spring Harbor Laboratory, P.O. Box 100, Cold Spring Harbor, New York 11724, USA
2 - 4 September 1987	From Cell Receptors to Gene Regulation, Wye College, Ashford, Kent, UK. Details from: J. Knowland, Dept. of Biochemistry, South Parks Road, Oxford OX1 3QU, UK
2 - 6 September 1987	Eukaryotic DNA Replication, Cold Spring Harbor, New York, USA. Details from: Meetings Co-ordinator, Cold Spring Harbor Laboratory, P.O. Box 100, Cold Spring Harbor, New York 11724, USA
7 - 9 September 1987	FEMS Symposium: Biochemistry and Genetics of Cellulose Degradation, Paris, France. Details from: J.P. Aubert, Dept. Biochim et Gen. Mol., Institut Pasteur, 25 rue du Dr. Roux, Paris F-75724, France

7 - 11 September 1987	Euroanalysis 7I, La Villette International Conference Centre, Cité des Sciences et de l'Industrie, Paris, France. Details from: GAMS 88, Boulevard Malesherbes, 75008 Paris, France
9 - 13 September 1987	Modern Approaches to New Vaccines Including Prevention of AIDS, Cold Spring Harbor, New York, USA. Details from: Meetings Co-ordinator, Cold Spring Harbor Laboratory, P.O. Box 100, Cold Spring Harbor, New York 11724, USA
10 - 19 September 1987	Khimia-87, Moscow, USSR. Details from: USSR, Moscow 107113, Sokolnicheski val. 1-a, V/O Expocentr, Chemistry-87
13 - 17 September 1987	T-Cell Activation in Health and Disease, Trinity College, Oxford, UK. Details from: Prof. Marc Feldmann, Charing Cross Sunley Research Centre, Lurgan Avenue, Hammersmith, London, W6 8LW, UK
15 - 18 September 1987	Separation for Biotechnology, Reading, UK. Details from: Soc. of Chemical Industry, 14/15 Belgrave Square, London SW1 X8 PS, UK
16 - 20 September 1987	Translational Control, Cold Spring Harbor, New York, USA. Details from: Meetings Co-ordinator, Cold Spring Harbor Laboratory, P.O. Box 100, Cold Spring Harbor, New York 11724, USA
28 September - 1 October 1987	Hepatitis B Viruses, Cold Spring Harbor, New York, USA. Details from: Meetings Co-ordinator, Cold Spring Harbor Laboratory, P.O. Box 100, Cold Spring Harbor, New York 11724, USA
28 September - 2 October 1987	7th World Congress of Food Science and Technology, Singapore. Details from: Congress Secretariat, c/o Singapore Professional Centre, 23 Outram Park, Singapore 0316
4 - 8 October 1987	Molecular Neurobiology of Drosophila, Cold Spring Harbor, New York, USA. Details from: Meetings Co-ordinator, Cold Spring Harbor Laboratory, P.O. Box 100, Cold Spring Harbor, New York 11724, USA
4 - 8 October 1987	1st Latin American Congress on Biotechnology, Tucuman, Argentina. Details from: Prof. F. Sineris, MIRCEN-PROINI, Av. Belgrano y Pasaje Caseros, 4000 S.M. de Tucuman, Argentina
4 - 17 October 1987	Molecular Development of the Mouse (practical course), EMBL, Heidelberg, FRG. Details from: Erwin F. Wagner, EMBL, Meyerhofstrasse 1, D-6900, Heidelberg, FRG
5 - 9 October 1987	III International Workshop on Carcinogenesis Studies in Human Tissues and Cells, Elsinore, Denmark. Details from: Dr. M.I. Nielsen, Danish Cancer Society, Rosenvaengets Hovedvej 35, DK-2100, Copenhagen O, Denmark
5 - 9 October 1987	International Symposium on Biotechnology and Food Industry, Budapest, Hungary. Details from: Hungarian Scientific Society for Food Industry (MÉTE), P.O. Box 5, H-1361 Budapest, Hungary
6 - 12 October 1987	China Pharm 87, Beijing, China. Details from: Larry Tang, Tradeshow Consultant International, 1605 World Commerce Centre, 11 Canton Rd., Tsimshatsui, Kowloon, Hong Kong
11 - 25 October 1987	Terrestrial Space Radiation and its Biological Effects, Washington, D.C., USA. Details from: Dr. P. McCormack, Division of Life Sciences (Code EB), NASA, HQ, Washington, D.C. 20546, USA
15 - 17 October 1987	North American Cystic Fibrosis Conference, Toronto, Ontario, Canada. Details from: Cystic Fibrosis Foundation, 6931 Arlington Road, Bethesda, MD 20814, USA
19 -21 October 1987	Biotechnology in Agriculture, Food Processing and Dietetics, Naples, Italy. Details from: Fond. Giovanni Lorenzini, 23 via Monte Napoleone, I-20121 Milan, Italy
20 - 21 October 1987	Novel Biotechniques for the Food Industry, Tara Hotel, Kensington, London, UK. Details from: Online Conferences Ltd., Pinner Green House, Ash Hill Drive, Pinner HA5 2AE, Mid, UK
2 - 3 November 1987	Symposium on Amino Acid Receptors: Allosteric Modulation and Therapeutic Implications, The Royal Society, London, UK. Details from: Dr. Ralph Kohn, Advisory Services Medical Symposia Ltd., 79 Wimpole St., London, W1M 7DD, UK

2 - 4 November 1987	7th International Symposium on HPLC of Proteins, Peptides and Polynucleotides, Washington, D.C., USA. Details from: Ms. S. Schlessinger, Symposium Manager, 400 East Randolph, Chicago, IL 60601, USA
4 - 5 November 1987	Fifth Annual International Symposium on Progress in in vitro Toxicology, Baltimore, USA. Details from: Mrs. Sheila Kuna, The Johns Hopkins Center for Alternatives to Animal Testing, 615 North Wolfe St., Baltimore, MD 21205, USA
4 - 6 November 1987	Fifth International Symposium on Rapid Methods and Automation in Microbiology and Immunology, Florence, Italy. Details from: Prof. A. Turano, Istituto di Microbiologia, Spedali Civili, P.O. Box 312, 25100 Brescia, Italy
9 - 12 November 1987	International Conference on Bioreactors and Biotransformations, Gleneagles, Scotland, UK. Details from: Ms. E. Gibson, N.E.L., East Kilbride, Glasgow G75 0QU, Scotland, UK
11 - 13 November 1987	Biotech '87, Los Angeles, USA. Details from: Online Conferences Ltd., Pinner Green House, Ash Hill Drive, Pinner HA5 2AE, MID, UK
9 - 11 December 1987	Innovations in Protein Therapeutics: From Research to the Clinic, Walt Disney World, Orlando, Florida, USA. Details from: M.L. Nucci, ENZON Inc., 300 C Corporate Court, South Plainfield, NJ 07080, USA
10 - 11 December 1987	New Developments in Biotechnology - Meeting the Challenges of the Food Industry, Birmingham, UK. Details from: Exhibitions and Events Division, The National Exhibition Centre Ltd., Birmingham B40 1NT, UK
9 - 11 December 1987	Biotechnology Food Industry, Conference and Exhibition, London, UK. Details from: Society of Chemical Industry, 14/15 Belgrave Square, London SW1 X8 PS, UK

Advance notice 1988:

12 - 15 April 1988	Progress in Food Preservation Processes, Brussels, Belgium. Details from: Mr. D. Tsevmans, Head of Biochemical Engineering Dept., CERIA-IILF-IMC, Ave. Emile Gryson 1, B-1070 Brussels, Belgium
5 - 11 June 1988	Achema 88, Frankfurt-am-Main, FRG. Details from: Dechema, Organisation Achema, P.O. Box 97 01 46, D-6000 Frankfurt-am-Main 97, FRG

B. REPRINTED ARTICLES

Seeds of struggle: the geopolitics of genetic resources

(This article, which was written by Jack Kloppenberg, Jr., and Lee Kleinman, first appeared in Technology Review, February/March 1987, and is reprinted hereunder with the kind permission of Technology Review, Massachusetts Institute of Technology, Cambridge, Mass., Copyright 1987)

Last year's celebration of the Statue of Liberty's centennial highlighted the central role that immigration has played in American history. Yet few people recognize that our population of agricultural plants is as immigrant as our human population. If the United States had not introduced new crop plants from other regions of the world, the tide of human immigration could never have been sustained.

Few US crops of economic importance today are indigenous to North America. European explorers found Native Americans growing corn, beans, tobacco, and squash. But these crops had been introduced from Central America and the Caribbean. A truly all-North American meal would consist only of sunflowers, Jerusalem artichokes, blueberries, cranberries, pecans, and chestnuts. Northern Europe's contribution to the global larder has been similarly meagre: it includes currants, raspberries, oats, and rye.

In spite of the relative poverty of their original endowments, the advanced industrial nations are hardly agriculturally underdeveloped. But the crops that dominate these areas - corn, wheat, soybeans, potatoes, alfalfa, barley, sorghum, tomatoes, cotton, tobacco, and flax - originated largely in what is today known as the third world. The agriculture of the North has been predicated on transfers of plants from the developing nations of the South.

While the original transfers of plants and seeds occurred decades and even centuries ago, the advanced industrial nations still need regular infusions of plant genetic resources from the third world to maintain the vitality of their crops. Plant breeders require material from the original stocks to develop new strains that are able to resist pests and pathogens. Seeds from the third world are also the raw material of genetic engineers in the industrialized nations.

Plant "germplasm", the genetic information encoded in seeds, is therefore increasingly recognized as a resource of tremendous value. This recognition has given rise to what the Wall Street Journal has called "seed wars". The principal arena for this conflict has been the Food and Agriculture Organization (FAO) of the United Nations. Like so many debates within the UN, the controversy over plant germplasm finds the industrialized nations of the North pitted against the less-developed countries of the South. At issue is the equity of global patterns in the exchange of plant genetic resources.

In the world economy today, extracted natural resources are treated as commodities. Plant germplasm is a notable exception. For over two centuries scientists from the industrial nations have

appropriated plant resources from the third world without paying for them. This unrecompensed extraction has been predicated on an ideology that defines plant germplasm as the "common heritage" of humanity. Germplasm has been regarded as a public good for which no payment is necessary or appropriate.

In contrast, the plant varieties purveyed by the seed companies of the industrialized world are marketed as commodities for which payment must be made. Third world nations are beginning to question this difference. They claim that if the raw materials they provide are common heritage, so are the seeds and crops that scientists develop from this material. Breeders in the industrialized nations argue that they are the ones who give the plant genes value by incorporating them into new strains. Resolving this impasse will require a new international framework for the use of these resources.

The fourth resource

Soil, air, and water have traditionally been regarded as Earth's fundamental natural resources. But our planet's true distinction lies in the existence of life. Germplasm, the hereditary material contained in every cell, must therefore be counted as a fourth resource of prime importance. It is convenient to think of the world's plant genetic resources as seeds, for that is the form in which genetic information is embodied and usually collected and stored.

The vagaries of natural history have distributed plant species unevenly over the face of the globe. The upper reaches of the northern hemisphere lost much of their diversity under the grinding impact and extreme cold of the last glaciation, with the result that biotic diversity is concentrated in what is now the third world. Moreover, it is in the third world - specifically in the Near East and Southeast Asia - that plants were first domesticated and crops first produced.

In the process of growing crops over the millennia, peasant farmers have developed thousands of "land races" - genetically variable populations within any one species that respond differently to pests, diseases, and environmental fluctuations. The genetic diversity in these land races is a form of insurance: by planting many different varieties of a crop, peasant farmers can ensure that some of the seed they sow will grow to maturity. Their objective is not high yield but consistency of production. The result of their efforts is that great genetic diversity has been developed in relatively confined geographical areas.

The spread of such cultivated plants to new areas has occurred throughout human history, but until relatively recently most of this spread was slow and geographically limited. Europe had added barley, wheat, alfalfa, and a variety of vegetables to its original complement of crops by 1300, for example. But the major crop regions remained largely distinct until 1492.

The discovery of the New World touched off a dramatic and unprecedented movement of plants around the globe. When Columbus returned from his exploration in 1493, he brought not only news of his discovery but also maize seeds. The next year he was back in the New World carrying material for planting wheat, olives, chickpeas, onions, radishes, sugar cane, and citrus fruits, with which he hoped to support a colony. Thus was initiated what has been called the great Columbian Exchange.

