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UNITED NATIONS INDUSTRIAL DEVELOPMENT ORGANIZATION

Genetic Engineering and Biotechnology Monitor

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Dear Reader,

Meeting under the aegis of UNIDO, the International Centre for Genetic Engineering and Biotechnology's Preparatory Committee held a one-day special session on 2 July 1985 to set the Centre on an operational footing by approving an interim work programme for 1985-88.

Activities will commence this autumn with a workshop on plant biotechnology in New Delhi (India) to be held in September. A workshop on biotechnology and industrial commodities will be held in March next year at Trieste (Italy). Other highlights for this year include the installation of computer facilities to link members of the panel of 15 eminent international scientific advisers, another meeting of this panel, the design of training activities and the appointment of a director, together with the heads of components, a programme management officer and support staff.

The $559,000 for the 1985 programme, together with the estimated $15.8 million for 1986-88 are being donated by the Italian Government from its offer of support for the Centre. The programme for 1986-88 will include a research and training project at each site, as well as a project for affiliated centres and one for other activities. To enable these to begin as early in 1986 as possible, finalization of projects to be executed by UNIDO is expected at the Committee's next session scheduled for November in Havana (Cuba).

To date, the Committee is composed of the 36 states that signed the Centre's statutes. These are Afghanistan, Algeria, Argentina, Bhutan, Bolivia, Bulgaria, Chile, China, Congo, Cuba, Ecuador, Egypt, Greece, India, Indonesia, Iraq, Italy, Kuwait, Mauritania, Mauritius, Mexico, Morocco, Nigeria, Pakistan, Panama, Peru, Senegal, Spain, Sudan, Thailand, Trinidad and Tobago, Tunisia, Venezuela, Viet-Nam, Yugoslavia and Zaire.

The UNIDO Secretariat has also taken up the question of safety guidelines for biotechnology. The co-operation of the World Health Organization (WHO) and the United Nations Environment Programme (UNEP) has been secured. The ICGEB is also expected to concern itself with this question.

On a personal note, this will be the last issue in which my name appears in the "Dear Reader" column. Since I will be retiring from UNIDO at the end of this year, from now on kindly address your enquiries to the Editor of the Genetic Engineering and Biotechnology Monitor. If you should happen to be in India or wish to maintain correspondence with me, please contact me at the following address: Dr. G. S. Gouri, Khanapur, Belgaum District, Karnataka State, India.

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A. POLICY NEWS AND OTHER EVENTS

UNIDO News

International Centre for Genetic Engineering and Biotechnology

The Preparatory Committee on the Establishment of the International Centre for Genetic Engineering and Biotechnology (ICGEB) at its special session held at Vienna on 2 July 1985 examined the items on the agenda and arrived at the following conclusions and decisions:

Interim Programme of the ICGEB

The Committee approved the interim programme for the ICGEB as proposed by the Bureau and requested the Chairman to present to its future sessions a detailed report on the implementation of the interim programme and the deployment of resources therefor. The Committee requested the Bureau of the Preparatory Committee and the host governments to finalize the draft headquarters agreement at an early date and to submit the draft to the next session of the Preparatory Committee.

The Committee recalled its decisions at its fifth and sixth sessions that 31 December 1985 should be an adequate date for completion of ratification by all States signatories. It reiterated its request to representatives of member countries to convey to the respective governments the need to accelerate the process of ratification and its concern in this regard. It further requested the representatives of member countries to inform the Committee at its next session of the progress made in this matter in the respective countries.

The Committee recalled its request at its last session to representatives of member States to indicate to the Chairman at or before the next session of the Preparatory Committee the voluntary contributions that the respective member States would offer to the Centre.

The Committee recalled its agreement at its last session on the procedure for the nomination and selection of the Director of the ICGEB, and invited the member States to submit their suggestions of candidates before 1 September 1985.

In regard to the selection of the Heads of components, the Committee recalled its decision at its sixth session and agreed that while the Heads of the two components will be appointed by the Director, the process for their selection should be initiated without delay with the appointment of the Heads to be made after endorsement by the Preparatory Committee.

The Committee agreed with the recommendation of the Panel of Scientific Advisers at their meeting in June 1985 that the subject of the specialized workshop in Trieste be "biotechnology and industrial commodities".

The Committee noted that the Panel at its next meeting will have to consider, inter alia, nominations for the post of the Director, evaluation of affiliated centres and evaluation of the results of specialized workshops. The view was expressed that two days proposed for the meeting at Trieste, namely, 2 and 4 November 1985 might not be sufficient. It was also noted that the Panel would also meet with the Bureau to consider names of candidates for the post of Director. The Chairman was requested to arrange with the Bureau and the Panel members the exact duration of the Panel's meeting and the arrangements for discussions with the Bureau.

Social Issues

Agricultural controls

Agricultural R&D is drawing increasing attention and sparking controversy regarding the potential social and ecological consequences of the discoveries. University researchers are concerned about a double standard that holds them to stricter account than scientists in private industry. The University of California, famous for pioneering work in water management, pest control and biotechnology, is currently involved in a suit that accuses it of spending public funds to develop labour-saving machinery to help large corporate farmers and eliminates jobs. Another suit against the University attempts to prevent the spraying of a genetically engineered form of *pseudomonas syringae* bacteria on a potato patch to retard frost. Some members of the research community feel that strict controls are necessary to insure that biotechnology experiments are adequately reviewed beforehand and the risk of contamination fully weighed. Others worry that government attempts to regulate experiments will stifle research and cost the US its narrow lead in the emerging field of biotechnology. (Extracted from Wall Street Journal, 21 November 1984)

Regulatory Issues

US regulatory controls

In the face of proposals to create a new means to oversee genetic engineering, the US Recombinant DNA Advisory Committee (RAC) of the National Institutes of Health (NIH) has begun to assert itself with a new vigour. At the meeting of the committee in May, members voiced concern that other agencies moving to assert jurisdiction over recombinant DNA - in particular the Environmental Protection Agency (EPA) - lack the expertise that the RAC had accumulated in its 10-year existence and that basic research could suffer as a consequence.

The focus of concern is the lengthy proposal of the Office of Science and Technology Policy (OSTP) for the establishment of a "coordinated framework" for regulating biotechnology. Under that proposal, a Biotechnology Science Board would be created to address generic issues and settle interagency disputes; in addition, each agency dealing with biotechnology (US Department of Agriculture, National Science Foundation, EPA, Food and Drug Administration and NIH) would have its own RAC to provide advice within the agency.

Although most of this proposed bureaucracy would address only applications for marketing or development of commercial products and would not involve any new statutory authority, EPA has indicated its intention to claim some authority over research. The agency has already said that field tests of microbial pesticides produced by genetic engineering come under the Federal Insecticide, Fungicide, and Rodenticide Act. Under interim rules announced by the agency, anyone who wants to field-test a genetically engineered microbial pesticide on a plot of any size must notify EPA; the agency can then demand a formal application for an "Experimental Use Permit".

EPA also intends to view the DNA in novel microbes as "new chemical substances", subject to the notification and safety-testing requirements of the Toxic Substances Control Act (TSCA). Under that act, EPA must be notified 90 days before the manufacture of such a new substance commences; EPA can demand additional data and with cause can restrict or even ban the product. (Extracted from Nature, Vol. 315, 16 May 1985)

Type culture a source of gain

Researchers say the role of the American Type Culture Collection (ATCC) as a repository of materials for basic biological research is being threatened by commercial exploitation of cell lines deposited there. At least one molecular biologist has refused to send any more of his samples to the collection after a commercial company obtained an oncogene he had deposited and, without his knowledge, began marketing to researchers DNA probes derived from it.

ATCC, a non-profit organization, makes cell lines and other materials in its collection available to any qualified researcher who requests them, charging a nominal fee to cover its costs. Although primarily a service to basic researchers, the collection has played an increasingly important role in facilitating the patenting of recombinant DNA products and processes.

As a general rule, the Patent Office requires applicants to deposit novel cell lines or plasmids in a collection such as ATCC to satisfy the public disclosure requirements of patents - the traditional written descriptions are often insufficient to allow someone else to reproduce the invention, a fundamental requirement of patent law. In order to satisfy the legal requirements, no restrictions on the distribution of deposited materials can be imposed.

Some research groups, apparently concerned about the uncontrolled commercial exploitation of cell lines placed in the public domain through ATCC or otherwise, have taken to distributing samples themselves to other basic researchers and requiring a signed agreement that those receiving them will not pass them on to a third party or exploit them commercially without permission. Although there is some dispute over the enforceability of such agreements at law, in at least one case, the originators of the cell line won a sizeable out-of-court settlement from a company that had obtained and was using the material without their permission.

A spokesman for ATCC says that the collection may have to reconsider its policies on free distribution, but it would not want to be in the position to enforce restrictions against transfers or commercial development. (Extracted from Nature, Vol. 315, 23 May 1985)

General

Trapped biotechnology

Biotechnology firms whose scientists have spent the past few years in laboratories working on genetically-engineered drugs fear they have wasted their R&D money. Conventional drugs can be protected against imitation by patents, but the first biotechnology drugs are mass-produced versions of proteins that occur naturally in the body, so there is increasing doubt whether they can be exclusively owned.

Lawyers will take several years to frame secure patents for many present biotechnology products, if indeed they ever reach them. But the confusion in the industry could help participants to draw a useful, and profitable, distinction between the first generation of biotechnology drugs and the second.

The first round of products are not blockbusters. Genetically-engineered interferons, for example, have disappointed in clinical trials and have surprisingly caused side-effects even though they are natural products.

Improving and cross-licensing the technology could assist in helping the biotechnology industry to find the money it needs for R&D work on the second generation of its products, which promise to be the real money-spinners. These products will be more easily patentable because they will more nearly resemble conventional pharmaceuticals. (Extracted from the Economist, 1 June 1985)

Art and biotechnology

Fixed algae have been used for many purposes, but rarely for making what the French sculptor Ernest Pignon-Ernest calls "arbrorigènes". This pun on the French words for "tree" (arbre) and "aborigine" describes a collection of life-sized models carved out of polystyrene and containing fixed Porphyridium cruentum, a reddish single-celled alga that gives the polystyrene flesh tones. Pignon-Ernest's models now adorn the trees of the Paris Jardin des Plantes. The sculptor is fascinated by the idea that these sculptures need water and light. Pignon-Ernest conceived the idea of using fixed algae and approached biotechnologist Daniel Thomas of the University of Compiègne and his colleague Claude Gudin of the solar biotechnology laboratory at Cadarache for ideas. Thomas, who specializes in cell and enzyme-fixing, had the technology of fixing P. cruentum in polystyrene, and Gudin has been using it to produce polysaccharides using solar energy. (When its environment dries, the organism protects itself by secreting a sugary shell.) Pignon-Ernest found the material ideal, and the "breathing" arbrorigènes were the result.

Thomas, meanwhile, was also at work with another artist, Monet - or at least with his enormous "water-lilies", a 186 sq. m. canvas hanging in the Louvre gallery in Paris. This painting was damaged when it was first transported. Paper was glued to the surface of the paint to protect it, but the wrong glue was used and the picture remain misted and in danger of denaturing by interaction of glue and paint. Thomas came to the rescue, discovered the glue was starch-based and dissolved it off with enzymes. Which proves that biotechnology has its uses, even if those uses will have little effect on share prices... (Source: Nature, Vol. 314, 18 April 1985)

B. COUNTRY NEWS

Australia

New Legislation

The New South Wales government in Australia is planning to introduce legislation to cover biological control of weeds and pests. It would be the first government in the world to bring in such rules. (Source: European Chemical News, 18 March 1985)

Belgium

Biotechnology in Belgium

Belgium has a strong chemical industry, and outstanding strengths in its universities and research institutes in the biomedical sector (e.g. the Institute for Cellular and Molecular Pathology) and in plant genetics (University of Ghent), as well as in other areas (e.g. bacteriology in various institutions). The international pharmaceutical companies are also attracted by the high quality environment provided by the research teams in the various universities of the country.

At the level of the regional authorities, Wallonie, Flanders and Brussels are seeking to attract foreign investment in high technology sectors such as biotechnology; Wallonie and Flanders have each created two R and D companies. Hybritech (the US leader in hybridoma technology and marketing) has established a plant at Liège; Biogen (the Swiss and U.S.-based group owned by Monsanto, International Nickel, Schering-Plough and Grand Metropolitan Hotels) has established a subsidiary at Ghent (Biogent). At the level of the national authorities, the IRSIA - a national industrial research association - is coordinating R and D projects on biotechnology topics, and its Biotechnology Committee comprises 32 companies from various industrial sectors and university laboratories specialising in monoclonal antibodies, fermentation, immunology and genetic engineering. (Extracted from Industrial Biotechnology Wales, February 1985)

Canada

Wellcome in Canadian biotechnology venture

In a joint venture with the Terry Fox Medical Research Foundation a Canadian charity, The Wellcome Foundation is to establish a Biomedical Research Centre in Vancouver, British Columbia. Claimed to be a unique concept, the centre will combine laboratory facilities with on-the-spot in- and out-patient facilities, an arrangement which the company expects will allow ideas to move "quickly and efficiently forward from basic research in clinical application".

To be based on the campus of the University of Columbia, the centre's initial thrust is to be towards biologically active proteins, with "emphasis on new substances now emerging on a production scale from biotechnology, such as lymphokines, interferons and monoclonal antibodies", according to Bill Castell, managing director of Wellcome Biotechnology.

The British Columbian Provincial Government has helped finance the project through its Development Corporation. (Extracted from Manufacturing Chemist, May 1985)

China

Chinese set a virus to catch a virus

Virologists at Beijing University claim to have cured two-thirds of mice who would otherwise have died of Japanese viral encephalitis. They did it by infecting them with another, related virus called M14.

C.H. Huang, one of the researchers, told the International Congress for Infectious Diseases that M14 reduced the amount of macrophage-inhibiting factor, which blocks natural non-specific immunity. The Chinese do not know yet whether this effect will save a human with encephalitis. They plan first to try M14 in T-cell leukemia, another disease in which macrophage inhibition plays an important role.

M14 may eventually have its most important effects on encephalitis while the disease is still being carried by the mosquito. Huang said the encephalitis virus "disappears" from various organs of mosquitos which are infected with M14. Encephalitis is not cleared from the entire insect, but in several cases Huang says it disappeared from the salivary glands, which transmit the disease to humans.

What seems to happen is that the two viruses compete for binding sites in cells. M14 wins. The phenomenon is not new to science and several virologists in Cairo described the finding as "reinventing the wheel".

Huang has high hopes for his "new concept" of therapy with non-pathogenic viruses, however. He wants to block the transmission of dangerous viruses by the mass infection of wild mosquitos with M14 in places where the diseases are endemic. This could lead to the eventual eradication of encephalitis and perhaps another, more important viral disease spread by mosquitos, yellow fever. (Source: New Scientist, 30 May 1985)

Denmark

Biotechnology in Denmark

Biotechnology is very strong in Denmark, whose economy is based on agriculture (24 per cent of output), food processing (34 per cent) and chemical industry (10 per cent). Everyone has heard of the Carlsberg brewery, with its traditional skills in brewing, which have supported the creation of an international research centre with outstanding competence

in plant genetics and cell biology. Everyone has also heard of Novo, which dominates the world market in industrial enzymes. Novo practised biotechnology before the word was invented, and is now arguably the world's leading company in the field.

In 1978, the Danish Technical Research Council, under the chairmanship of Prof. O.B. Jorgensen, of the Technical University, took the first initiative in the field and supported projects in genetic engineering scale-up problems (with particular reference to genetic stability), product recovery (with special reference to selective recovery of intracellular products) and on protein synthesis. More recently, a Ministry of Industry "initiative group" recommended against creating a new institute specially for biotechnology because the subject was of such widespread interest that it needed to be practised widely. (Extracted from Industrial Biotechnology Wales, February 1985)

European Economic Community

European biotechnology

Agriculture and food processing, forestry, health care, pharmaceuticals and major sectors of the chemical industry are among the areas of activity which may be radically altered by the recent breakthrough in biological science, and their technological applications. Biotechnology is of fundamental importance to every society, and to many businesses. In the United States, over 200 new companies have been created, and several billion dollars invested in biotechnology, over the past 10 years; giant multinationals are reorienting their strategies towards the applied life sciences, and spending massively on research. In Japan, the expenditure is more modest, but the coordinating role of MITI's "Bio-industry Office" brings together all the major groups in a concerted assault on the commanding heights of this, the other "microtechnology". The dynamo of change is the breathtaking pace of scientific progress, and Europe is strong in all the key areas - molecular and cellular biology, microbiology, process engineering and fermentation science. But will the Old World, with its fragmented markets and complex political machinery, manage to hold its place in the race to commercialization?

The European Community cannot be passive, faced with the massive challenge of the new opportunities, and the sharp competitive threat from the other industrialised countries. The means exist within the Community - the human skills, the financial resources, the potential scale of the home market. These need mobilisation by a concerted effort, involving decision-makers both in private industry and the public sector; in small and large firms; at national Ministries, and in the Community institutions.

The studies and the experience are available, on which to build a Community effort. The Commission has argued since the mid-70s for a collaborative R and D programme in the key areas of genetic engineering and enzymology. The futures group FAST (Forecasting and Assessment in Science and Technology) argued for a comprehensive Community strategy for biotechnology - of what use the advanced research, if firms are being driven out of the Community because of the price of agricultural raw materials? Meanwhile, the development of biotechnology in the countries of Europe proceeds slowly and sporadically; constrained by history to gradual innovation and institutional change, condemned by future competition if it fails to move more quickly enough.

Biotechnology is a "knowledge based business", and therefore R and D capability is central. That capability has to achieve "critical mass", by developing centres in Europe with the equipment, the people (above all the broad interdisciplinary teams), the intellectual stimulus and density in "brains per square metre". The best young researchers in each area must be able to find and move to centres of world class within the Community. By all means, with transatlantic collaboration and exchange - but a two-way shuttle, not a one-way brain-drain.

To stimulate the development of these advanced technologies, at a precompetitive level under-pinning applications capability, the Community first launched a programme oriented towards the transfer of the scientific breakthroughs into European agriculture:

A Multi-annual (1982-86), 45 million ECU, cost-sharing Research and Training Programme

This programme, started in April 1982, now includes 104 research contracts, covering periods between 24 and 40 months, and involving Commission co-finance averaging 40,000 ECU per year per laboratory. The six areas, all oriented to agriculture and the food industry, comprise:

- development of advanced bioreactors for agriculture and the food industry;

- improved production of materials for stock breeding and for agriculture and the food industry through application of biomolecular engineering techniques;

- improvement of plant products;

- development of methods for the identification and transfer of new genetic information in plants;

- improvement of the symbiotic relations between cultivated plants and soil micro-organisms;

- development of methods for cell selection and regeneration in other plants.

Wider in its scope, the training programme covers all aspects of biomolecular engineering, including methods of risk assessment in biotechnology.

The need for a wider concept of strategy is reflected in the Commission's new proposals for a five-year, Biotechnology Action Programme (1985-89), of which Research forms only the first of six points.

1. Research and Training - prolonging the activities of the outstandingly successful first R and D programme, and enlarging its scope to a broader range of topics in basic biotechnology; ranging from such frontiers as "protein engineering", to work on the development of better health diagnostic tools, and better methods of toxicological testing for new drugs. A "Contextual Measures" sub-programme aims to strengthen the research infrastructure for biotechnology, in data banks, information services, and banks of genetic materials (cells, microorganisms, etc.).