Maize, potatoes, squash, sweet potatoes, cassava, peanuts, and cocoa went East while wheat, rye, oats, and Old World vegetables went West. This exchange had a profound effect on global diets and culture. Maize and potatoes were instrumental in the doubling of Europe's population in the hundred years after 1750. Cassava from Latin America was similarly important in the Asian and African tropics.

In addition to providing new food staples, the New World offered crops of great medicinal and industrial significance such as quinine, rubber, sisal, and tobacco. The Americas also provided new locales for producing tropical crops originally from Asia and Africa, including spices, tea, coffee, and indigo. The emergence of an expansive mercantile capitalism committed to the global transformation of agricultural production played an important role in this rapid plant migration.

While many food crops moved in all directions, tropical plantation crops moved among colonial possessions rather than from the colonial periphery to the European imperial centres. The banana, originally from Southeast Asia, was transferred to Central and South America as well as to the Caribbean and Africa. Coffee from Ethiopia made its way to the Caribbean, South and Central America, and Asia. Sugar cane from Southeast Asia was transferred to Africa as well as to Central and South America and the Caribbean.

As the commercial value of plant products increased, germplasm was recognized as a resource of tremendous strategic importance. European governments went to great lengths to prevent competitors from obtaining useful plant material. The Dutch, for example, destroyed all the nutmeg and clove trees in the Moluccas near Indonesia except those on the three islands where they established plantations. And the French made the export of indigo seed from Antigua a capital offence.

In Britain, a nascent botanical science was called into the service of empire early on. The Royal Botanic Gardens at Kew were established in the mid-eighteenth century to facilitate the development of both colonial and domestic agriculture. Kew botanists made systematic - and sometimes illegal - efforts to collect plant materials from around the world and ascertain their commercial utility. This material and information, passed along to colonial administrators and plantation owners, proved crucial to the success of many plantation crops and plant-based industries.

In the young United States, the need to collect germplasm for both food and industrial crops was particularly acute given the relative genetic poverty of the North American continent. Thomas Jefferson is widely quoted as asserting that "the greatest service which can be rendered to any country is to add a useful plant to its culture". The introduction of plants into the United States was much more than a great service. It was an absolute imperative.

In 1819 the Secretary of the Treasury directed all consular and naval officers abroad to collect seeds and plants that might be useful to US agriculture. Admiral Perry's gunboats not only opened the harbours of Japan to US commerce in the 1850s; they also brought back seeds and cuttings of rice, soybeans, vegetables, and citrus fruits.

With the creation of the Plant Introduction Office in 1898, the Department of Agriculture (USDA) formally institutionalized the global collection of plant genetic material - an effort that then accounted for one third of the agency's annual budget. In what has been called the "golden age of plant hunting", the first third of the twentieth century saw some 50 USDA-sponsored expeditions scour the world in search of useful plants. The

US Government distributed the plant varieties it then developed to American farmers, who provided a testing ground for the plant cultivars that allowed the country to become a modern industrial Power.

Germplasm and genetic vulnerability

By 1900 the American and European Powers had appropriated the plant types they needed to become the breadbaskets of the world. However, these countries have had to continue to replenish their stocks from the countries where the plants originated. This is because in the process of working plant material into extremely productive elite varieties, breeders have often eliminated characteristics that do not contribute directly to high yield, such as resistance to disease and pests. Moreover, since a large proportion of US farm acreage is devoted to a small number of varieties, these crops are vulnerable to new diseases and pests in a way that genetically heterogeneous land races are not.

The material consequences of this vulnerability were brought dramatically home by the US corn blight of 1970. Fifteen per cent of that year's harvest was lost to one disease organism that attacked a genetic character carried by over 90 per cent of the country's corn varieties. A subsequent study by the National Academy of Sciences found American crops "impressively uniform genetically and impressively vulnerable".

Since World War II, the advanced industrial nations have collected third world germplasm specifically to improve the stocks that become vulnerable to pests, disease, and environmental factors. The collected materials are stored in climate-controlled "gene banks" developed for this purpose.

The ideology of common heritage and the norm of free exchange of plant germplasm have been worth billions of dollars to the developed nations. Every species of economic importance in the United States has been improved by genes originating elsewhere. For example, the genes that code for resistance to yellow dwarf disease in barley, obtained from a Turkish land race, have been worth $150 million per year to US farmers. And new soybean varieties developed by University of Illinois plant breeders using germplasm from Korea may save US agriculture $100 million to $500 million in yearly processing costs.

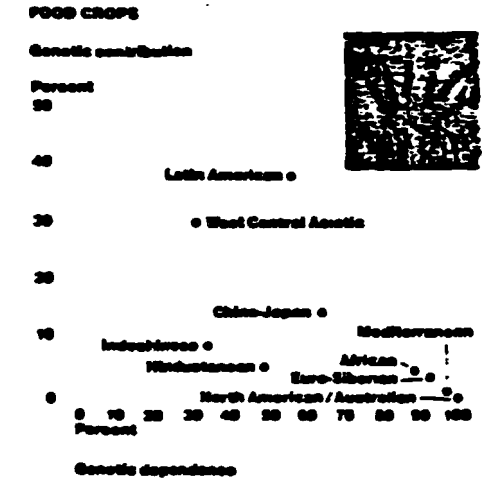
Controversy erupts

While third world plant materials have been available free of charge as the common heritage of humanity, the elite cultivars developed by seed companies have been accorded the status of private property: they are commodities obtainable by purchase. A number of factors have combined to galvanize global political conflict around this inequity.

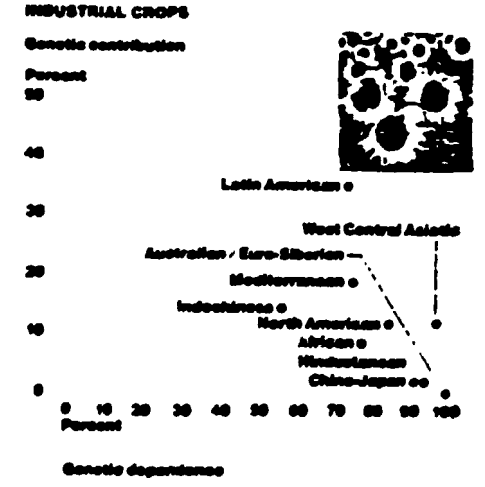
Perhaps most significant, growing concern about species extinction and the narrowing of the world's genetic base has led to a new awareness of the vital importance of plant resources. Scientists first realized that, as part of the Green Revolution, poor countries were replacing their traditional cultivars with high-yielding strains originally developed from those very plants. Disasters such as the US corn-blight epidemic reinforced the idea that the loss of germplasm in the third world also has material consequences for the developed nations. Efforts to conserve the biotic diversity of third world countries have emphasized the economic value of these resources.

The internationalization of the seed industry during the 1970s further highlighted the distinction between the two types of plant material. As North American and European seed companies reached out for global markets, they sought international recognition of the monetary value and proprietary status of their seed varieties. As both developed and developing nations were asked to recognize patent-like "plant-breeders' rights", awareness of the value of plant germplasm increased. Advances in biotechnology promise to accelerate demands that countries legally recognize plant genetic information as private property.

This chart shows the percentage of global food production planted in crops that originally came from each region. The chart also shows the percentage of each region's crop production that is planted in varieties that originated in other areas. For example, Latin America is the region of origin for 36 per cent of the 20 crops that lead global food production, while 56 per cent of the region's own production is based on plants introduced from elsewhere.



This chart gives similar information for the production of the world's industrial crops. In this case, regional contributions to genetic diversity are more evenly distributed.



Yet amid third world demands for a more equitable "new international economic order", the distinction between "elite" commercial germplasm and "primitive" germplasm seems less than persuasive. To many observers in the developing world, this supposed

difference is sleight of hand designed to maintain their subordinate position in the global economy.

Mounting third world dissatisfaction with this inequity found expression at the 1983 biennial conference of the UN Food and Agriculture Organization. Despite vehement opposition from the advanced industrial nations, delegates to this meeting approved an International Undertaking on Plant Genetic Resources. The "undertaking" affirms the principle that these resources are the "heritage of mankind and consequently should be available without restriction". And the resolution includes "special genetic stocks (including elite and current breeders lines)" under the rubric of plant resources. That is, the measure claims that the proprietary lines of the seed industry are no less the common heritage - and therefore the common property - of humanity than the peasant-developed land races of the third world.

Such an arrangement is unacceptable to industrial nations with powerful seed industries. The United States, Denmark, Finland, France, the Federal Republic of Germany, Netherlands, Norway, Sweden, the United Kingdom, and New Zealand have all officially indicated that they do not accept the validity of the undertaking, or said that they will do so only with restrictions. Conversely, virtually every third world member of the FAO that has responded has expressed "support without restriction" for the undertaking.

Angered by what they see as a lack of co-operation by the North, some third world nations have suggested that no germplasm should be exchanged freely. There has been talk of a "genetic OPEC", and several nations, including Ethiopia, have closed their borders to the export of certain types of plant germplasm.

The seed industry intends to do all it can, including heavily lobbying various governments, to retain the distinction between the two types of germplasm. Unrestricted exchange of privately held genetic stocks would be inconsistent with the laws of most industrial nations, and they are simply not about to dismantle the system that gives companies proprietary rights to their products. Indeed, current developments are bearing in the opposite direction. The US Board of Patent Appeals recently established the patentability of plant germplasm, Japan permits patenting of plants, and similar decisions will probably be forthcoming in Europe. Thus, the prospect for achieving common-heritage status for all types of plant germplasm is not bright.

Yet the third world nations have legitimate concerns. The natural resources that the developed nations have extracted for the longest time, derived the greatest benefits from, and still depend upon the most are those for which no compensation is paid. Politicians, business executives, and scientists in the developed world argue that this "raw" germplasm cannot be given a price because it is impossible to predict the utility of the genes in any particular sample of seed. But neither are coal, oil, and timber useful before they have been processed, yet no one suggests that these resources should be extracted without payment. Even though plant genetic resources are not depleted when they are extracted, the seed companies are still receiving all the benefits from access to them. Moreover, unlike coal, oil, and timber, land races are not the simple gift of nature but the product of human labour: their diversity is the direct result of the daily activities of peasant farmers throughout the world.

Ironically, in a world economic system based on private property, each side wants to define the possessions of the other as a common good. As long as the terms of the debate remain unchanged, resolution is unlikely. But a rapprochement may be possible if both sides admit that the principle of common heritage is unworkable. Third world nations should recognize that, given the international balance of power, developed nations will not declare proprietary plant lines a public good. And the advanced industrial nations should recognize that they cannot insist upon free access to a natural resource, however difficult it is to value. Replacing the principle of common heritage with that of national sovereignty would help resolve this impasse by providing a framework for compensating third world nations for their plant resources.

A new international arrangement

The UN charter already guarantees nations sovereignty over all their natural resources, so there is a firm precedent for international acceptance of this principle in the case of plant germplasm. Moreover, while seed companies are vehemently opposed to the "decommodification" of their own plant lines, there are indications that they would be willing to pay nations for the use of their plant germplasm. Recently, for example, Occidental Petroleum purchased a collection of rice lines from China, and Zoecon Corp. bought a set of soybean land races from the Chinese. Companies will undoubtedly consider such payments preferable to continued conflict and possible restrictions on the flow of what is for them an essential raw material.

One problem with providing compensation based on national sovereignty is that genetic resources are distributed unequally within the third world as well as between North and South. This means that third world nations might not benefit uniformly under the new system, and could even suffer if they charged one another for their plant germplasm. A market approach in which each country charged for the use of its genetic resources would also pit poorer nations against one another as suppliers of plant germplasm.

More preferable would be an approach that builds on the third world's willingness to confront the issues surrounding plant genetic resources in a unified way. The Undertaking on Plant Genetic Resources could provide a vehicle for compensating developing nations by mandating the creation of a global network of gene banks and a plant gene fund managed by the FAO. Advanced industrial nations could pay into the fund according to the size of their seed industries, the value of national agricultural production, or the frequency and size of their drafts upon the gene banks. The fund could be used to develop the banks, support efforts to conserve global plant resources, and train third world plant breeders.