2. Concertation Action - for monitoring coordination, and the essential communication functions, between Commission services, between biotechnology policy makers at Community and national levels, between the various scientific disciplines and economic sectors, through informal networks spanning the internal national frontiers of the Community.

3. Access to Raw Materials - sugar, starch or some such organic and digestible energy source is fundamental to all the fermentation industries of biotechnology; but it must be available at a competitive price, if Europe's biotechnology firms are to thrive. Proposals for the necessary changes of agricultural régimes have been put to Council. The development, through biotechnology, of high-added-value and non-food uses for agricultural materials is of strategic importance for the future of Europe's agriculture.

4. Regulatory Régimes - the long-standing effort towards the creation of a true Common Market acquire a new urgency from the needs of biotechnology, which include the need for a clear, responsible and uniform regulatory environment. In pharmaceutical products, foodstuffs, feedstuffs, chemicals and other areas, the need is the same: to derive the economies of scale and consequent benefits of a market of 300 million people.

5. Protection of Intellectual Property - the law of patents, and the conventions for the protection of plant varieties, find some of their basic concepts brought into question by the radical innovations of biotechnology. Thus the existing proliferation of different national systems, both within the Community and world-wide, is further complicated by technical uncertainties at the interface between science and jurisprudence. Industry - particularly within Europe - chafes at its impediments, and at the more advantageous conditions in the USA and Japan; while jurists at national, European and OECD level wrestle with the slow processes of legislative innovation and the modification of international conventions. The Commission's working group on patenting in biotechnology is battling to assert in this complex domain the urgent and growing need for a Community approach.

6. Demonstration Projects - and other forms of closer collaboration with industry, are seen as essential to the Community's long-term strategy.

Action and proposals on this plan have been intensifying through 1984, the new five-year research Programme being timed to start in early 1985, to run at roughly 15 million ECU per year to 1989.

The Commission's plan attempts to address the strategic challenge, but the resources are modest, the constraints on implementation, many and complex.

The role of the European Community

The strength and diversity of European capabilities in biotechnology include all application areas in industry, agriculture, health care and environmental or resource management, and all the relevant areas of fundamental science and advanced technology. Of no single European country could this be said. Industrialists need to recover the heavy R and D costs and capital investments by the economies of scale achieved only at European and world level. Students and researchers need access to worldclass centres where the key resources and accumulated multi-disciplinary expertise are available; such access, for collaboration, service and training, is no less necessary for those concerned with applications.

To create in biotechnology this "espace européen", continuing Community initiatives are needed in several policy areas: in research, in agriculture, in regulations, in industrial policy. These policy initiatives have to be based on a concerted approach, not only within the Commission services, but between the Community institutions and national administrations, and in association with those groupings or institutions which command the key scientific, industrial and agricultural strengths. (Extracted from Industrial Biotechnology Wales, February 1985)

Clean incentive

The European Commission has invited applicants for its biotechnology and "clean" technology programmes. The biotech programme runs from 1985-89 and covers training and basic research proposals. On clean technology, the EEC will put up 30 per cent of the investment costs for development of processes which produce less waste or use less resources. (Source: European Chemical News, 20 May 1985)

Federal Republic of Germany

Biotechnology in the FRG

Germany was amongst the first to give official recognition to the importance of the field, when in 1974 the Ministry for Research and Technology (BMFT) took up the suggestions of a DECHEMA report (the German Chemical Equipment Manufacturers' Association). This association has remained an active promoter of biotechnology, both in Germany and at the European level: being a founder association and secretariat of the European Federation of Biotechnology (founded in 1978, and now comprising 49 scientific societies, from 18 European countries). The German research effort is focussed on major centres at Braunschweig and Jülich, as well as at many other public or private institutions, such as the Technical University of Berlin.

Hoechst, the world leader in pharmaceutical (particularly antibiotic) production, has also pioneered production of single-cell protein for human consumption (with BMFT cofinance). Boehringer Mannheim is a leader in the new biochemicals - restriction enzymes and oligonucleotides - used in genetic engineering. Boehringer Ingelheim produces speciality chemicals by fermentation (citric acid). Bayer, number two in pharmaceuticals world-wide, applies enzymology to the production of semi-synthetic penicillins. Schering uses microbial transformations in producing steroid hormones. Degussa produces amino acids (for animal nutrition) using immobilised biocatalysts. There are some twenty other significantly active companies, although these are usually established firms rather than venture capital activities on the U.S. model. (Extracted from Industrial Biotechnology Wales, February 1985)

Bacteria eat up sewage

Although much of the environmental damage is recognised nowadays, the causes are often still a mystery to scientists, especially in the case of massive damage to forests, even though much information has been gathered on the subject. The figures are alarming: almost half of German forests are already damaged, while the scientists are still disputing how and to what extent air pollution, the condition of the ground, climatic fluctuations or pests are to blame for it.

Recently the bark beetle, also called the "engraver", has developed into a veritable plague. These greedy creatures prefer to attack ailing trees. Bark beetles signal to other members of the species by means of a particular scent where they have found food, and it is possible to synthesise this odiferous substance. The success is sensational: in the Federal State of Hesse alone over one hundred million of these beetles went into the scented traps set for them.

In the area of water conservation, great progress has been achieved in recent years, not least owing to the research work of the chemical industry since the regulations for protecting the environment have been drastically tightened.

A pioneer in the development of new methods of water purification is Hoechst AG, which has invested some 330 million marks in clean water in the last four years. The Frankfurt chemical giant is first and foremost backing the development of so-called large-scale bio-reactors, the third generation of biological purification plants developed by Hoechst. This largest chemical group in the Federal Republic of Germany spends about five per cent of its total turnover on environmental protection, equal to 18 per cent of its overall investments.

The bio-reactor method has been copied from nature, whereby bacteria feed on organic substances, convert them into cellular materials or oxidise them to produce energy. The organically dirty sewage is literally thrown down for the bacteria to eat. In order to give these minute organisms ideal working conditions either oxygen or granulated active charcoal is added, since for their work the bacteria need air. Active charcoal also helps to detoxicate particularly obnoxious sewage. In this way over 95 per cent of organic impurities can be removed. Dangerous alkaline and acid solutions and heavy metals are filtered out of the sewage before it is piped into the bio-reactors. The tower-like plants have the added advantage that there are neither objectionable smells nor any noise during the process. Although the bio-reactors constitute the essential item in purifying very dirty effluent, they alone are not enough. Part of the Hoechst AG's "Purification Programme" is also a so-called "Demercurising Plant", which removes mercury from the effluent of potassium chloride electrolysis. Since its introduction, the mercury passed into the River Main, which is already polluted to some extent, has decreased considerably. (Extracted from Scala, No. 5, 1985)

France

French biotechnology

The country of Louis Pasteur seemed to be falling behind in biotechnology until a strongly renewed government interest was signalled in 1979-80 with the publication of strategic analysis and reports, by Gros, Jacob and Roger ("Sciences de la Vie et Société"), de Rosnay ("Bio-Industrie"), and subsequently Pelissolo ("La Biotechnologie, Demain?"). The Pelissolo recommendations for the creation of a "Mission Biotechnologie" were accepted, leading to the launch of the national "Programme Mobilisateur" now being implemented. This focuses national efforts in biotechnology on four 'poles' in particular: Toulouse, Compiègne (long known for its enzyme engineering and bio-process technology), Pasteur Institute (a private foundation, 50 per cent financed by government, with capabilities in genetic engineering, hybridoma technolgoy, virology and immunology), and ParisGrigon (the newly rebuilt centre of fermentation technology in INRA, the National Institute for Agricultural Research). A particular objective of these centres is to improve the transfer of knowledge into industry. The strong molecular biology at the University of Strasbourg should also be mentioned.

In addition to the many multi-nationals with strong bases in France, major French companies using biotechnology in fine chemicals and pharmaceuticals include Rhone-Poulenc (antibodies, and world leader in production of vitamin B12), with its subsidiaries Institut Mérieux (for vaccines) and Genetica (for genetic engineering); and Roussel-Uclar (a subsidiary of Hoechst) for antibodies and steroids. But the largest commitment to biotechnology comes from the oil company Elf Aquitaine. In human biologicals, it has acquired Sanofi, Clin Midy, Choay and Institut Pasteur Production. Elf Bioindustries and Elf Bioresearch are developing biotechnology in the food and agricultural sectors. There are research-minded companies in the dairy industry (Bel-Industries, BSN-Gervais-Danone, Entremont), and in starch conversion, Roquette Frères are world leaders in sorbitol production. In animal feeds, amino acids are produced by Orsan, Eurolysine (associated with Ajinomoto) and Rhone-Poulenc.

Of new biotechnology companies set up, Genetica has been mentioned; and Transgène, in genetic engineering, benefits from its proximity to the University of Strasbourg. (Extracted from Industrial Biotechnology Wales, February 1985)

Biomechanics and biomaterials training and research in Marseille

The successful treatment of a wide range of traumatic injuries, such as are encountered by military personnel, requires a close integration of surgery with a knowledge of the properties and characteristics of an ever-growing list of natural and synthetic materials. The Faculty of Medicine of the University of Aix-Marseille, France, has designed a teaching and research programme aimed at providing orthopaedic surgeons and others with a broad and comprehensive diploma built around biomechanics and biomaterials. This programme which trains 10 to 40 students per year, is led by Professor Agrege D. Poitout; it is the first of its kind in France, embracing the technological application of materials in medicine and cooperative work between hospitals, research laboratories, and industry.

France currently implants annually a total of 50,000 hip prostheses; 5,000 knee prostheses; 15,000 cardiac valves; 15,000 vascular prostheses; and 20,000 cardiac pacemakers. Many of the materials were actually developed for nonmedical uses in, for example, the aeronautics industry, the electronics industry, or agriculture. While the functional aspects of implanted materials can usually be predicted with a certain degree of accuracy, estimation of the biological performance still needs much research in order to be considered reliable in many cases. The progress which has been made in recent years in the study of the interface between materials and living tissues has enabled the development of implants which are far more reliable and effective. However, the biocompatibility of the materials used is still not completely satisfactory, and this would seem to justify an intensification of research and collaboration between designers (engineers) and users (clinicians).

The course of study in the Poitout's programme is designed to be of interest to medical students who are preparing for orthopaedic, cardiovascular, neurological, or general surgery; general anatomy; and dentistry. Some students who are in physical and biomedical sciences may also enter the course.

Through close cooperation with manufacturers and researchers, the course aims to provide students with in-depth knowledge of new materials and new technologies to enable them to take their place at the forefront of current practice and to orient their research in terms of industrial needs. In a like manner, manufacturers will acquire a better understanding of practical problems, enabling them to solve them more satisfactorily and to provide materials that are better adapted to the needs of the clinician. (Source: European Science News, 39-6 (1985))

Greece

Biotechnology in Greece

In Greece, the Ministry of Coordination, in consultation with the Ministries of Science and Technology, Education and Agriculture, is currently developing plans to stimulate awareness, education and application of biotechnology, in the context of the 1983-88 five-year plan for economic and social development. This includes a programme for scientific and technological development, and an element of which concerns "key technologies", containing three themes:

(a) microelectronics and informatics
(b) biotechnology
(c) technologies relating to marine exploitation.

This choice reflects top-level political decisions, and ambitious plans are now being implemented to create the necessary foundations.

Biotechnology and life sciences research are being vigorously promoted at the new Institute for Molecular Biology and Biotechnology in Heraklion, Crete; as well as at several other universities (Athens, Patras, Thessalonika) and at research centres such as the National Hellenic Research Foundation, the Cancer Research Centre (Salonika), and NRC Demokritos (Athens).

Professor Stavropoulos, associated with the science-based biotechnology company Vioryl (food additives, preservatives, flavourings, plant nutrients), is working with the government planners to identify new industrial opportunities in biotechnology. There has been created a national company, "Bio-Hellas", which will work in close association with the research centres mentioned. (Extracted from Industrial Biotechnology Wales, February 1985)

India

India sets five-year-plan

India has earmarked $400 million for biotechnology over the next five years, sealed a long-delayed science agreement with the U.S.A. and sought a joint bio-collaboration with the Soviet Union.

The Gandhi-Reagan Science and Technology Initiative (GRSTI) agreement lays particular focus on applied biology, genetic engineering and plant biotechnology. While GRSTI is broad in its scientific scope, it emphasizes Indo-U.S. cooperation in developing recombinant vaccines and pharmaceuticals for measles, cholera, typhoid, malaria, non-A/non-B hepatitis, human and animal rabies and leprosy - with particular attention to preclinical leprosy diagnosis - and development of a male contraceptive vaccine.

Coordinating the five-year bio-plan is India's National Biotechnology Board (NBB). Created in 1982, it has initiated postgraduate biotechnology programmes in six Indian universities, and aims to open five more by year's end. NBB will set up embryo-transfer and animal-breeding centres, gene banks, genomic libraries, and biotechnology manufacturing units.

Meanwhile, India is about to sign an agreement for collaboration in biotechnology with the Soviet Union. Later this year the two nations will identify four to six areas of mutual Indian-Soviet interest, including biomass conversion and macromolecular interactions. (Extracted from McGraw-Hill's Biotechnology Newswatch, 6 May 1985)

Biotechnology in India

India is now posed to become the first developing country in this part of the world to make use of biotechnology to solve many problems being faced in medicine, agriculture and industry.

In recent years, biotechnology has emerged as an important discipline which can be broadly defined as the development of biological forms and systems for obtaining maximum benefits to man and other forms of life while maintaining an optimum ecological balance.

The recent epoch-making discoveries which have led to the development of techniques of genetic engineering, cell-cell fusion amongst plants and animals and micro-organisms and manipulation of enzyme and metallic pathways have opened up new possibilities for the cost-effective production of fuel from renewable resources, cloning and mass fertilization of crops, better yielding varieties of plants, cheaper products, better methods for early diagnosis of diseases, selective methods of pest control and stabilisation of waste water.

Several basic disciplines of science like biochemistry, physics, mathematics, chemistry and engineering have an interface with biotechnology. The grounding and advances in basic research in Indian universities and institutes over several decades have made possible the emergence of biotechnology as an interdisciplinary thrust area of research with a potential future.

Genetic engineering: Work on genetic engineering has been taken up at a number of institutions. In the capital, various institutions are active in the field. Studies are being carried out on transfer of "nif" genes into plant cells at the School of Environmental Sciences, Jawarharlal Nehru University. Construction of M-Laprae DNA library and cloning of DNA and coding the hormones, HCG and human placental lactogen is in progress at the National Institute of Immunology.

At the Indian Agricultural Research Institute an active group is working on characterisation of translation and transcription process in E. coli during cell division and gene expression in plant tissues. At the Indian Institute of Technology, Delhi, stress is given on conversion of cellulose to alcohol and this is the major facility for detailed studies on all aspects of fermentation. At the CSIR Centre for Biochemicals, a support facility has been created to ensure that restriction enzymes and other strategically important materials are readily available.

Two of the major institutions in Bombay active in the field of genetic engineering are the Tata Institute of Fundamental Research and the Bhabha Atomic Research Centre. The Department of Zoology at the Poona University and the Department of Biochemistry at the National Chemical Laboratory house two important groups working in the field of genetic engineering at Pune.

Several groups are active in the Indian Institute of Science, Bangalore, working in diverse areas like gene expression in Rinderpest virus, Histone gene expression in rice embryos, structure and expression of genes regulating silk, fiboin synthenis in Bombyix mori, regulation of nitrogen fixation etc. Work on molecular cloning and sequencing of genes, coding for restriction and anti-restriction proteins in E. coli and Shigella dysenteriae as well as cloning of biocide gene from Bacillus shaericus and B. Thuringiensis is pursued at the Madurai Kamaraj University, Madurai, the Osmania University and the Centre for Cellular & Mollecular Biology, Hyderabad, the Indian Institute of Chemical Biology, the Bose Institute and the Saha Institute of Nuclear Physics are leading Institutions in Calcutta where several groups work on application of genetic engineering techniques, studies of biological nitrogen fixation and insertion of genes of applied importance to bacteria.

At Banares work on studies on cloning of genes of the bacteriophage in E. coli is being pursued at the Institute of Medical Sciences. Other centres of the activity include the Central Drug Research Institute, Lucknow and the Aligarh Muslim University, Aligarh.

Fermentation technology: The Biochemical Engineering Research Centre at IIT, Delhi, has several research groups working on different aspects of fermentation technology starting from strain improvement using mutagens/genetic engineering right up to pilot plant fermentations with computer controls. The Department of Microbiology at the MS University, Baroda, the Indian Institute of Science, Bangalore, the National Chemical Laboratory, Pune, the Jadavpur University, Calcutta, the National Sugar Institute and the Harcourt Butler Technology Institute, Kanpur, the Regional Research Laboratories at Jammu and Jorhat, the Central Food Technology Research Institute at Mysore, the Department of Microbiology, the Punjab University, Chandigarh, are some of the other important centres where basic studies on fermentation technology are carried on.

Among industries, work on fermentation technology is being actively conducted at the Hindustan Antibiotics Ltd., Pimpri, Pune, Anil Starch Products Limited, Ahmedabad, Bharat Serums and Vaccines, Thana, Cadilla Laboratories Pvt. Ltd., Ahmedabad, Hindustan Lever, Bombay and Hoechst Pharmaceuticals, Bombay.

Enzyme engineering: Major centres in India where work on immobilisation of enzymes is going on include Hindustan Antibiotics Ltd., Pimpri, the Biochemical Engineering Research Centre, IIT Delhi, National Chemical Laboratory, Pune, the Jadavpur University, Calcutta, the Indian Institute of Science, Bangalore, IIT Kanpur and the Indian Institute of Chemical Biology. The work being done covers immobilised enzymes for use in medicine, industrial fermentation, food processing and waste water treatment.

Tissue culture: A large number of establishments are active in the field of plant tissue culture. These include National Botanical Research Institute, Lucknow, National Chemical Laboratory, Pune, Regional Research Laboratory, Jammu, Department of Botany, University of Delhi, Calicut University, Calicut, MK University, Madurai, Indian Institute of Science, Bangalore, Central Arid Zone Research, Institute Jodhpur, Bose Institute, Calcutta, Rajasthan University, Jaipur, Department of Botany, MS University of Baroda, BARC Bombay, JNU, New Delhi and IARI, New Delhi.

Work in various areas including clonal propagation and protoplast fusion and regeneration of fruit and forest trees, plantation crops like sugarcane, papaya, banana, cardamom etc. for applied use, as also basic studies in subjects like cell diversification, immobilisation of plant cells, submerged tissue culture, etc. is being pursued in these institutions. Recently the Central Plantation Crops Research Institute, Kasaragod has successfully propagated coconut plantlets in test tube.

In addition, work on different aspects related to biotechnology including immunology, photosynthesis, diagnostics, vaccine production by improved methods is being done in a number of laboratories spread throughout the country.

The National Biotechnology Board (NBTB), was set up to promote and oversee research in this field. It has completed the working plans for implementing various decisions on major issues namely, integrated short term training courses for manpower development: formulation of long term plan with time schedule; finalisation of NBTB fellowships, visiting scientist programme; formulation of proposals for creation of infrastructural facilities; safety regulations to be followed for DNA research in India, supply of radio-labelled chemicals and restriction enzymes required for genetic engineering; and preparation of feasibility reports for setting up biotechnology based manufacturing units.