A variety of international arrangements, including agreements among third world nations to control the price of and access to commodities such as copper and cocoa, prove that such multilateral initiatives can work. World recognition of nations' sovereignty over their plant resources and creation of a system of compensation would redress a significant inequity between developed and developing nations. The specific provisions of such a system would have to be negotiated. But the sooner such efforts begin, the sooner plant genetic resources will be recognized and preserved as essential to the well-being of all humanity.

Below: Every plant species of economic importance in the United States has benefited from infusions of genes from diverse sources of germplasm. Furthermore, as indicated in the case of wheat, each species has been improved in many different ways.

EXOTIC GERMPLASM AND CROP IMPROVEMENT IN THE UNITED STATES

Crop	Characteristic	Germplasm source
Alfalfa	Stem nematode resistance	Turkey
Barley	Yellow dwarf virus resistance	Ethiopia
Bean	Fusarium root rot resistance	Mexico
Cabbage	Black rot resistance	Japan
Cauliflower	Disease virus resistance	Iran
Cucumber	Bacterial wilt resistance	Burma
Lettuce	Lettuce aphid resistance	Egypt
Muskmelon	Powdery mildew resistance	India
Oat	Crown rust resistance	Uruguay
Onion	Thrips resistance	Iran
Pea	Disease virus resistance	Iran
Potato	Late blight resistance	Panama
Sorghum	Greenbug resistance	India
Soybean	Cyst nematode resistance	China
Spinach	Downy mildew resistance	Iran
Tomato	Resistance of cuticle cracks	Peru
Watermelon	Wilt resistance	Africa
Wheat	Dwarf-dwarfing	Japan
	Leaf rust resistance	Brazil, China, Russia
	Stripe rust resistance	Turkey
	Dwarf resistance	Russia, Turkey, Australia
	Septoria resistance	Brazil, Bulgaria
	Stem rust resistance	Russia, Kenya, Egypt, Ethiopia, Palestine
	Hessian fly resistance	Turkey, Greece, Uruguay
	Cereal leaf beetle resistance	Russia, China, Ethiopia
	Aluminum tolerance resistance	Brazil

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Beyond the green revolution: new approaches for third world agriculture by Edward C. Wolf (Worldwatch Paper 73, October 1986). (This article is reproduced with kind acknowledgement to the Worldwatch Institute)

After 20 years, the green revolution stands as a touch-stone in international agricultural development. At a time when famine seemed imminent, new varieties of wheat and rice introduced to Asia and Latin America along with fertilizers, pesticides, and mechanized farm equipment dramatically increased harvests. This agricultural strategy, which transformed the lives and prospects of hundreds of millions of people, is considered the most successful achievement in international development since the Marshall Plan and the reconstruction of Europe following World War II. India, whose food prospects once seemed bleak, today holds grain reserves that provide insurance against famine. Indonesia, once the world's largest rice importer, is now self-sufficient and exports rice.

But the agricultural progress that made the green revolution possible has not been distributed evenly. New seeds, fertilizers, and pesticides boosted the crop yields of Asian and Latin American farmers who had access to irrigation systems and markets for their crops. The aggregate statistics hide a large group of third world farmers who did not benefit from the new technologies: subsistence farmers raising food for their families on marginal, rainfed land. Because their agriculture remains unproductive and vulnerable to crop failure, drought, and natural catastrophe, these rural people remain among the poorest in their societies. Failing to address their needs has slowed economic progress in dozens of countries. The recurrent famines in Africa, and persistent pockets of starvation on that continent, demonstrate the unacceptable human costs of this neglect.

High-yielding varieties of wheat and rice have been introduced to less than a third of the 423 million hectares planted to cereal grains in the third world. The rates of adoption vary widely by region: 38 per cent of the grain area in Asia and the Middle East, 22 per cent of Latin America's grain area, and only 1 per cent of Africa's grain fields grow improved varieties of wheat and rice. Other crops including barley, sorghum, potatoes, and especially maize have also been improved by research and breeding, and new varieties distributed to farmers. The local contributions of these advances have been substantial. For example, Zimbabwe's maize surpluses in recent years stem largely from plantings of improved hybrids by commercial and communal farmers alike. But none of these crops have had an effect on total food production, average productivity, and rural incomes as widespread or significant as the green revolution wheats and rices. 1/

Not all wheat and rice farmers can afford the new seeds and the inputs they require. Others raise crops for which systematic research is just beginning. Overall, nearly 100 million people in Latin America, 280 million in Africa, and over 990 million in Asia raise food under difficult conditions at yields little changed since mid-century. But grain yields in more agriculturally advanced regions are already near their biological ceilings; thus this group of near 1.4 billion people holds the key to future increases in world food production. 2/

The case for increasing yields remains as compelling today as it was a generation ago. Over the next 13 years, world population will expand from today's 5 billion to over 6 billion. Few analysts expect a significant expansion of cultivated land by then. Just to maintain current consumption levels will require a 26 per cent increase in the world's average grain yields. And by 2020, feeding the projected population of 7.8 billion will require grain yields 56 per cent higher than 1985 levels. Unlike past yield increases achieved under favourable cropping conditions, future improvements in average yields must come from raising the productivity of traditional farmers who cultivate low-yield crops under marginal conditions - perhaps the most demanding challenge that national governments and the international development community have faced. 3/

Small farmers cultivate their crops under extraordinarily diverse ecological conditions, ranging from the rain-soaked volcanic archipelagos of South East Asia to the arid savannas south of the Sahara and Latin America's high altiplano. Farming methods, and staple foods, vary enormously as well. In South East Asia, for example, where one third of the farms are less than half a hectare in size, most farmers depend exclusively on manual labour and draft power supplied by water buffalos in order to cultivate their rice. On Africa's small farms, cultivated more with hoes than ploughs, families grow root and tuber crops including cassava and yams as the primary staples. Despite such variety, subsistence farms around the world share common features: farmers often mix different crops in the same field to reduce the risk if a particular crop fails, they grow a variety of staple crops and vegetables to meet family food needs, and they rarely purchase artificial fertilizers or pesticides. 4/

Green revolution approaches will only be part of the answer for the 230 million rural households in Africa, Asia, and Latin America that use farming methods almost identical to those of their ancestors. One reason is energy. Past advances have come from increasing the energy intensity of farming: fuel to run machinery, fossil-fuel-based artificial fertilizers, and diesel fuel or electricity to run irrigation pumps. Few of the rural poor can afford these costly materials and

services. Even if they had the income to purchase such inputs, many farmers are not served by roads or markets that could reliably supply them.

In addition, subsistence farmers grow crops that have received comparatively little research attention. There is as yet no research base for achieving high yields in many staple crops. Third world farmers cultivate on poor soils under harsh climates that require finely tuned agricultural practices. As rural populations grow, these farmers will need agricultural advances that are labour-intensive, rather than capital- and energy-intensive. Such conditions demand different research approaches from those that raised yields in the past.

A new strategy of efficiency and regeneration could help meet the needs of subsistence farmers, and begin to address the environmental and economic problems linked to more intensive cropping practices as well. Such a strategy would stress the efficient use of fertilizers, chemicals, water, and mechanized equipment. As a supplement to efficiency, farmers would blend biological technologies and traditional farm practices to increase the contribution that the land's natural fertility makes to food production.

Two sets of technical opportunities, already stirring the agricultural research community, promise rapid progress toward better resource management and regenerative approaches. One is the reappraisal of traditional farming practices, once judged backward and unproductive. Shifting cultivation, multiple cropping, and traditional soil management methods, though often practised under pressures that make them counterproductive today, are governed by ecological principles that can serve as models for sustainable farming.

Biotechnology can also offer new solutions to third world farming problems. The ability to modify the genetic makeup of plants and animals poses environmental risks that must be carefully evaluated. But biotechnology's benefits lie in the potential to allow breeders to develop new crop varieties more quickly than conventional breeding. Crops may be tailored to use water and nutrients more efficiently, and to perform well in the mixed cropping practices that many poor farmers employ.

Joining biotechnologies with the ecological insights of traditional farming promises innovative solutions to agriculture's economic and environmental problems. Government policies do not fully recognize that promise yet. But opportunities have never been greater for moving agriculture toward sustainability and reaching the quarter of the world's people - and quarter of the world's cropland - left out of the green revolution.

Productivity reconsidered

The pursuit of productivity has been central to agriculture since farmers first selected the wild grasses ancestral to today's crops. In recent years, harvests have outpaced population growth, not only because more land has been brought under the plough, but because different plant varieties, more irrigation, fertilizer, and improved tools and equipment allow farmers to produce more from each hectare of land and each hour worked. World grain production increased from 620 million tons in 1950 to 1,560 million tons in 1985, and the average yield per harvested hectare climbed from 1.1 tons to 2.0 tons. These rapid increases have no precedent. 5/

The postwar increase in yields rested on a simple formula. Researchers and extension agents encouraged farmers to use more fertilizers, pesticides, and irrigation in combination with newly bred crop varieties. According to the conventional approach, substituting these capital- and energy-intensive inputs for the traditional resources of land and labour would allow farmers to expand harvests each year.

Some countries succeeded handsomely; hundreds of millions of people are better fed and better off than they would have been without these gains. But because of their exclusive focus on improving yields, policymakers and researchers emphasized regions where the economic return on investment in fertilizers would be highest, rather than seeking to distribute inputs more widely. This approach naturally overlooks farmers on marginal land, for whom raising yields may not be as important as increasing resistance to drought and other natural catastrophes.

Despite its drawbacks, enthusiasm for the conventional productivity formula is understandable. The increase in world food production in the last decade has been associated with a comparable increase in the use of artificial fertilizers. Regions that have used the most additional fertilizer have reaped the largest benefits. (See Table 1.) Asia and North America, the areas that harvested nearly four fifths of additional world grain production, accounted for 56 per cent of the increase in fertilizer use. And while North America's average harvested area also expanded over this period, virtually all the growth in Asian harvests came from fertilizer. Yet Eastern Europe and the Soviet Union demonstrate that additional fertilizer alone does not necessarily mean proportionately larger harvests. Relying on central planning rather than farmers to allocate fertilizer supplies accounts for much of the inefficiency.

Table 1: Increase in Average Grain Production and Fertilizer Use by Region between 1978-74 and 1980-84

Region	Grain Production		Fertilizer Use	
	Total Increase	Share of World Increase	Total Increase	Share of World Increase
	(Million tons)*	(percent)	(Million tons)	(percent)
Asia	211.1	56	19.2	45
North America	86.0	23	4.6	11
Western Europe	31.1	8	2.8	7
Latin America	23.9	7	3.2	8
Eastern Europe and Soviet Union	8.8	2	10.7	25
Oceania	8.4	2	0.6	1
Africa	6.2	2	1.9	5
World	366.9	100	42.6	100

*Million metric tons

Sources: U.S. Department of Agriculture, Economic Research Service, "World Indices of Agricultural and Food Production 1950-85," unpublished printout, Washington D.C., April 1986; U.N. Food and Agriculture Organization, Fertilizer Yearbook (Rome: 1982 and 1984).

Average grain yields in the world's most populous countries reflect in part variations in rainfall and soil fertility, but they also illustrate the productivity gap that must be closed in the effort to raise the world's average yield above 2.0 tons per hectare. (See Table 2). The 11 countries shown in table 2 are home to nearly two thirds of the world's population and represent the entire economic and ecological spectrum. Slightly fewer than a third of the world's people live in four countries where land productivity, measured as tons of grain harvested per hectare of agricultural land, exceeds 3.5 tons, well above the world average. Another third live in the five countries where productivity is less than 2 tons per hectare. While

the highest yields occur in affluent industrial nations, China and Indonesia demonstrate that low income need not be associated with low yields.

Table 2: Land Productivity in World's 11 Most Populous Countries, 1985

Country	Average Grain Yield (tons per hectare)	Population (millions)
Japan	5.8	122
United States	4.8	241
China	3.9	1,050
Indonesia	3.7	168
Bangladesh	2.1	104
Mexico	2.1	82
Brazil	1.8	143
India	1.6	785
Pakistan	1.6	102
Soviet Union	1.6	280
Nigeria	0.8	105
Total Population		3,182

Sources: Population Reference Bureau, 1985 World Population Data Sheet (Washington, DC: 1985); U.S. Department of Agriculture, World Indexes of Agricultural and Food Production 1950-85," unpublished, Washington, D.C., April 1986.

The first step most countries can take to increase harvests is to correct the inefficient application of chemical fertilizers. Even China's high grain yield conceals a substantial opportunity to expand total harvests by distributing fertilizers more equitably to Chinese farmers. China's remarkable increase in food production from less than 200 million tons in the mid-seventies to over 300 million tons by 1985 was made possible in large part by an equally dramatic increase in fertilizer use. By 1983, Chinese farmers were applying 115 kilograms of artificial fertilizers per hectare planted, about as much as US farmers. But according to Bruce Stone of the International Food Policy Research Institute, most of this was d[illegible] for just a third of Chinese cropland, the [illegible]e country's most fertile and most market-oriented areas. Adding another sack of fertilizer to these fields now produces much less additional gain than fertilizing neglected areas. Distributing fertilizer to the other two thirds of Chinese cropland could yield three to 15 times more grain per ton of additional fertilizer than the State and market-oriented farms could produce under the existing distribution system. 6/

In addition, farmers achieve less than optimum production when they apply the nitrogen, phosphorus, and potash in artificial fertilizers in incorrect ratios. Nitrogen is often in short supply in Chinese soils, but if other nutrients are also lacking, just adding nitrogen cannot raise yields. Addressing the inequities in fertilizer distribution and correcting nutrient imbalances can increase food output faster and at lower cost than simply expanding fertilizer supplies, even in countries that now use little fertilizer. 7/

Another reason for using fertilizer more efficiently is the high environmental costs linked to heavy use. Government subsidies in Europe, Japan, and North America encourage farmers to expand production by applying more fertilizer than either sound agronomic practices or world market conditions warrant. One result of this subsidized over fertilization is that as much as one fourth of the nitrogen fertilizers used in these regions leaches into groundwater. Increasing concentrations of nitrates in drinking water, which pose a health threat to bottle-fed infants, have been reported in Denmark, England, France, Germany, and the Netherlands. Ironically, at the levels of fertilizer applied by European farmers, the losses of nitrogen may amount to 30 to 45 kilograms per hectare - more fertilizer than is applied to cropland in many third world countries. 8/

Farmers in Africa, Latin America, and Oceania have used the least additional fertilizer and contributed least to expanded food supplies. In Latin America, the challenge of managing enormous external debts has forced many countries to curtail imports of fertilizers in an effort to conserve foreign exchange for interest payments. In Africa, few farmers can afford conventional fertilizers, and limited water supplies often make them unprofitable. Yet, African and Latin American farmers need to expand food production, which has fallen behind population growth in both regions. Using additional fertilizer efficiently would help, but these farmers also need less costly alternatives to the conventional methods of raising productivity.

Correcting inefficiencies in the use of purchased resources is not the only way to raise and sustain agricultural productivity. As the circumstances facing Africa and Latin America suggest, helping farmers achieve more stable yields, manage soils and water supplies more effectively, and control spending on costly chemicals could make farming practices in many settings more sustainable. Redefining productivity to encompass these concerns could broaden options for poor farmers in developing countries and suggest new directions for financially strapped farmers in industrial countries.

Farmers have another set of productive resources that publisher Robert Rodale has aptly labelled the "internal resources" of agriculture: the inherent fertility of the soil, rainfall and climate patterns, the dynamics of pest populations and their natural enemies - in other words, the natural resource base. The productive potential of these internal resources is sometimes masked or even diminished by heavy use of artificial fertilizers and other farm chemicals. 9/

"The rapid introduction of external inputs into agricultural production over the past century has unnecessarily diminished the strength, vitality, and usefulness of the internal resources of farmers," Rodale argues. 10/ Research on nitrogen fixation by legumes shows how this can happen. Micro-organisms in the roots of these crops convert nitrogen from the air into a form plants can use; the excess that remains in the soil can help nourish a subsequent grain crop. Soil scientist David Bezdicek and his colleagues at Washington State University have found that residual nitrogen from artificial fertilizer can reduce the amount of nitrogen fixed by a legume crop such as chickpeas. A heavy dose of fertilizer applied at the start of the growing season suppresses biological activity, while in some cases a small amount of fertilizer can actually stimulate nitrogen fixation. More nitrogen might be supplied by the correct balance of artificial fertilizer and biological nitrogen fixation than by using artificial fertilizers alone. 11/

The regenerative approach seeks to maximize biological contributions to agricultural productivity. It makes the most of the natural sources of nitrogen, phosphorus, and potash, as well as the way these nutrients are cycled and conserved in natural ecosystems. Regenerative farming practices include sowing different crops together to use fully the soil's fertility, rotating food grains with nitrogen-fixing legumes, and planting trees and shrubs whose roots draw nutrients from deep soil layers to the surface. Purchased fertilizers and pesticides are used sparingly in these practices. Although regenerative methods require more careful farm management, they are less costly than conventional approaches. 12/

Agricultural research that emphasizes biological approaches to raising productivity can help poor farmers better cope with the risks imposed by erratic rainfall and less fertile soils. Conventional agricultural modernization, based on fossil fuels, is already beyond the means of many third world farmers. Offered better methods for managing their internal resources, these farmers can reduce their vulnerability to crop failure and famine.

Beyond the Green Revolution

Two decades have passed since new, high-yielding varieties of wheat and rice were introduced to farmers in Mexico, the Middle East, and South Asia. The new varieties, which were more responsive to artificial fertilizers and irrigation than traditional varieties, "spread more widely, more quickly, than any other technological innovation in the history of agriculture in the developing countries". 13/

Modern grain varieties were quickly taken up in Bangladesh, India, Pakistan, and throughout Southeast Asia. (See Figures 1 and 2.) In Latin America, the area planted to new wheat and rice varieties

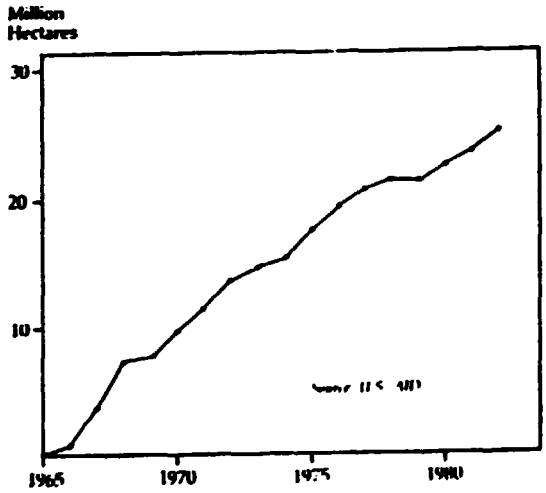

Figure 1: Area Planted to High-Yielding Varieties of Wheat in South Asia, 1965-82

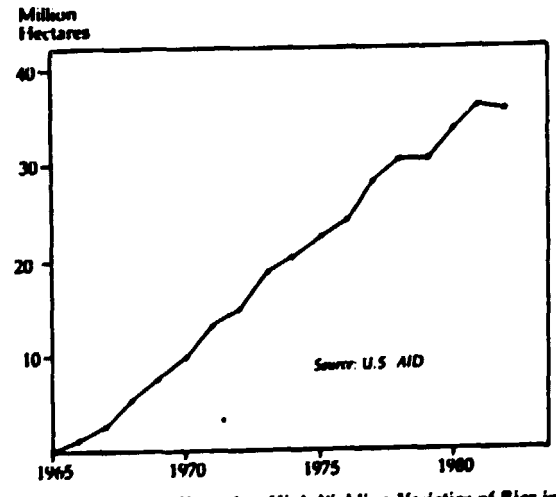

Figure 2: Area Planted to High-Yielding Varieties of Rice in Southeast Asia, 1965-82

increased from 270,000 hectares in 1970 to 9.6 million hectares by 1983. By the mid-eighties, roughly half the wheat area and nearly 58 per cent of the rice area of all developing countries had been sown to high-yielding varieties. In major wheat- and rice-growing regions, the percentages are far higher: 82 per cent of Latin America's wheat area and 95 per cent of China's rice area were sown to high-yielding varieties in 1983. 14/

The amount of rice and wheat grown in developing countries increased 75 per cent between 1965 and 1980, while the area planted to those crops expanded by only 20 per cent. The ability to harvest two crops a year with the new seeds contributed to these increases. In 1980, the additional wheat and rice produced by green revolution technologies were worth an estimated $56 billion, of which $10 billion was due to the improved genetic potential of the new varieties. This expansion of the food supply is crucial to many countries with rapidly growing populations. As Michael Lipton of the University of Sussex wrote in 1985, "If the farmers of the third world today used the same cereal varieties as in 1963-1964, and everything else were unchanged, then tens of millions of people would this year die of hunger." 15/

Africa benefited least from the green revolution. Few of Africa's 50 million rural families grow wheat or rice, and only in the last decade have researchers turned their attention to millet, sorghum, cassava, yams, and cowpeas that are the subsistence staples of most rural Africans. Only 6 per cent of sub-Saharan Africa's wheat and rice area is planted to modern varieties. Improved maize varieties and hybrids have boosted harvests in countries including Kenya, Zimbabwe, and South Africa, but on the whole, scientific plant breeding has not decisively changed the continent's food prospects. And Africa's conditions are not unique; many farmers in Latin America and Asia are still prevented from planting improved varieties by poor soils, erratic water supplies, and poverty. 16/

High-yielding varieties of wheat and rice are still spreading, however. Though the early green revolution seeds were planted almost exclusively by farmers with well-irrigated land who could afford to purchase the necessary supplements of fertilizers and pesticides, modern varieties are now grown by farmers under less-favoured circumstances. More than half of the high-yielding wheat in Bangladesh is watered only by rain, as is about 85 per cent of the high-yielding rice in the Philippines. Varieties bred and released today perform better than traditional varieties even without costly inputs. 17/

The green revolution's early benefits were by no means equally shared. Relatively prosperous farmers who controlled more land, and so had the financial means to purchase fertilizers, pesticides, and equipment, gained most by adopting high-yielding wheat and rice. Small farmers in areas favoured by abundant water, who tended to adopt new varieties and technologies later, also profited, but not as much. Grain prices dropped because of bigger harvests on the larger landholdings. Consumers enjoyed the lower food prices - or at least the brake on price increases - that expanded harvests made possible.

Governments also gained. India, for example, used the expanded production of the late sixties to offset its dependence on costly grain imports rather than to significantly increase food consumption among its poor. A drain on the country's treasury was plugged but there was little progress in raising per capita food consumption. 18/

Others, however, lost from the new technologies. The biggest losers were farmers in areas where the new varieties performed poorly, and those growing crops primarily for subsistence. These farmers earned no new income from bigger harvests, and may have become poorer as prices for their occasional marketable surpluses declined. On some

300 million hectares in the third world, supporting over a billion people, productivity has not measurably improved. 19/

That the record of the green revolution is mixed should come as no surprise. The scientists who developed the new varieties of wheat and rice never expected their work to provide an open-ended solution to the world's food problems. Many believed that the new technologies offered a means to buy time until population growth rates could be slowed. Harvests could not increase indefinitely; birth rates would have to fall. Twenty years later, countries like China that both promoted new seeds and instituted economic reforms and national family-planning programmes to lower birth rates have done the most to improve the welfare of their people.