One of the charters of NBTB is to identify priority areas in biotechnology and prepare programmes in these areas for carrying out research and development work, for generating know-how required for the application of biotechnology in areas of national relevance such as health (human and animal) and family planning, food and agriculture, industry, energy, chemicals, environment etc. and survey the work done by various agencies in the area of biotechnology. In this connection a long-term plan has been formulated. It was suggested that the sectoral long term plan should be discussed with member agencies and a time schedule drawn up.

The Board was entrusted to set up and provide centralised assistance for procurement of materials required for genetic engineering from abroad and to initiate follow-up action for production of these materials. In view of the urgency, the department initiated a coordinated, multi-institutional programme on production of restriction enzymes which are essential for genetic engineering research. Management and monitoring of the project is being done by NBTB. In the first phase of the project, production of five enzymes has been completed. As an interim measure, NBTB arranged for bulk import and distribution of restriction enzymes with the help of the Centre for Biochemicals at the VP Chest Institute, Delhi. The Board is also arranging the centralised import of radio-labelled nucleotides through the Bhabha Atomic Research Centre, Bombay.

Simultaneously, effort is being made for the production of radio-labelled nucleotides by BARC. The CSIR has agreed to provide laboratory space and other facilities in the Centre for Cellular and Molecular Biology Campus, Hyderabad.

NBTB has formulated an integrated plan for conducting short term training courses. Training programme in plant tissue and cell culture; methods and application; workshop-cum-seminar on enzyme engineering; training programme on recombinant DNA techniques in genetic engineering and workshop course on "gene cloning and allied techniques" under genetic engineering programme. Fellowships were also given by NBTB to scientists for short or long term training within the country and abroad. It has been decided to send some scientists abroad in different sectors for training in advanced techniques to expose them to the recent developments wherever infrastructural facilities and expertise are not existing within the country. NBTB will award 30 junior and 12 junior overseas fellowships of 1-2 years duration and 5 senior overseas fellowships of 3 months duration.

Realising the hazard involved in recombinant DNA research, the Board desired to evolve safety regulations. The task was entrusted to a special committee, which on the basis of guidelines followed in other countries viz. the US National Institute of Health, formulated guidelines relevant to Indian conditions which were subsequently approved by the Board.

Research and development effort in the field of biotechnology would become crippled for lack of certain essential infrastructural support facilities. The authenticity of microbial culture, animal cell lines, plant cell lines primate and small animals used in the production of biotechnological product/metabolite is an essential prerequisite for a successful industrial production of the product concerned. Such a rigorous demand can only be met by proper preservation, maintenance, consistency and monitoring of the desirable pool which becomes, therefore, paramount. The need for such centralised facilities having collections of these is, thus acute. Noting that any organised effort in this direction is yet to take place the following proposals have been formulated in consultation with the experts:

(a) Germplasm banks for microorganisms, protozoa and other parasites, plant and animal tissues and cell lines and viruses; (b) Experimental facilities using non-human primates and specialised small laboratory animals; (c) Pilot plant and other bioengineering scale up facilities for process development and optimisation and for producing sufficient quantities of new products for field trials; (d) Procurement/manufacture of enzyme, reagents and labelled isotopes essential for R&D work in bioengineering and related fields; and (e) A network of information disseminating system to provide up-to-date S&T information to the scientists working in the frontier area of modern biotechnology.

An International Centre for Genetic Engineering and Biotechnology is being set up at the Jawaharlal Nehru University, Delhi with the help of the United Nations Industrial Development Organisation (UNIDO). It will take up research and development work in agriculture, human and animal health, industrial technology for pharmaceuticals and other products.

If and when advances in biotechnology are achieved, it would benefit not only India but the world as a whole. As a result of the stimulus of the green revolution, developing countries are aware of potentials for improving crop yields and are maintaining indigenous agricultural stations capable of acting as centres for technology transfer. (Source: The Hindu, 27 February 1985)

Italy

Italian biotechnology

A new centre for biotechnology research and development is being founded at Pomezia, 45 km south of Rome, by Menarini SaS, the Florence-based pharmaceutical company. Dr. Alberto Aleotti, president of Menarini, says the company is investing 28,000 million lire in the new biotechnology centre.

The first goal of the centre will be the manufacture of TPA (tissue plasminogen activator) and its derivatives for human pharmaceutical purposes, using recombinant DNA technology developed by Creative Biomolecules, a California corporation founded in 1982 by Roberto Crea and Charles M. Cohen.

The agreement between Manarini and Creative Biomolecules is aimed at the production of an economic drug for the international market. The Pomezia team will include researchers from Italy, the United States and Britain. The first TPA for chemical and biological evaluation is expected in the summer.

Inaugurating the Menarini centre (and the toxicology research facility on the same site), Italian minister of research Luigi Granelli pointed to several encouraging signs of development in Italian biotechnology by way of international co-operation. The International Genetic Engineering Centre of the United Nations Industrial Development Organization, to be based at Trieste, is one of these. But Granelli added that developments in this field in Europe as a whole are still not a sufficient counter to developments in Japan and the United States, perhaps because governments see their interests as stronger than supra national ventures.

Italian biotechnology is in part held back by the lack of venture capital, with the result that most of the companies involved are either well established in some related field such as pharmaceuticals or are public enterprises. The companies with declared interests include Farmitalia-Carlo Erba (Montedison group, now under the umbrella of Erbamont), Lepetit and Serono. Sorin Biomedica (wholly owned by Fiat), Farmitalia and various companies of the ENI group have declared an interest in protein chemistry; Sclavo, an ENI company, plans to produce beta-interferon. Biotechnology in agriculture is quite advanced at ENEA, the public corporation for nuclear and alternative sources of energy, and Assoreni (ENI group) has interests in agricultural biotechnology.

University researchers have been drawn into biotechnology in various ways. Thus the multinational Roche facility at Milan has an agreement with the Pharmacology Institute of the University of Milan, headed by Professor Rodolfo Paoletti, for applications to molecular neurobiology. The Italian Society for Biotechnology (SIB) has signed a convention with IASM, the public sponsor of development in the south of Italy, and with FINAM, a financial holding for agriculture, to set up a centre for biotechnology transfer in the south.

The first objective of the centre will be to evaluate the degree of innovation in small and medium-size industries so that by the end of 1985 agricultural experiments on a pilot-plant scale may be started. (Source: Nature, Vol. 314, 14 March 1985)

The Netherlands

Dutch biotechnology

The Netherlands is outstandingly strong in biotechnology, in industrial companies, academic departments, and a light but well-organised structure for national cocrdination.

It has an excellent tradition of microbiology, biochemistry and process engineering, and retains a leading international position in effluent treatment, developed in response to the needs of the food industries.

The company Gist-Brocades is Europe's major producer of penicillin, with corresponding expertise in fermentation technology. It is also one of the world's major producers of enzymes, and is carrying out intensive study on their production, isolation and application, on laboratory and commercial scale. Related research is under way to the universities of Delft and Wageningen. In the food industry, Dutch breweries and dairy plants are sophisticated and internationally competitive.

Academic strengths in biotechnology include the universities of Amsterdam (microbial physiology), Leiden (genetics), Groningen (protein crystallography, molecular dynamics), Wageningen (which along with the various research institutes there, covers a wide range of agricultural sciences) and Delft (where the Technical University has a close association with industrial fermentation). (Extracted from Industrial Biotechnology Wales, February 1985)

Genentech and Cetus talk to Dutch

U.S. biotech concerns, Genentech and Cetus, are negotiating with the Dutch Government Industrial Projects Company, MIP, an investment promotion body to set up subsidiaries in the Netherlands. The two companies say their eventual settlement in Holland will be conditional upon government financial support.

Genentech had earlier considered establishing a research centre for its "genemachine" venture with Hewlett Packard in the Netherlands in 1983, but finally chose Benders of Austria, a Boeringer Ingelheim subsidiary. If government support is adequate, production facilities to build machines to synthesise genetic material may be located in the Netherlands.

Cetus is interested in working jointly with Leiden University on genetic manipulation of plant cells. Leiden University recently joined biotech ventures with Centocor and Molecular Genetics of the USA. (Source: Manufacturing Chemist, April 1985)

Switzerland

Fixed binding sites

Fixed binding sites exist to hold DNA to a protein scaffold, according to Dr. U. Laemmli of the University of Geneva. A loop of DNA may represent a single gene or a set of adjacent genes that are coordinately expressed. A major protein in the scaffold is an enzyme called topoisomerase II. The enzyme is used in untangling DNA. The attachment sites may be sites where topoisomerase II binds DNA. The function of the attachment sites is uncertain. (Extracted from Science News, 23 February 1985)

Basel Institute for Immunology

The Basel Institute for Immunology (BII) conducts basic research with full academic freedom, even though it has been and still is supported entirely by F. Hoffmann-Laroche AG, a family-owned Swiss pharmaceutical company. The work of this institute helps indicate the Swiss pharmaceutical industry's commitment to basic research.

BII was founded in 1968 and began operation in 1971 with Dr. Niels Jerne as its first director. (Jerne shared the Nobel Prize in Medicine and Physiology with Drs. Milstein and Kohler for the concept and development of the methods for monoclonal antibody production.) Dr. Fritz Melchers is the present director of the BII. There is a board of directors which is responsible for the operation of BII and for ensuring its independence. BII also has a board of advisors which has an international representation. Most of the members of the board of advisors are former Nobel Prize winners, making this a very high-powered group.

In addition to the above-named boards, the institute also has a board of consultants. This board consists of scientists working in other Swiss laboratories. It acts in a capacity similar to the board of advisors and encourages cooperation among immunologists in Switzerland.