The unique research network launched by the Rockefeller Foundation in Mexico in 1943 may be a more significant contribution of the green revolution than the expanded harvests achieved so far. Supported by the Rockefeller and Ford Foundations, plant breeders developed new crop varieties appropriate for conditions in Mexico, Pakistan, India, and Turkey. Success in these countries led to the creation of the Philippines-based International Rice Research Institute (IRRI) in 1962, the International Center for the Improvement of Maize and Wheat near Mexico City in 1965, and ultimately to the creation of a system of 13 international agricultural research centres funded through the Washington-based Consultative Group on International Agricultural Research (CGIAR). The research agenda of the centres today covers 21 food crops, conservation of the genetic resources used for plant breeding, animal husbandry and livestock diseases, and policy issues related to agricultural research. 20/

A high priority of the CGIAR centres is the need to defend the gains already achieved. Farmers who plant high-yielding varieties of wheat and rice need continuous research to sustain their yields. This "maintenance research" emphasizes breeding crop varieties to increase their natural ability to resist pests and disease. Maintaining stable yields at high levels can be a more complex task than raising yields in the first place. New plant varieties must be on hand to replace old ones that succumb to pests and disease. This requires a vast breeding programme and an extensive system of gene banks. 21/

National and international research programmes are turning to a new challenge: developing crops and technologies for farmers who do not irrigate their fields and who lack the income to purchase fertilizers and pesticides. The rice-breeding agenda at IRRI illustrates the shift in research priorities that will help meet their needs. In the sixties, the effort to raise yields of irrigated rice led to IR-8, IRRI's first widely planted high-yielding variety. When IR-8 began to experience serious pest infestation, breeders sought a wider variety of agronomic traits. IR-36 combined high yield with broad genetic resistance to pests, and it matured even more quickly than earlier varieties, permitting two crops to be harvested each year. IRRI's next successful rice strain, IR-64, was selected both for its broad resistance to pests and disease and for its more flavourful grain. 22/

In the eighties, breeders have further expanded their goals to developing rice varieties suited to adverse growing conditions - varieties that will be profitable for marginal and disadvantaged farmers. IRRI's breeding goals have evolved from a nearly exclusive emphasis on achieving peak yields with inputs of water and fertilizer to dependable production under a range of farming conditions.

In addition to appropriate crop varieties, poor farmers need alternative sources of plant nutrients. IRRI has begun to investigate opportunities to substitute farm-grown nutrient sources for purchased artificial fertilizers. Promising approaches for Asian farmers include the nitrogen-fixing blue-green algae sustained by a fern called Azolla that thrives in flooded rice paddies, and types of bacteria that could enhance soil fertility. Chinese farmers already use some of these methods quite successfully, and researchers in the Philippines have found that farmers who grew Azolla in their paddies were able to reduce their use of purchased fertilizer by 50 per cent without lowering yields. 23/

Such innovations are not restricted to Asia. Scientists at the International Institute of Tropical Agriculture in Nigeria have identified a leguminous African shrub called Sesbania that may prove to be a low-cost nitrogen source for African rice farmers. Research in Colombia indicates that farmers can cut their needs for phosphate fertilizers in half by using certain fungi that help plant roots absorb phosphorus. IRRI recently created the International Biofertilizer Germplasm Conservation Center at its Philippines headquarters, where promising microbial sources of plant nutrients can be evaluated, stored, and distributed to researchers all over the world for testing. 24/

A range of other food crops is beginning to receive deserved research attention. Wheat and rice tend to be grown under relatively homogeneous conditions. Breeders of these crops drew on an enormous backlog of improved wheats and rices already available in Japan and North America, varieties whose pedigrees predated World War II. By contrast, improving the staple crops widely grown in Africa, and the potatoes, yams, and legumes grown throughout the third world, is a much more challenging task. Such crops grow under widely divergent conditions, and have no comparable history of improvement. Systematic work on cassava and cowpeas in West Africa or potatoes in the Andes is little more than a decade old.

Efforts to raise the productivity of all staple crops in the years ahead depend on gathering a wide range of traditional varieties, crop relatives, and wild plants for breeding. Breeders need this genetic sampling to select the traits that strengthen resistance to pests and disease, and to tailor crops to grow under varied ecological conditions. Collecting and storing crop germplasm is co-ordinated by the International Board for Plant Genetic Resources (IBPGR). It is now a major responsibility of all the international centres. The value of distant crop relatives is likely to increase as biotechnology techniques are introduced that can speed up and simplify the tasks of breeding new varieties. IBPGR has initiated genetic resources programmes in 50 countries, and national committees concerned with conservation of germplasm have been set up in over two dozen others. 25/

For most major food crops, germplasm collections of modern and traditional crop varieties are impressively broad. (See Table 3.) Except for wheat, however, scientists have not thoroughly investigated or collected the wild relatives of these crops. The unique genetic combinations of wild crop relatives are often lost as modern varieties and monocultures replace traditional farming methods. Such wild species may hold the key to improvements in the productivity of crops like sorghum and cowpeas that are crucial to Africa's food prospects.

Most of the world's food is supplied by a handful of crops selected by our neolithic ancestors. While farming technologies have advanced

Table 3: Estimated Number of Germplasm Samples Collected for Major Food Crops, and Coverage of Traditional Varieties and Wild Species

Crop	Samples in Major Genebanks	Estimated Share of Diversity Collected	
		Traditional Varieties	Wild Species
	(thousands)	(percent)	
Wheat	400	95	60
Rice	200	70	10
Maize	70	90	—
Barley	250	40	10
Sorghum	90	80	10
Potato	42	95	—
Cowpea	18	75	1

Source: Adapted from Consultative Group on International Agricultural Research, "International Agricultural Research Centers: Achievements and Potential," unpublished draft, Washington D.C., August 1985

steadily, there have been few significant botanical innovations since the origins of agriculture. Most international research deals with just 16 widely grown crops, although at least 3,000 plants have been used for food at one time or another in history. Crops like teff, a hardy grass grown as a staple grain in Ethiopia, or amaranth, a grain and vegetable crop native to the Americas that is both nutritious and drought-tolerant, may prove better-suited than conventional crops to the environmental and economic conditions facing many third world farmers. 26/

The network of international research centres may not be the well-spring of work on promising but unproven crops. By their charters, the centres are instructed to work on the most widely grown food crops. Research efforts focus on crops with proven potential and regions where the return to research investment is likely to be high. But restricting research to familiar crops may foreclose some important agricultural opportunities.

Naturalist Gary Nabhan, who has studied traditional food and medicinal plants native to the Sonoran Desert in the southwestern United States, believes that research on unconventional crops may be as valuable for insights on how to manage familiar crops as for novel agronomic possibilities. He writes, "By evaluating native desert plants as potential economic resources, and comparing them with conventional crops, we stand to learn something about the tradeoffs between short-term productivity and long-term persistence in unpredictable environments." 27/

Independent research centres have an important role to play in pursuing the agricultural opportunities that fall outside the mainstream of international research. The privately funded Rodale Research Center in Pennsylvania co-ordinates worldwide research on amaranth and maintains a germplasm collection containing 1,300 amaranth samples from Asia and Latin America. Scientists at Rodale and at the Land Institute in Kansas are investigating perennial grain polycultures as possible alternatives to today's annual corn and wheat monocultures, particularly for marginal lands. Agriculture based on perennials, though probably decades away, would offer several advantages over current practices, including reduced soil erosion, simplified weed control, improved water management, and enhanced soil fertility. Understanding perennial-based cropping practices could shed new light on how to reduce the environmental impact of more conventional farming practices. 28/

New crop varieties and technologies for farmers in developing countries will be essential in the years ahead. Biotechnologies may provide new generations of crop varieties to farmers left out of the green revolution. But to avoid the environmental and social costs associated with the last generation of agricultural technologies, tomorrow's innovations will have to be more consistent with regional agricultural traditions and better matched to the ecological context into which they are introduced.

Rediscovering traditional agriculture

Agricultural research has been needlessly hindered for two decades by pejorative attitudes toward traditional farming. Some scientists assumed that because peasant farmers produced low grain yields, their practices had little relevance to twentieth-century agriculture. Until recently, few researchers recognized the ecological and agronomic strengths of traditional practices that had allowed farmers over the centuries to maintain the land's fertility. In pursuit of higher productivity, many agricultural scientists overlooked the need for long-term sustainability.

Economic analysis reinforced the belief that traditional practices had little to offer in solving contemporary agricultural problems. In Transforming Traditional Agriculture, published in 1964, University of Chicago economist Theodore Schultz argued that peasant farmers were rational and efficient individuals who had reached the limits of their technologies. His conclusion: No significant increase in harvests could be achieved using only the resources and methods that traditional farmers had at their command. Schultz advocated investments in agricultural research, new technologies, and rural education that would allow traditional farmers to choose innovations to increase their productivity. 29/

Many scientists and policymakers, however, saw traditional methods as an obstacle to be eradicated rather than a basis for introducing new seeds and farming methods. The food crisis in India and throughout Asia in the late sixties lent a sense of urgency to efforts to promote the green revolution. The strengths of traditional practices and the reasons for their persistence were swept aside. A report by US President Lyndon Johnson's Science Advisory Committee warned in 1966 that "the very fabric of traditional societies must be rewoven if the situation is to change permanently." 30/

Agricultural scientists have recently begun to recognize that many farming systems that have persisted for millennia exemplify careful management of soil, water, and nutrients; precisely the methods required to make high-input farming practices sustainable. This overdue reappraisal stems in part from the need to use inputs more efficiently, and in part from the growing interest in biological technologies. The complex challenge of Africa's food crisis in the early eighties forced scientists to look more closely at the methods used by peasant farmers. Many researchers today seek to "improve existing farming systems rather than attempting to transform them in a major way", according to William Liebhardt, director of research at the Rodale Research Center. 31/

Traditional farming systems face real agronomic limits, and can rarely compete ton for harvested ton with high-input modern methods. It is important to recognize these limitations, for they determine both how traditional practices can be modified and what such practices can contribute to the effort to raise agricultural productivity.

First, most traditional crop varieties have limited genetic potential for high grain yields. They are often large-leaved and tall, for example. These traits help farmers meet nonfood needs, supplying thatch, fuel, and fodder as well as food to farm households. Traditional varieties respond

poorly to the two elements of agronomic management that make high grain yields possible: dense planting and artificial fertilizer. Despite these limitations, traditional varieties also contain genetic diversity that is invaluable to breeders in search of genes for disease- and pest-resistance and for other traits. 32/

Second, peasant farmers often have to plant in soils with serious nutrient deficiencies, where crop combinations and rotations are needed to help offset the limitations. Many tropical soils, for instance, lack sufficient nitrogen to sustain a robust crop. Soils in vast areas of semiarid Africa are deficient in phosphorus. High-yielding varieties, more efficient in converting available nutrients into edible grain, can rapidly deplete soil nutrients if they are planted in monocultures by peasant farmers who cannot afford to purchase supplemental fertilizers. 33/

Traditional agriculture, practised under biological and physical limitations, often breaks down under growing population pressure. As rural populations grow, farmers try to squeeze more production from existing fields, accelerating the loss of fertility. Or they may cultivate new, marginal, or sloping land that is vulnerable to soil erosion and unsuited to farming.

None the less, traditional methods can make an important contribution to efforts to raise agricultural productivity. They offer what Gerald Marten of the East-West Center in Hawaii calls "principles of permanence". They use few external inputs, accumulate and cycle natural nutrients effectively, protect soils, and rely on genetic diversity. "Neither modern Western agriculture nor indigenous traditional agriculture, in their present forms, are exactly what will be needed by most small-scale farmers," says Marten. "The challenge for agricultural research is to improve agriculture in ways that retain the strengths of traditional agriculture while meeting the needs of changing times." 34/

Farming methods like the traditional agroforestry systems of West Africa's Sahel region offer improvements in water-use efficiency and soil fertility that subsistence farmers can afford. Sahelian farmers traditionally planted their sorghum and millet crops in fields interspersed with a permanent intercrop of *Acacia albida* trees. Acacia trees fix nitrogen and improve the soil. In the Sahel, grain yields are often highest under an acacia's crown. 35/

Fields that include acacia trees produce more grain, support more livestock, and require shorter fallow periods between crops than fields sown to grain only. *Acacia albida* naturally enhances productivity by returning organic matter to the topsoil, drawing nutrients from deep soil layers to the surface, and changing soil texture so rainwater infiltrates the topsoil more readily. All of these benefits make farming on marginal lands more productive and profitable without requiring the farmer to purchase fertilizers year after year. 36/

Equally important, such improvements in soil structure, organic matter content, water-holding capacity, and biological nitrogen fixation allow the most productive application of conventional fertilizers. Programmes promoting acacia-based agroforestry could complement fertilizer extension in semiarid countries - agroforestry playing a role analogous to irrigation. Governments that have modest fertilizer-promotion programmes may find that they can maximize the benefits from fertilizer by promoting agroforestry as well. 37/

Legume-based crop rotations and traditional intercropping systems husband organic material and nutrients much more carefully than do modern monoculture practices. While organic manures and composts contribute significant amounts of nutrients in their own right, they can, like agroforestry, also magnify the contribution of small amounts of artificial fertilizers.

Research in Burkina Faso illustrates the complementary effect. (See Table 4.) This study looked at the contributions of straw, manure, and compost to sorghum yields with and without the addition of small amounts of artificial nitrogen. The results show that the most productive organic method, applying compost, can increase sorghum yields from 1.8 tons per hectare to 2.5 tons. Artificial fertilizer alone produced grain yields slightly higher than any of the organic practices. But the best result was achieved by combining compost with artificial fertilizer; this raised sorghum yields to 3.7 tons per hectare. The three organic practices increased the efficiency of nitrogen application by 20 to 30 per cent. Given responsive crop varieties and small amounts of artificial fertilizer, traditional practices that cycle organic materials effectively would raise yields in the same manner. 38/

Table 4: Complementary Effect of Artificial and Organic Fertilizers on Sorghum Yields in Burkina Faso, 1981

Treatment[1]	Sorghum Yield	
	Without Artificial Nitrogen	With 60 kg/ha Nitrogen
	(metric tons per hectare)	
No Organic Treatment	1.8	2.8
Sorghum Straw	1.6	3.4
Manure	2.4	3.6
Compost	2.5	3.7

[1] All organic materials applied at a rate of 10 tons per hectare.

Source: M. Sedogo, "Contribution à la valorisation des résidus culturaux en sol ferrugineux et sous climat semi-aride," doctoral thesis, Nancy, France, 1981, quoted in Herbert W. Ohm and Joseph G. Nagy, eds., *Appropriate Technologies for Farmers in Semi-Arid West Africa* (West Lafayette, Ind.: Purdue University International Programs in Agriculture, 1985).

Some conventional analysts looking at the study would argue that fertilizer outperforms the organic practices. Yet exclusive reliance on fertilizer would sacrifice a significant part of the additional harvest. As French researcher Christian Pieri, who has worked in West Africa, points outs, "Fertilization is a prime technique for increasing agricultural productivity in this part of the world, but in order to obtain a greater and lasting production it is indispensable to combine the effects of mineral fertilizers, the recycling of organic residues and biological nitrogen fixation, and also to optimize the use of local mineral resources such as natural phosphates." 39/ Neglecting the local internal resources can undermine a farmer's investments in conventional inputs.

Intercropping, agroforestry, shifting cultivation, and other traditional farming methods mimic natural ecological processes, and the sustainability of many traditional practices lies in the ecological models they follow. This use of natural analogies suggests principles for the design of agricultural systems to make the most of sunlight, soil nutrients, and rainfall.

Shifting cultivation practices, such as bush-fallow methods in Africa, demonstrate how farmers can harness the land's natural regeneration. Farmers using bush-fallow systems clear fields by burning off the shrubs and trees. Ashes fertilize

the first crop. After a couple of seasons, as nutrients are depleted, harvests begin to decline, so farmers abandon the field and move on to clear new land. Natural regeneration takes over; shrubs and trees gradually reseed the field, returning nutrients to the topsoil and restoring the land's inherent fertility. After 15 to 20 years, the land can be burned and cultivated again. 40/

The bush-fallow system has obvious limitations. It requires enormous amounts of land, and when population growth pushes farmers to return too quickly to abandoned fields, serious environmental deterioration can result. Declining land productivity in crowded countries like Rwanda is testimony to this danger. But even disintegrating systems offer a basis for designing productive and sustainable farming practices.

Researchers at the International Institute of Tropical Agriculture, for instance, have adapted the principles of natural regeneration in bush-fallow systems to a continuous-cultivation agroforestry system called alley cropping. Field crops are grown between rows of nitrogen-fixing trees; foliage from the trees enhances soil organic matter, while nitrogen fixed in root nodules increases soil fertility. A high level of crop production is possible without a fallow interval. Traditional shifting cultivation provided the model for this system. 41/

Conventional research tools can also be used to overcome the agronomic constraints that have limited traditional systems to low productivity. For decades, crop breeders have tailored varieties to respond to high levels of artificial fertilizers, assured water supplies, and dense monoculture plantings. Working with the genetic diversity available in traditional crop varieties, they can apply the same breeding methods to produce varieties better matched to the conditions faced by subsistence farmers. At an Agency for International Development workshop on regenerative farming practices, Charles Francis of the University of Nebraska concluded, "A new generation of varieties and hybrids adapted to marginal conditions and to intercropping could be the start of a new revolution aimed at meeting the needs of the majority of limited resource farmers in the developing world." 42/

Traditional practices exemplify efficiency and the regenerative approach to agricultural development. Yet until recently, a kind of myopia has kept the research community from recognizing the opportunities for agricultural innovations that lie in traditional practices. In West Africa, for example, 70 to 80 per cent of the cultivated area is sown to combinations of crops in traditional intercropping systems. Cowpeas, one of Africa's most widely grown food staples, are always planted as an intercrop. But only about 20 per cent of the research effort in sub-Saharan Africa focuses on intercropping. 43/

As the African examples described here show, researchers can use traditional principles to develop new techniques that preserve the land's stability and productivity even as populations increase. Though traditional methods have limitations, they are not archaic practices to be swept aside. Traditional farming constitutes a foundation upon which science can build.

Toward appropriate biotechnology

Most agricultural innovations of the past have been based on gradual refinements of technologies known at least since the Industrial Revolution and in some cases since the dawn of farming. But the 1953 discovery of the structure of DNA and the 1973 development of "recombinant DNA", or gene-splicing techniques, promise to change irretrievably the familiar landscape of agricultural development. Biotechnologies based on these insights allow scientists to identify the genes that control certain physical traits and to combine the genes of distantly related or unrelated plants and animals - two barriers that conventional plant breeders have never been able to overcome. Many analysts believe that agricultural applications of biotechnology will mark a watershed in the effort to raise productivity.

From 1920 to 1950, agriculture in industrial countries was dominated by mechanical technologies that dramatically increased the amount of food produced per worker and per hour. Shortly after World War II, the mechanical age gave way to the chemical age as farmers worldwide began to adopt artificial fertilizers and synthetic chemical pesticides, which vastly expanded their harvests per hectare. Biotechnologies shift the focus of research toward crop plants themselves. They have inaugurated a new era of agriculture likely to reshape research, development assistance, and farmers' choices. Biotechnologies may offer cheaper and quicker ways to improve third world staples - including millet, cassava, and yams - than the costly innovations of the mechanical and chemical eras. 44/

Biotechnology encompasses an array of tools and applications that allow researchers to manipulate the genetic material of plants, microbes, and animals. These methods provide ways to modify the characteristics that are passed from one generation to the next. The vaccines, antibiotics, and reproductive technologies created through biotechnology and genetic engineering are already revolutionizing animal husbandry. Biotechnologies are not yet as widely applied to cultivated crops, in part because scientists understand less about plant genetics and physiology than about domestic animals.

Technical hurdles are not the only constraints on agricultural applications of biotechnology. So far, advances have been made in industrial countries, where public scrutiny is intense. The environmental risks posed by releasing gene-spliced microbes or plants into the environment remain poorly understood. Developing guidelines for the newly emerging technologies has led to a contentious public debate about genetic engineering. In the United States, debate has centred on proposals to release bacteria modified to retard the formation of frost on strawberry and potato plants. Because the bacteria could reproduce in the natural environment and thus spread beyond the fields where they were released, predicting environmental impacts is both more crucial and more complex a task than with many other technologies. Developing the "predictive ecology" that critics say is necessary for thorough environmental review, and enacting regulations that guard against the uncertainties will slow the marketing of commercial biotechnology products to industrial country farmers. 45/

The genetic engineering of plants is far more complex than modifying microbes, but it is also less controversial on environmental grounds. Crops with modified traits are under a farmer's direct control, and their reproduction and spread in the environment are both slower and more predictable. Crop characteristics like drought-tolerance, ability to withstand salty water, and pest resistance - the traits that have always concerned breeders - are a likely focus of the new technologies.

Thus, the major applications of biotechnologies to third world crops will complement rather than replace conventional plant breeding. Developing new

crop varieties can be an extraordinarily complex and time-consuming process. Identifying desirable characteristics, crossing parents, planting and growing the first generation of the cross, selecting the progeny that have the right mix of desired traits, and refining those characteristics through further breeding and screening can easily take a decade or longer. Conventional breeding of a new variety of wheat may involve thousands of carefully selected crosses.

By contrast, tissue culture, gene transfer, and other genetic techniques allow much of this work to be done in the laboratory, because researchers can manipulate single cells rather than entire plants. This saves space and time. Gene-splicing techniques allow researchers to transfer only specific traits into a crop. Such precision can help reduce the need to identify and eliminate full-grown plants carrying undesired genetic baggage - a problem when distantly related species or varieties are crossed.

Tissue culture techniques may revolutionize international gene banks by making it easier to store and manipulate crops that do not reproduce by setting seeds. These methods - which allow single plant cells to be sustained in laboratory flasks, multiplied, and regenerated into adult plants - are especially important for crops that propagate by roots or cuttings, such as cassava, potatoes, and yams. Tissue culture is also useful for propagating slow-growing species, including trees that hold promise for reforestation. 46/

Given the ability to modify virtually any plant characteristic and to tailor plants in precisely defined ways, biotechnology would seem to offer tools well-suited to agricultural development strategies that emphasize resource efficiency and farming's internal resources. According to the US Office of Technology Assessment, "Most emerging technologies are expected to reduce substantially the land and water requirements for meeting future agricultural needs." 47/ For example, it should eventually be possible to modify a plant's physiology to improve its efficiency in photosynthesis, enabling grains to produce more carbohydrate and thus, higher yields. The adaptations that allow some plants to lose very little water through their leaves in transpiration, transferred to more widely grown crops, could reduce irrigation needs. Developments like these could indeed diminish pressures on marginal lands and perhaps eliminate the need for costly capital investments in water supply projects.

There is nothing in the nature of biotechnologies that renders them inherently appropriate to a strategy of efficiency and regeneration, however. Many biotechnology innovations pose trade-offs rather than clearcut benefits. Although increasing photosynthetic efficiency could raise yields, it would likely lead to accelerated depletion of soil nutrients and heavier dependence on artificial fertilizers.

Another trade-off centres around herbicide resistance, a relatively uncomplicated genetic trait, which makes it an attractive research target. Researchers have already put considerable effort into developing crop plants that resist herbicides, allowing farmers to apply more of these chemicals. Much of this work is supported by the chemical companies that market herbicides. 48/

Herbicides have to come to play a major role in industrial-country farming in recent years. High fuel costs and the need to conserve soil have prompted US farmers to adopt reduced-tillage practices on 42 million hectares. These methods, which involve less ploughing and leave topsoil covered with crop residues, employ herbicides rather than cultivation to control weeds. Conservation tillage is no longer restricted to industrial countries; scientists at the International Institute of Tropical Agriculture are also investigating more labour-intensive forms of these practices for small farmers to protect fragile tropical soils. In both industrial and developing countries, the soil- and energy-saving benefits of conservation tillage practices could be offset by the hazards of increased reliance on chemical herbicides. 49/

The most significant factor that will affect the direction of agricultural biotechnology is the rapid shift of research from the public to the private sector. This is especially evident in the United States. For nearly a century, public agricultural experiment stations and land grant universities sponsored by the US Department of Agriculture (USDA) performed most agricultural research. Private seed companies often used the plant varieties developed by government-supported breeders. Over the last three decades, however, the private sector has assumed control of research efforts. Private companies now perform two thirds of US agricultural research. 50/

In biotechnology, the deck is stacked even further in favour of the private sector. USDA's Agricultural Research Service and Co-operative State Research Service support most public work in agricultural biotechnology, and these two federal programmes spent less than $90 million on biotechnology research in 1984-1985. Monsanto, which has the largest but by no means the only plant biotechnology research programme among private US corporations, has already invested $100 million in agricultural biotechnology development. Biotechnologies that affect agriculture in the years ahead will have a decidely private-sector cast. With the exceptions of mechanization and the development of hybrid corn, that has not generally been true of important innovations in agriculture. 51/

Leaving research priorities to the marketplace may eclipse promising opportunities. Research efforts on crops will be proportional to the value of the crop and the size of the market. Because improving crops for small farmers in developing countries means producing low-cost agronomic innovations, many of which must be site-specific and thus not suitable for mass-marketing, crop improvement for the vast majority of the world's farmers offers little profit. New private companies are likely to enter such an unpromising market. Consequently, investigations of minor crops like sorghum and millet, grown primarily by third world subsistence farmers, will be neglected.