About one-third of the projects have been cooperative work with scientists from Austria, Canada, Denmark, Finland, France, West Germany, Great Britain, The Netherlands, Sweden, Switzerland, and the U.S. The research projects encompass the following topics: gene structure; DNA cloning and transfection; structure and function of immunoglobulin; structure and synthesis of surface antigens; repertories of T and B cells; biochemical studies on activated lymphocytes; activation of lymphocytes by lectins and antibodies; lymphokines; hemopoietic factors; differentiation in vitro and in vivo; cell surface of lymphocytes; formal genetics; lymphocyte migration; idiotypes; T cell lines and hybridomas; helper T-cells and T-B collaboration; autoimmunity; and development of new methods for immunological studies.

Research at BII has led to the development of new reagents and techniques. Monoclonal antibodies with interesting specificities have been generated. These include large libraries of gamma light chain-producing antibodies from mitogen-stimulated spleen cells of kappa light-chain-suppressed mice, and of antibodies from mitogen-stimulated as well as ovalalbumin-primed spleen cells in which rheumatoid autoantibodies could be found. Conditions for serum-free cultures of chicken lymphocytes were improved. Antibodies secreted by a B cell clone in semisolid agar can be detected, and single cells can be probed in situ for the expression of specific messenger RNA (mRNA), for example, B lymphocytes for the expression of Ig-specfic mRNA. A mouse fibroblast line has been established in culture that offers an alternative to L cells and NIH 3T3 fibroblasts for DNA transfection experiments. Methods for DNA transfection have been further refined. For the first time, a complete epitope-binding, biologically active Ig molecule was produced by gene-transfer techniques. With present methods for modifying genes, research is being carried out to construct new Ig genes, such as a variable region of heavy chains linked to a constant region of light chains. New alleles of genetic markers were found, and new halotypes and recombinants were bred. Two-dimensional gel electrophoresis is being used to analyze the phenotype of cells. A fully automated oligonucleotide synthesizer has been built at the institute's workshop. It uses the chemistry of ologonucleotide synthesis developed at the Roche Research Department to prepare probes for gene isolation and modification.

BII offers an ideal environment for a research scientist. Since the institute is entirely funded by the Hoffman-LaRoche Company, the scientific staff does not have to apply to the Swiss Government or to any other sources for research funds.

The main criterion for a research project is that it be innovative, without the requirement of any direct application to a potential product for Hoffmann-LaRoche. Thus, the independence of the scientific staff is equivalent to that at any university. Many of the scientists at the institute also teach at the University of Basel and train graduate students

as well as post-doctoral fellows. Since most of the staff positions are on a temporary basis of 3 to 5 years - in some cases, 8 years - there is a continuing influx of new ideas and projects. In addition, the international composition of the staff is conducive to the generation of new concepts and to collaboration with scientists from other countries. The organization of the institute, in that there are no departments or sections and no chairmen, facilitates collaboration rather than competition among the scientific staff. They are also permitted to publish freely the results of their research. The excellence of the research has led to international recognition of the institute as an organization devoted to research of the highest quality. (Source: European Science News, 39-6 (1985))

The Friedrich Miescher Institute, Basel

The institute was established in 1970 as an independent foundation by Ciba-Geigy Limited. The aims of the institute are: (1) to engage in basic research, originally in the fields of biochemistry and medicine and, more recently, in plant science; and (2) to provide an international centre for research, study, and training for young scientists. This institute is entirely funded by Ciba-Geigy, but the staff scientists carry out research without constraints by Ciba-Geigy. Thus this institute has the same independence in research projects as the Basel Institute of Immunology and the Roche Institute of Molecular Biology in the U.S., the latter two being entirely funded by the Hoffmann-LaRoche Company. The director of the Friedrich Miescher Institute is Dr. Edward Reich.

The institute was originally housed at the Biozentrum, University of Basel, but is now in new and larger quarters in the Rosental complex of Ciba-Geigy. These quarters are well equipped with supporting facilities required for modern research in the life sciences. Current work at the institute spans a wide range of subject matter in cell and molecular biology of eukaryotic organisms. The institute maintains a programme of internal research seminars and journal clubs, seminars, and lectures by a constant stream of visitors from Europe and overseas, as well as meetings on special topics of interest. The staff scientists as well as research fellows comprise an international group representing, in addition to Swiss nationals, other European countries as well as Japan and the U.S. Some of the staff scientists as well as research fellows have temporary appointments for periods from 2 to 5 years, similar to the situation at the Basel Institute of Immunology. This turnover allows for an influx of new ideas and approaches to research projects.

A board of trustees is responsible for overseeing the long-term activities of the institute. It is helped in its assessment of the institute's work by an independent scientific advisory board that consists of an international group of distinguished scientists.

A large number of diverse research projects are carried out at the institute: gene expression in yeast; plant development; culture and genetic modification of cereal protoplasts; regulation of storage proteins in corn seeds; biochemical genetics of cultured plant cells; studies on cauliflower mosaic virus; gene expression in plants; neuronal microdifferentiation; desensitization of β-adrenergic receptors; glia-derived modulations of neurite outgrowth in neuronal cells; human oncogenes; human interferon; mechanisms of DNA repair; hormonal regulation of gene expression; regulation of tumour functions by hormones; structure, function, and hormonal regulation of specific eukaryotic genes; regulation of protein synthesis and S6 phosphorylation; molecular aspects of protein phosphorylation; structure and function of plasma proteases; hemopoietic cell differentiation and transformation; biochemistry of fibrinolysis; translational control mechanisms and clinical immunology; regulatory events of the cell cycle. (Source: European Science News, 39-6 (1985))

United Kingdom

Britain planning biotech research

The British Government is planning to establish a joint biotechnology research programme involving industry, public and private sector research bodies and universities, according to Geoffrey Pattie, industry minister responsible for biotechnology.

Five U.K. food and chemical groups - Unilever, ICI, Shell, Rank Hovis McDougall and Cadbury-Schweppes - have already discussed the proposal with the minister. So have three Government research councils and Agricultural Genetics Co.

Under discussion is a joint R&D programme of £5-10m a year over five years, with the Government contributing a large part of the cost. The object would be to carry out basic research to enable food and agro-chemical companies to exploit new areas such as genetic engineering.

Participating companies would form partnerships with universities, polytechnics and research council laboratories. Study groups set up to investigate three separate areas - food science, plant science and animal sciences - are due to report to the Government in June. The programme could be launched later this year.

Of the European Community countries, the United Kingdom has the strongest research base in biotechnology, with world class centres in many of the key disciplines. The institutes of the Medical Research Council (e.g. Molecular Biology, Cambridge), and of the Agricultural and Food Research Council (e.g. The John Innes Institute, Norwich) complement strong university departments; and another public institute of special importance of biotechnology is the Centre for Applied Microbiology and Research at Porton Down, strong in fermentation science, and home of a recently founded centre for animal cell lines.

Industrial biotechnology in the U.K. is represented by leading chemical firms, as in ICI's "Pruteen" plant for single-cell protein combining a major innovation in engineering (the air-lift continuous fermenter) with a major innovation in nutrition. In fermentation for pharmaceuticals, Glaxo and Beechams are well known, and G.D. Searle and Wellcome are also noted for their capability in genetic engineering. In agro-food, Unilever's success in cloning cells of the oil-palm is a breakthrough in applied genetics of major practical benefit; Rank Hovis McDougall's mycoprotein is another promising food innovation.

The U.K. also has many smaller, venture-capital companies, with special skills or application areas, or providing ancillary services and supplies to the larger firms. Celltech, launched by government co-finance with industry, is strong in animal cell culture and in the production of monoclonal antibodies (for diagnostic or analytical applications), as is to be expected in view of its original links with the institutes of the Medical Research Council; a similar link with the agricultural institutes provides access to the knowledge base for Agricultural Genetics Co. Ltd. (Source: Industrial Biotechnology Wales, February 1985 and European Chemical News, 29 April 1985)

U.K. Biotechnology

One of the most unusual arrangements yet for turning public investment in research into industrial channels, Porton International, announced an arrangement with the British Government that gives it the right of first refusal on biotechnology innovations at the Centre for Applied Microbiology and Research (CAMR).

The new arrangement is the outcome of several years of negotiation. Porton International already has agreements with CAMR for the exploitation of two of its proprietary developments, asparaginase (used in cancer chemotherapy) and a vaccine for herpes simplex virus (based on developments at the University of Birmingham as well as at CAMR).

In a joint statement, the company and the Public Health Laboratory Services Board said that the new arrangement will run for thirteen years from 1 April, and that the arrangement might be continued thereafter. A spokesman for Porton International said that developments not taken up by the company would remain the property of CAMR, and might be offered to other companies. But he suggested that such happenings would be few and far between.

The management of the laboratory will remain the independent responsibility of the director, Dr. Peter Sutton, the Public Health Laboratory Service and ultimately the Department of Health and Social Services. But the existence of the new agreement is likely to divert the scientific interests of many members of the laboratory into directions that may be profitably exploited.

Porton International Ltd. is for the time being a holding company, with a number of subsidiaries (such as LH Fermentation) active in fields related to biotechnology. The recent development appears to have been financed by capital contributions from a number of financial institutions, including the pensions funds of several public companies and a number of insurance companies. (Extracted from Nature, Vol. 314, 18 April 1985)

British thalassaemia

Britain seems to have its own form of α-thalassaemia, a genetic disorder that disrupts the synthesis of -globin chains, which form part of the oxygen-carrying haemoglobin in the blood. Researchers at the John Radcliffe Hospital in Oxford have diagnosed the rare genetic defect in eight people with no known foreign ancestry (British Medical Journal, Vol. 290, p. 1303).

Normal individuals have two α-genes on each of the relevant paired chromosomes (number 16). People with only one functional α-gene ($--/-\alpha$) suffer from a moderately severe anaemia, whereas people with no α-genes die early on. The discovery of the heterozygote

condition (--/--, which causes no illness) in British people is interesting because researchers have long thought that only people of Mediterranean or Southeast Asian origins showed deletions of both α-genes on one chromosome. The study has implications for genetic counselling: we now know that a child of either British-Mediterranean or British-Southeast Asian parents could suffer from the lethal (--/--) form of α-thalassaemia. (Source: New Scientist, 16 May 1985)

United States of America

U.S. biotechnology policy

Most technologically developed countries have a well defined science policy, in which biotechnology is targeted for support as a national goal. The United Kingdom, France, West Germany, the Soviet Union, and, even more vigorously, Japan have national efforts involving government support of industrial-academic collaborations, financial support of private companies, legislative support, and rapid modification of scientific guidelines.

In contrast, the United States' policy appears to be in some turmoil. The Environmental Protection Agency has not been given any specific authority in this area, but has loosely interpreted the Toxic Substances Control Act and the Federal Insecticide, Fungicide, and Rodenticide Act to encompass DNA as a potentially hazardous chemical. The Departments of Defense, Commerce, and State debate the extent of restrictions on exporting biotechnology to other countries. Lawsuits filed in U.S. courts challenge a host of biotechnology issues ranging from deliberate release of microorganisms, to patent questions (particularly those involving universities and industry), to the rights of patients to share in profits of biotechnology created from their body tissues. In all of these areas, industrial participation in formulating national policy has been largely restricted, if not nonexistent. Many initiatives need to be addressed in terms of a comprehensive national science policy in biotechnology: supporting basic research; targeting in areas like bioprocessing, plant molecular biology and biochemistry; improving intellectual property law; regulating technology transfer rather than products; modifying import-export regulations, to name a few.

The National Institutes of Health (NIH) originally established guidelines for recombinant DNA research under the Recombinant DNA Advisory Committee (RAC). Both academia and industry have adhered to the guidelines and have sought RAC approval as necessary. This single scientific oversight system of review and recommendation is considered by nearly all to have functioned in an exemplary fashion. The gamut of controversial issues and experimental proposals has been brought forward, accepted for discussion, and acted upon in the light of current knowledge - all with dispatch. These issues include deliberate release to the environment and human gene therapy, and will probably include the issue of "convertibility" for military uses. With the exception of hybridoma technology, the major recent discoveries leading to modern biotechnology have been made in the United States. These include methods for manipulating, reading, cutting, and splicing DNA chains. Seen in this light, the disarray of U.S. policy seems surprising.

In the last half of this decade, the United States will clearly compete with coordinated efforts in biotechnology from most of the industrialized countries. The U.S. Office of Science and Technology Policy (OSTP) has published a Proposal for a Coordinated Framework for Regulation of Biotechnology, (Federal Register, 49: 50856, December 31, 1984). The Proposal recommends establishing separate rDNA Advisory Committees within the Food and Drug Administration (FDA), EPA, Department of Agriculture (USDA), NIH, and National Science Foundation (NSF). The FDA, EPA, and USDA have provided position statements, included in the Proposal, but NIH and NSF provided none. The statements from the FDA and USDA acknowledge that they have no need for additional authority for regulation and will deal with biotechnology on a case-by-case basis. There are inconsistencies in the FDA statement. The agency says on one hand that it intends to regulate products "based on a rational and scientific evaluation of products and not on a priori assumptions about certain processes," yet it says that animal and food additive products must be subject to approval "even if the active substance is shown to be identical to that in approved products produced by conventional methods." In contrast, the USDA policy statement notes that agriculture and forestry products developed by biotechnology will not differ fundamentally from conventional products.

The OSTP proposal provides for a second or different review process for biotechnology products by establishing a Biotechnology Science Board (BSB). This creates a two-tiered system in which submissions are made to the appropriate authority, which forwards them to BSB, which may send the proposal back with recommendations or send them on to yet another authority for further consideration. Products of biotechnology are not inherently different from "conventional" products. (Extracted from Bio/Technology, Vol. 3, May 1985)

USSR

Two-stage bio-oxidation used to purify postfermentation mash

At the Kropotkin Chemical Plant a method has been introduced for biological purification of afteryeast mash (PDB) which, in addition to lowering pollutant content of PDB, makes it possible to recover an additional amount of biomass. Under the conditions at the Kropotkin plant, the method is the most suitable and effective, since the plant processes vegetation waste from agriculture mixed with molasses slops into feed yeast, and along with augmenting output, this causes significant increase in pollutant content of PDB passing into the general discharge channel of the plant. Unutilized nutrients remain in PDB (carbohydrates, organic acids, nitrogen and phosphorus salts, trace elements) which have high parameters for chemical and biological oxygen demand.

The biooxidation process takes place in two stages in yeast-growing fermenters as follows: the nutrient substrate delivered for first-stage biooxidation (in 600 m^3 tank) consist of mash that has risen and wash from the bottom separators of the basic production fermenters. Partially purified PDB is discharged from the bottom separator of the vat and directed as nutrient medium to the second-stage biooxidizer (1,300 m^3 tank). Purified PDB is discharged into general discharge channel of the plant. The cultivated biomass is recovered from the top separators of the fermenters, mixed in a flotation unit with the general flow of yeast suspension and delivered for separation and drying.

The yeast-like fungus, Trichosporon cutaneum, serves as the main culture for biological purification of PDB. Pure culture of the fungus is added once a week to each biooxidizer; however, there is mostly the basic production yeast culture in the first-stage bio-oxidizer, whereas in the second-stage one there is prevalence of the fungus.

Aeration of the biooxidation process is effected on the level of yeast fermentation at a temperature of 39-40°C; medium pH is controlled with sulfuric acid; the concentration of biomass in the fermenters is kept at 15-17 g/l; PDB remains in the first- and second-stage fermenters for 2.7 and 7.0 h, respectively.

Thus, introduction of technology for two-stage biooxidation of afteryeast mash made it possible to lower contamination by 40-45% according to chemical oxygen minimum and by 50-55% according to biochemical oxygen demand, as well as to produce an additional 2,662 kg per day of commercial yeast. The economic effectiveness of obtaining additional biomass constituted 212,300 rubles/year. (Extracted from Microbiologicheskaya Promyshlennost'. Ekspress-Informatsiya, No. 5, 1984)

C. RESEARCH

Research on human genes

Anti-cancer hormone

A human hormone with potential anti-cancer properties has been isolated by scientists working at the US National Cancer Institute at Bethseda, Maryland, USA. The hormone, called human leukoregulin, is made by lymphocytes. It is molecularly and biologically distinct from previously discovered anticancer substances that occur naturally, including lymphotoxin, the interferons, interleukins 1 and 2 and macrophage activating factor. Leukoregulin has two modes of action. It can directly burst or supress human tumour cells including sarcoma and leukaemia cells. Secondly it can enhance the ability of natural killer cells to lyse tumour cells.

This second activity makes the hormone distinct from the interferons. The hormone's mode of action appears to be the alteration of tumour cells surface permeability. Preliminary experiments with the substance as an anticancer therapy have been encouraging. Mice, given human tumour xenografts have shown as much as 50 per cent inhibition of tumour cell proliferation when treated with leukoregulin. (Source: New Scientist, 16 May 1985)

Human white blood cells as carcinogens

Blood cells that normally protect the body from bacterial infection sometimes can produce enough germ-killing toxic substances over a long enough time to cause normal tissue to become malignant. Researchers at Massachusetts General Hospital and Harvard Medical School in Boston reported they believe some cancers can be caused not only by toxic substances in the environment but also by toxic substances released by cells called phagocytes to fend off environmental carcinogens.

The researchers showed that human neutrophils - phagocytic white blood cells that ingest bacteria and foreign substances - release toxic free radicals (oxygen metabolites) that can cause normal mouse connective tissue to become malignant. They injected 43 mice with cells treated with human neutrophils activated to produce toxic oxygen metabolites and injected a control group of 53 mice with untreated cells. Five of the mice given treated cells developed malignant tumors and six developed benign tumors. None of the control mice developed tumors.

The most common human model in which phagocytes accumulate and ultimately cause cancer is ulcerative colitis, a chronic bowel inflammation.

The researchers believe the mechanism of phagocytic accumulation and production of toxic metabolites might also help explain the origins of lung and breast cancer.

The researchers do not know the specific molecules ultimately responsible for causing normal tissue to become malignant. Phagocytes produce superoxide, hydrogen peroxide and hydroxyl radicals, as well as other toxic substances. These substances can interact with membrane components of phagocytes or their target cells to generate other toxic products, such as peroxides and aldehydes. (Extracted from Science News, Vol. 127, 9 March 1985)

Anemia: A defence against cancer?

Scientists have long suspected that iron plays a role in cell proliferation processes, such as cancer. Researchers at the University of Florida-Gainesville have shown that supplemental iron can enhance tumor growth in laboratory animals, and they suggest that anemia may be a defense mechanism in cancer patients.

The researchers injected leukemia cells into mice treated with iron at levels "comparable to clinical doses for humans" and into untreated mice. They found that tumors grew faster in iron-treated mice and that these animals succumbed to the disease faster than did untreated animals.

Most living things, from microorganisms to cancer cells, need iron to grow. When bacteria invade the body during an infection, the body removes iron from the bloodstream and "hides" it in the liver, making it unavailable for bacterial growth. Such a mechanism might also take place in certain cancers and explain why many cancer patients have anemia, according to the report in the March JOURNAL OF NUTRITION. However, the researchers warn against extrapolating the results of the present study to humans since the study involved only one type of cancer - mouse leukemia. (Extracted from Science News, Vol. 127, 6 April 1985)

Plan from genes to embryo

A recently discovered segment of DNA, called a "homeo box," is thought to direct the development of the body plan in a wide variety of animals (SN: 7/14/84, p. 21). Walter Gehring of the University of Basel in Switzerland and colleagues are examining fruit fly embryos to determine when and where genes containing homeo boxes are active. They have studied three fruit fly genes containing homeo boxes and find that each is active in specific periods and locations in the early embryo corresponding to the recognized roles of the genes. For example, flies with a defective form of one of these genes have legs instead of antennae extending from their heads. In normal embryos, the gene is active only in the region destined to become the head. Similar experiments on genes that influence segmentation produced stripes of gene activity. (Extracted from Science News, Vol. 127, 23 February 1985)

Smoke gets in your genes

Cigarette smoke rots your genes - quite literally. Japanese researchers have found that cigarette smoke causes human DNA to break up into smaller strands. In experiments, they found that one cigarette can cause about 10 000 single-strand breaks in the DNA of one cultured human cell. They suggest that this "clastogenic" action of breaking DNA strands could be the reason why cigarettes can cause cancer.