National research programmes and the international research centres have an obvious stake in applying biotechnology. Refinements in plant breeding, technologies for germplasm storage and for plant evaluation and propagation, and new alternatives in pest control are exactly the kinds of innovations scientists need to extend research on developing-country food crops. It took decades of work to produce high-yielding varieties of wheat and rice. With biotechnology, comparable improvements in millet, sorghum, cassava, or tropical legumes could come more quickly.

The private-sector domination of biotechnology raises questions about the role new technologies will play in international research programmes. Private companies may become competitors with the CGIAR-sponsored centres, particularly when it comes to improvements in major, widely traded crops like wheat and rice. The full exchange of scientific information that is essential to the international centres may be curtailed if it appears to compromise proprietary corporate research. Moreover, international centres may increasingly have to

purchase or license new technologies that were formerly freely available through public channels. Finally, private firms will compete with the centres for scientific talent, and the centres may be unable to match the salaries, facilities, and security that corporate laboratories offer. 52/

Uncertainties cloud the prospects for national biotechnology programmes as well. A few developing countries, notably Indonesia, the Philippines, and Thailand, have established national programmes in agricultural biotechnology. The Philippines views its programme as the first step toward an industrialization strategy based on biological materials that can help free the country from dependence on imported oil. Philippine scientists hope to use crop residues and by-products as raw materials to produce liquid fuels and industrial chemicals, and to develop food-processing industries with biotechnology methods. W. G. Padolina, of the National Institute of Biotechnology and Applied Microbiology at the University of the Philippines, writes, "The national strategy is to transform biomass biologically into food, fuel, fertilizers, and chemicals." 53/

Achieving these goals is certain to be costly. Few countries can afford the investment in equipment that major biotechnology programmes entail, and some countries lack sufficient trained scientists to staff such programmes. Agricultural biotechnology contrasts sharply in this regard with conventional plant-breeding programmes, which require relatively modest capital investment.

Biotechnologies offer promising tools for more resource-efficient and sustainable agriculture. Technical hurdles must be overcome and environmental risks evaluated before that potential can be realized. But more troublesome from the standpoint of third world agriculture is the degree to which the private sector will dominate agricultural biotechnologies. An expanded commitment to public research, at both the national and international levels, is needed to correct distortions of the research agenda and ensure that third world priorities command attention. Public research in biotechnology consistent with resource-conserving and low-cost farming practices could counterbalance private-sector priorities.

Research for sustainable agriculture

The sense of urgency with which the green revolution was launched has largely disappeared from international agricultural development efforts. That several developing countries, formerly food importers, now have achieved food self-sufficiency has led some policymakers to question the value of assisting poor countries to increase food production further. But for third world farmers who never shared in the agricultural advances of the green revolution, the issue is economic survival. Only by husbanding their scarce resources, regenerating their land, and raising their yields can these farmers improve their economic prospects. The reorientation of agricultural research and development assistance to meet their needs has begun, but deserves more attention and support.

An important bellwether of trends in international agricultural research is the funding of the world's 13 CGIAR-sponsored research centres. The budget grew from $21 million in 1972, when the system included just four centres, to over $100 million by 1980. This growth expanded the research mission to new crops and ecological zones. Spending increased more slowly to a level of about $170 million by the mid-eighties. While support for the centres remains strong, sufficient financial resources in the years ahead to underwrite more complex research tasks and changing technologies are by no means assured. 54/

CGIAR centres have established an important foundation of basic knowledge about staple food crops in the last 15 years. Opportunities to apply that knowledge could slip away if funding support stagnates. A large measure of responsibility for adapting crop research to local conditions rests with national research programmes. Scientists at CGIAR hope that national programmes will assume most of the responsibility for crop breeding in the years ahead. This would allow the international centres to focus on more "strategic" issues, including co-ordinating the conservation of crop genetic resources and applying biotechnology to staple crops. 55/

The international research agenda is shaped as much by new technologies as by critical agricultural needs. Biotechnology, now the principal focus of private-sector agricultural research, has captured the limelight; research administrators are scrambling to hire molecular biologists and redirect research programmes. Taking this trend too far could be a serious mistake for public research institutions worldwide. As Cornell University sociologist Frederick Buttel counsels, "One must be cautious in assuming that there is only one scientific trajectory along which agricultural practices evolve." 56/

After supporting much of the work that led to the green revolution, the Rockefeller Foundation is now looking at ways to apply biotechnology to the crops overlooked by private-sector research. In 1983, the foundation redirected its programme in agricultural sciences to emphasize biotechnology research on rice, the grain of least interest to private firms in industrial countries. In 1986, the foundation outlined a new agenda that includes plans to extend biotechnology research to the improvement of sorghum, millet, and other neglected staple food crops - partly to counterbalance the private-sector emphasis on more widely grown commercial crops. 57/

The public research agenda can complement and compensate for the interests of the private sector in other ways as well. One way is to focus some portion of agricultural research on ecology. Robert Barker of Cornell University argues that public institutions like the US land grant universities should shift their attention to the "development of the ecosystem sciences". 58/ Agricultural technologies and practices that emphasize efficient use of resources and regenerative approaches are more likely to draw on the insights of ecology and evolutionary biology than on biochemistry.

In the past, responsibility for advances in resource efficiency and regenerative approaches has been left to independent institutions like the Rodale Research Center and some US universities that have developed programmes in agroecology. Participants in a 1980 Office of Technology Assessment workshop on biological technologies for agriculture noted that "much of the development of innovative technologies is occurring outside of, and perhaps in spite of, the national and international institutions normally considered responsible for maintaining natural resources and for dealing with problems of land quality and productivity". 59/ That bias is slowly changing.

At the international level, the CGIAR centres have begun to acknowledge the importance of agricultural sustainability. The directors of the centres agreed in May 1986 to devote more research to raising crop productivity in ways that avoid environmental deterioration. The new emphasis on resource management goes beyond crop yield to encompass soil conservation, water management, and ways to help farmers reduce their reliance on purchased chemicals and fertilizers. In addition, the centres will work to develop technologies that can restore degraded croplands. 60/

The 230 million rural households in Africa, Asia, and Latin America that this research must reach are more isolated and face a far more complex set of agricultural constraints than their market-oriented counterparts. Actual conditions, rather than the ideal conditions in the experimental fields of research stations, determine the success or failure of new seeds, tools, or farming practices. Several international research centres have adopted a new approach to better understand the constraints faced by farmers on marginal lands. "Farming systems research" involves farmers and rural households directly in the research process. But how can the comparative handful of scientists in national and international research begin to reach a quarter of a billion households and refine technologies that match their individual circumstances? The answer must be a far more decentralized research effort that builds on farmer-scientist collaboration and equips farmers to produce innovations for themselves. 61/

The reappraisal of traditional practices is a step toward this collaboration. According to Paul Richards of University College in London who has worked with Nigerian farmers, indigenous agricultural knowledge is "the single largest knowledge resource not yet mobilized in the development enterprise". In his book, Indigenous Agricultural Revolution, Richards documents how traditional farmers in West Africa have modified farming practices on the basis of carefully controlled experiments, ranging from selection of rice varieties to the control of grasshoppers. He suggests that mainstream researchers have as much to learn from the partnership with small farmer as the farmers themselves. 62/

The challenge for agricultural research at all levels is no longer a problem of one-way "technology transfer", as so many people perceived the green revolution. Innovations and insights that help raise agricultural productivity will flow in both directions - between researchers and farmers, between developing and industrial countries. Success in the low-productivity fields of the third world can suggest new ways of managing agricultural resources that farmers in Iowa or France could employ as well.

The conservation and use of crop genetic diversity illustrates the international convergence of interests in raising agricultural productivity in the third world. The tools of biotechnology are needed to store, evaluate, and manipulate the genes in traditional crop varieties and wild plants needed for crop breeding. Yet much of the diversity itself still resides in farmers' fields, where crops are adapted to the idiosyncracies of local rainfall, soils, and cultivation methods. "Neither money, talent and technology, nor unimproved germplasm alone can create improved crop plants - the former must be applied to the latter," points out Steven Witt in his book Biotechnology and Genetic Diversity. "And that means co-operation between those who have the talent and technology and those with the necessary germplasm." 63/

The world is far from having solved the problems of agricultural productivity. The conventional approach to raising productivity - combining new crop varieties with fertilizers, pesticides, and heavy use of energy - succeeded dramatically in increasing food production in industrial countries and in parts of the third world. But new approaches are needed to reach farmers who could not afford the conventional technologies, as well as to correct inequities in the distribution of resources and confront widespread environmental problems. Complementing the use of conventional resources with innovative biological technologies that maximize agriculture's internal resources can ensure the affordable and sustainable gains in agricultural productivity that the world needs in the years ahead.

Notes

1. Data on adoption of high-yielding varieties are from Dana G. Dalrymple, Development and Spread of High-Yielding Rice Varieties in Developing Countries (Washington, DC: US Agency for International Development, 1986) and Dana G. Dalrymple, Development and Spread of High-Yielding Wheat Varieties in Developing Countries (Washington, DC: US Agency for International Development, 1986). Regional grain area data are from US Department of Agriculture (USDA), Economic Research Service (ERS), "World Indices of Agricultural and Food Production 1950-85", unpublished printout, Washington, DC, April 1986.

2. Population data are based on estimates of agriculturally active populations from Food and Agriculture Organization, 1984 Production Yearbook (Rome: 1985).

3. Population projections are from Population Reference Bureau, 1985 World Population Data Sheet (Washington, DC: 1985). Grain-yield projections are by Worldwatch Institute, based on world grain utilization data from USDA, Foreign Agricultural Service, Foreign Agriculture Circular - Grains, FG-9-86 (Washington, DC: 1986).

4. For descriptions of traditional farming, see D. B. Grigg, The Agricultural Systems of the World (Cambridge, England: Cambridge University Press, 1974); Gerald G. Marten, ed., Traditional Agriculture in Southeast Asia (Boulder, Colo.: Westview Press, 1986); and US Office of Technology Assessment (OTA), Africa Tomorrow: Issues in Technology, Agriculture, and US Foreign Aid (Washington, DC: US Government Printing Office, 1984).

5. USDA, ERS, "World Indices".

6. World Bank, China: Agriculture to the Year 2000 (Washington, DC: 1985); Bruce Stone, "Chinese Fertilizer Application in the 1980s and 1990s: Issues of Growth, Balance, Allocation, Efficiency and Response", in US Congress, Joint Economic Committee, China's Economy in the Eighties (Washington, DC: US Government Printing Office, forthcoming).

7. Stone, "Chinese Fertilizer Application in the 1980s and 1990s".

8. Organisation for Economic Co-operation and Development, The State of the Environment 1985 (Paris: 1985).

9. Charles A. Francis and Richard R. Harwood, Enough Food: Achieving Food Security through Regenerative Agriculture (Emmaus, Penn.: Rodale Institute, 1985).

10. Robert Rodale, "Internal Resources and External Inputs - The Two Sources of All Production Needs", in Rodal Institute, Regenerative Farming Systems (Emmaus, Penn.: 1985).

11. D. F. Bezdicek, R. F. Mulford, and B. H. Magee, "Influence of Organic Nitrogen on Soil Nitrogen, Nodulation, Nitrogen Fixation, and Yield of Soybeans", Soil Science Society of America Proceedings, March-April 1974; D. F. Bezdicek, "Biotechnology and Farming Systems: On-Farm Applications and Consequences", in Institute for Alternative Agriculture, Biotechnology and Agriculture: Implications for Sustainability (Greenbelt, Md.: 1986); and D. F. Bezdicek, Washington State University, Pullman, Wash., private communication, 6 August 1986.

12. For a review of regenerative practices, see Francis and Harwood, Enough Food; Rodale Institute, Regenerative Farming Systems; and Proceedings of Workshop on Resource-Efficient Farming Methods for Tanzania (Emmaus, Penn.: Rodale Press, 1983).

13. Dana G. Dalrymple, "The Development and Adoption of High-Yielding Varieties of Wheat and Rice in Developing Countries", American Journal of Agricultural Economics, December 1985.

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Third world and biotechnology

By David Dembo, Clarence Dias and Ward Morehouse. Excerpted from a discussion paper presented by the authors for Working Group 1, World Food Assembly, Rome. (This article first appeared in Asia-Pacific Tech Monitor, May/June 1986)

The introduction into the third world of biotechnology as it is presently being developed in the first world is likely to generate a number of adverse consequences. In view of such consequences, governments and social action groups in the third world may well be tempted to adopt a nihilistic approach to biotechnology and feel that they want no part of the biorevolution. Such an approach would be both impractical and undesirable. Third world countries will be affected (negatively) even if they choose not to have anything to do with the biorevolution. Moreover, such a nihilistic approach would be undesirable given the tremendous potential of biotechnology to help provide a solution to the pressing problems faced by third world peoples. Most third world countries must therefore seek to devise policies and strategies which will help maximize the benefits and minimize the burdens resulting from biotechnology both for the country as a whole and for the underprivileged masses within the country.

Biotechnology, food and hunger

Techniques and products resulting from developments in biotechnology will have a range of agricultural applications for both plants and animals.

In plant production, tissue culture technology and genetic manipulation have already had a role to play in speeding up traditional plant breeding techniques as well as in providing increased control over the breeding process. These techniques, while allowing for the improvements from traditional breeding methods to be realised more swiftly, have also opened up a whole new realm of possibilities, previously hoped for and dreamed of, and now within reach. These include increased stress tolerance of plants to allow for production of foodstuffs under adverse conditions (including tolerance for salt, to allow use of salt water); growth in arid conditions; and increased efficiency in the utilization of fertilizers to allow fo. fewer inputs.

New developments in biotechnology will increase the ability of farmers to use herbicides on crops which previously did not respond well to such inputs. They will also result in the development of new varieties of plants, as well as plants with improved characteristics, allowing for the growth, almost anywhere, of most major food crops.

Some of the first products of biotechnology to reach market in the first world, receiving clearance from the appropriate regulatory agencies, have applications in the field of animal husbandry. In this area as well, biotechnology has/will have a broad range of applications. New antibiotics (including those against scours and hoof-and-mouth disease) are possible which could eliminate many of the most serious animal diseases afflicting developing countries. Not only will biotechnology

have a role to play in keeping animals alive, it already has resulted in advances in breeding techniques to allow selection and reproduction at a much faster rate. Products are under development which will greatly increase the growth rate of animals, as well as the overall amount of growth, in a manner which will not use comparable amounts of inputs.

Other applications of biotechnology include the production of food and animal feed from gas.

Potential impacts of biotechnology on developing countries

These applications of biotechnology to agriculture have the potential for vast improvements in the food producing capacity of developing countries. Yet, as should be obvious to those familiar with previous advances in agricultural technology (especially the Green Revolution), the development of the technology does not take place in a social/political/economic vacuum. In fact, depending on who develops the technology toward what ends, biotechnology applications to agriculture could have the exact opposite impact on the third world, and especially the poor and hungry in these countries.

As far as crop production is concerned, biotechnology will also allow for increased use of chemical inputs (fertilizer and pesticides) and could provide a means for corporations to tie the purchase of seeds to use of these chemicals. Biotechnology provides the potential for development of agriculture on a small-scale basis, as opposed to applications of Green Revolution technology which have led to increasingly large farms and inability of smaller farmers to compete.

Related to the development of new and improved crops are the impact that development in other areas of biotechnology applications will have on crop production. Applications such as the production of fuel alcohol will affect the current use and production of crops. The use of sugar cane for this purpose, for example, results in lessened availability of sugar cane for other purposes. Added to this is the possibility of expanding land use for alcohol production, resulting in the removal of these lands for food and animal food production. This will be countered, to some extent, by the ability, through biotechnological applications, to grow crops on previously unproductive land.

In a similar vein, the application of biotechnology to animal husbandry does not lead necessarily to an increase in animal protein available to developing country populations especially the poor in these countries. In the worst case, the possibilities for increase in animal consumption by the rich as well as in production for export, could divert crops from food sources for the poor.

Biotechnology provides a means by which chemicals formerly produced by plants in developing countries and sold at high prices in developed countries, can be produced in laboratories anywhere, thereby displacing important sources of income to farmers and peasants as well as export revenues in these countries.

The technology also leads to the displacement of export crops as the end products from these crops (e.g., drugs based on medicinal plants) can be made through biotechnological methods thereby avoiding and undermining controls by developing countries.

Although it is possible in the distant future that biotechnology will provide the means for recreation of lost plant and animal varieties, at present, and for the forseeable future, the most that can be hoped for is better techniques for storage and maintenance of endangered species. At the same time, use of fewer new varieties developed through biotechnological methods, will have the same disastrous impact on plant genetic resources as development of high yielding varieties (HYVs) resulting from the Green Revolution have had. In production and processing of agricultural products, biotechnology will play a role in increasing efficiency, reducing pollution, and cutting costs.

Consumers as well will be affected by the technology. Costs of some products will drop, availability may increase, and environmental impacts could conceivably be beneficial, although some sort of trade-off between harmful environmental effects (e.g., increased use of pesticides/herbicides/fertilizers and loss of plant genetic resources) and more beneficial ones (e.g., pollution control) is likely. On the other hand, issues of product and worker safety relating to products and processes from biotechnology are far from decided in industrialized countries, let alone developing countries.

Policy and strategy options for developing countries

Because biotechnology will have, and already has begun to have, such pervasive negative and positive implications for developing country agriculture, it is imperative that these countries establish the capability to monitor and develop strategies to deal with its negative impacts. Some illustrative policies and strategies which have been identified by third world experts and activists in their publications and at meetings and workshops are the following:

1. Access, privatization, dependency

Privatization refers to a variety of processes which result in a resource, a product, or a technology being moved from out of the public domain (i.e., the commons) and into the control (and often the ownership) of private hands, individual or corporate. Privatization inevitably creates problems of access: what was freely accessible earlier becomes, as a result of privatization, either totally inaccessible or accessible under restricted conditions.

Three concurrent strategies seem essential if concerns relating to the above are to be effectively addressed:

(a) Development of indigenous capabilities in countries of the third world. This must be accorded highest priority and, in particular, the role of public sector institutions must be safeguarded and strengthened so that such institutions can act as an equal partner with or provide adequate countervailing power to first world trans national corporations operating within such countries. It is also vital, in this regard, that realistic policies be adopted to arrest 'brain drain' and effective measures be taken to preserve the 'open community of scholars' and to protect the public interest in university-industry relationships in third world countries.

(b) Strengthening of an international system as an alternative to the private sector for third world access to biotechnology. A key component of such an international system would be an international agreement governing access, on equitable terms, to all countries (first world and third world alike) to plant genetic resources which will often be the vital basic raw material for biotechnology.

(c) Strengthening the negotiating capacity of third world countries which need selective linkages

with the private sector in first world countries both in order to gain access to technology from abroad as well as to speed up the commercialization of indigenously-developed technologies.

2. R&D priority setting in biotechnology

Biotechnology is being developed overwhelmingly in industrialized countries, and primarily by corporations in those countries. Priorities for R&D programme are therefore determined by profit and risk minimizing considerations, not by the needs of developing countries or the poor and hungry.

Effective strategies to ensure appropriate priority setting in the third world must, in the long run, necessitate the development of indigenous capabilities. In the short run, however, it may be possible for certain third world countries (and with regard to certain biotechnology applications) to pursue R&D in their own priority areas through careful negotiations with either venture capital financed companies or with transnational corporations.

3. Proprietization of biotechnology

It is vital that third world solidarity be maintained in resisting proprietization of biotechnology. Third world countries should, with one voice, say no to the introduction of patent law protecting biotechnology. Of course, third world countries with indigenous biotechnology capabilities, have a legitimate interest in safeguarding technological innovations developed indigenously. But this can be achieved in a variety of ways other than by creating property rights in such innovations. Within the country itself, the author of the innovation can be rewarded through a variety of devices: user fees, taxes on sales, fiscal incentives, etc. If developing countries choose the option of adopting their own biotechnology patent laws, they will be creating the last link in the privatization process and will enable the transnational corporations to secure global market monopolies for their products. At any event, third world countries stand to lose more than they will gain if they join the rush to patent.

4. Displacement of third world products

Third world governments and social action groups must accord priority to monitoring developments in biotechnology R&D in industrialized countries and devising 'early warning systems' regarding displacement of their products by biotechnology application. Responses to such warnings might take many forms: R&D efforts to devise new uses for the displaced product; adjustment assistance (analogues to that used regarding sick industries) to cushion the harmful effects and relocate the human resources dislocated by product displacement; seeking to compete (through joint ventures with first world partners) by entering into production of the biotechnology-produced substitute.

5. Biotechnology and the poor

Biotechnology, in theory, offers the possibility of breakthroughs which can be targeted to the poor. With biotechnology, it will become possible for technologies to be developed which have the potential for disproportionately benefiting the poor, e.g., the development of high-yielding, disease-resistent strains of cassava, or vaccines against pervasive infectious cattle diseases in Africa.

The danger is that the highly profitable initial products of biotechnology will cause significant harm to the third world's poor before the products and processes of more direct benefit to the poor come on line. Thus, there is a crucial need to strengthen the capabilities of third world social action groups to monitor (and play advocacy roles with regard to) the harmful effects on the poor of the introduction (often in collaboration with third world governments) of such biotechnology innovations.

6. Information systems on biotechnology

Of crucial importance to any third world effort to devise appropriate policy or strategy responses is access to relevant information on biotechnology developments. Given the general character of the emerging biotechnology revolution and its likely impact on developing countries, especially poor and marginalized groups within these countries, it becomes all the more important to see that third world actors have access to critical information on which to make the best possible action choices. Among the more significant of these actors are: farmers' associations (upgrading and technology mix; coping with crop displacement; developing appropriate biotechnology); social action groups (environment and health organizations, and conservation, consumer, people's science movements, disarmament groups, etc.); private sector contracting parties such as third world companies involved in joint ventures, licensing or purchase of inputs from external sources, public-sector contracting parties with similar concerns; regulatory agencies (e.g., those concerned with protection of environment, public health and worker safety); national policymakers concerned with the role of biotechnology in the country's economic and social development; private-sector R&D institutions with access problems; and public-sector R&D institutions seeking to initiate the research appropriate to locally determined needs and priorities.

Since it is predictable that other actors, including first world governments and transnational corporations, will have access to and substantial capabilities for acquiring social intelligence, third world actors, and especially poor and marginalized groups of small farmers, landless agricultural labourers, and poor urban workers, and support groups of professionals working with them - need to have, in so far as possible, comparable access to and capacity for acquiring such intelligence.

Challenges and fallacies

The biorevolution poses serious challenges and also offers unique opportunities to third world countries to restructure their societies on a more equitable basis. The challenges lie in finding ways to:

- Bridge the gap between technology policy and the needs and concerns of those likely to be affected by such policy;
- Establish the relevance of biotechnology at the grassroot level;
- Monitor the social and distributional impacts of innovations based on biotechnology;
- Sensitize the scientific and bureaucratic communities to such social impacts;
- Secure greater participation and social accountability in decision making with regard to biotechnology;
- Create and sustain an environment that fosters indigenous creativity and innovation; and
- Devise an effective yet flexible institutional and regulatory framework governing biotechnology R&D and its applications.

While there is no room in a short discussion paper to elaborate on such matters, it is important to note that several characteristics of biotechnology make its development more readily adaptable to third world needs and capabilities. Among these are lower scientific barriers to entry than for a number of other areas of frontier technologies; location specificity of products and inputs, increasing the bargaining power of developing countries vis-à-vis TNCs; existence of markets, or at least demand for many products of TNCs relted to biotechnology; lower labour costs; lower investment per unit of production; and the small scale of the "biological" factories used in biotechnology applications.

The characteristics inherent to the very nature of biotechnology which will become identifiable once greater experience in developing countries has been built up after the introduction of such technology, make it clear that the range of policies and strategies are available, at the present juncture, to deal with concerns regarding biotechnology identified above.