The team of researchers, from Tokyo's National Cancer Center Research Institute, says that "there has been no previous direct demonstration that cigarette smoke can cause single-strand breaks in DNA". The team suggests that the breaks could be caused by active oxygen (such as hydrogen peroxide and the free oxygen radical, O_2) that is generated by cigarette smoke.

"Although, in the body, most [single-strand breaks] caused by cigarette smoke are expected to be efficiently repaired, some would remain unrepaired and the accumulation of such [breaks] over a long period may have serious consequences, especially for heavy smokers," the researchers say. (Source: New Scientist, 11 April 1985)

Genetic code is not so universal

Any textbook of genetics or evolution will tell you that the genetic code - the relationship between the nucleotide sequence of a gene and the amino acid sequence of the protein it codes for - is universal. All creatures, from bacteria to humans, use the same genetic code. This neat simplicity was disturbed slightly a few years ago, when the small genomes of mitochondria were found to use slightly deviant codes. Now, some more deviations from the standard code have turned up in some free-living ciliated protozoons and mycoplasmas implying that the genetic code is really not universal after all.

The deviations from the standard code, which five separate groups of scientists in America, Europe and Japan have now found, are very small. In each case a series of three nucleotides (a codon) which normally marks the point on messenger RNA at which protein manufacture should stop, instead codes for the incorporation of an amino acid. But they are deviations from a major biochemical doctrine.

The main significance of these new discoveries concerns our version of early evolution. Current textbooks often state, not only that the genetic code is universal, but that it has to be universal because any alteration of the code would destroy the organisms concerned by wrecking all of their vital genetic messages. Such reasoning is based on the assumption that all modern life is derived from a single ancestral line in which the standard genetic code was already fixed. The modern code has been described as a "frozen accident", chanced on by the first life and then fixed forever because changes would cause damage.

The discovery of slightly altered versions of the code probably simply means that the organisms concerned diverged from the common stock at an early stage and that some geneticists have been overly dogmatic in asserting the inevitability of a universal code.

Completely different codes would be a major shock but there are no signs of them so far. It does appear however that the "frozen accident" may have experienced the occasional thaw. (Extracted from New Scientist, 11 April 1985)

Breakthrough in search for malaria vaccine

This summer, the first trials in humans of the first synthetic vaccine against malaria should take place. Teams of researchers working for government institutes and a pharmaceutical company in the US reported last week that they had persuaded bacteria to produce a protein found on the surface of one stage of the malaria parasite's life cycle. When the researchers inoculated mice with the protein, the animals produced antibodies which prevented infections by real parasites.

Over the past few years, researchers in Europe and the US have found that it is possible to immunise the body against the first and crucial stage of the parasite's life cycle in humans. This is the sporozoite, the form in which Plasmodium enters the blood.

Sporozoites are tiny organisms which enter the blood from the saliva of anopheles mosquitoes. When in the blood, they make their way to the liver, where they develop into another form, called metazoites. The metazoites go back into the blood stream, to produce the symptoms of malaria.

An ideal vaccine against malaria would stimulate the body to produce antibodies which would seek out and destroy sporozoites in the blood. Researchers have known for years that this is theoretically possible. Experiments on animals and humans have shown that inoculations of parasites killed by irradiation stimulate the body's immune system. But P. falciparum has evaded attempts to be grown in culture, thus making this type of vaccine impossible to produce on a large enough scale.

The goal of research now is to find ways to produce large quantities of the bit of the parasite that stimulates the body's immune system. This is a protein on the organism's surface, called CS or circumsporozoite protein. Again, it is impractical to separate adequate amounts of the protein from malaria parasites. But last year, John Dame and colleagues from the US's National Institutes of Health managed to identify and clone the gene responsible for making the CS protein. This work opened up the possibility of introducing the gene into another organism, thus programming it to make large quantities of CS protein.

James Young and colleagues of the pharmaceutical firm SmithKline French, together with teams from the Walter Reed Army Institute of Research, the Naval Medical Research Institute and the National Institutes of Health, report successfully carrying out this piece of genetic engineering.

The teams isolated the sequence of DNA, 2337 base pairs long, which carries the code for CS protein, and introduced likely-looking fragments of it into plasmids of the bacterium Escherichia coli. The engineered bacteria produced three varieties of the peptide sequence, which seemed to account for the immunological activities of CS protein. When inoculated into mice, all three sequences stimulated the animals to make antibodies. The two longer sequences were the most effective, producing large quantities of antibodies.

Further tests, including ones on liver cells, "all demonstrate the strong immunogenic potential of these E. coli-produced CS protein derivatives," the authors report. "These recombinant proteins may be appropriate for development of a human malaria vaccine."

Although researchers are confident that a vaccine based on synthesised CS protein will soon be ready for trials in humans, no one is saying that vaccination against malaria is about to become routine. Even if the substance lives up to its promise, work is still needed to devise practical and stable formulations to use as vaccines. (Extracted from New Scientist, 23 May 1985)

Malaria parasites

Malaria parasites can propagate in red blood cells that are deficient in an enzyme they need by producing the missing enzyme.

The enzyme is glucose-6-phosphate dehydrogenase (G6PD). Women with a certain X-linked chromosomal disorder cannot produce this enzyme, and because the malaria parasites rely on the enzyme for their development, its deficiency protects some women against the disease. But E.A. Usanga and L. Luzzatto, of the Royal Postgraduate Medical School, in London, have found that malaria parasites can produce their own G6PD. (Nature, Vol. 313, p. 793)

The parasites invade both the normal cells and the G6PD-deficient cells, and gradually adapt to the G6PD-deficient cells by producing increasing amounts of their own enzyme. They thus possess the gene for this enzyme but are unable to express it in normal red cells.

The study shows that the expression of a parasite's gene can be determined by the host cell. But it also provides insight into how the malaria parasite might cope with other red cell deficiencies, and even antimalarial drugs. (Source: New Scientist, 11 April 1985)

Acquired Immune Deficiency Syndrome (AIDS) Virus

The acquired immune deficiency syndrome deserves all the scientific attention it receives. AIDS differs from many categories of diseases - old and new. It takes years to manifest itself and it claims the lives of most of those who contract it. So long is the gestation period of AIDS that many of the people now dying from it were infected with the virus before the first scientific paper on the disease appeared. Even worse than this is the fact that the research under way will do little for someone exposed to the virus today. Responsible medical opinion is that researchers will find no "cure" for AIDS in the next five years.

This does not prevent newspaper headlines from announcing "cures" and "vaccines". Nor does it prevent some researchers from attacking the press for sensationalising AIDS. If this has happened, then the scientists must carry some of the responsibility. Researchers have made rash claims of rapid progress and have talked of developing vaccines. Others have warned that the disease shows every sign that it will spread at an alarming speed to the whole of society. This was the message of numerous papers presented at a meeting on AIDS, in Atlanta, Georgia, but it did not stop one researcher from berating the press for so much as mentioning the possibility that AIDS will spread beyond the homosexual community.

With such contradictory messages it is no wonder that the press and the general public receive a confused picture. This would not matter were it not for the fact that among the ranks of the confused are not only those with AIDS but also those who are expected to diagnose and treat the disease.

The virus that causes acquired immune deficiency syndrome (AIDS) may also be responsible for the brain disease seen in some patients with AIDS. Doctors blame opportunistic infections for the brain degeneration associated with AIDS, but new research presented by Dr. Leon Epstein at an international conference on AIDS in Atlanta, Georgia, suggests that the virus may show as much tropism for tissues of the brain as it does for cells of the immune system.

If the AIDS virus is proven to cause brain disease, Epstein, of the University of Medicine and Dentistry in New Jersey, and the Laboratory of Central Nervous System Studies at the National Institutes of Health in Bethesda, Maryland, says "we could have the biggest neurological problem we have had on our hands for years".

Encephalopathy means, literally, brain disease. In adults with encephalopathy, AIDS results in mental disorder affecting knowledge and intellect, resembling dementia. In children, however, it results in retarded development. In adults it causes profound atrophy, shrinkage or destruction, of brain tissues. In children, this manifests itself as delayed brain growth.

It was the effects in children that first suggested to Epstein that the AIDS virus might be responsible.

Epstein told delegates at the meeting the reasons behind his frightening speculations. He took brain tissue from people who died from AIDS, homogenised it in saline and injected it into the brains of eight healthy chimpanzees. Four animals now show evidence of infection either by the presence of antibodies to the AIDS virus in their blood or by the fact that virus can be isolated from their blood. Fifteen months is the longest time any animal has been infected. Although no animal has developed clinical or immunological features of AIDS, it is still early days.

Epstein said that the AIDS virus may infect the brain more heavily than any part of the body. He drew attention to the "striking similarity" between the AIDS virus and the visna virus of sheep. Both diseases look the same under the electron microscope, both share similarities in the sequence of nucleic acids that make up the genome, and, finally, in their preference for replication in neural cells.

Two other pieces of evidence support the idea that the virus could be the cause of encephalopathy in AIDS. First, the AIDS virus has the propensity to attack well-differentiated cells and persist for a long time. Secondly, the brain is a good place to live from the virus's point of view because it is said to be "immunologically privileged" - the immune surveillance system does not patrol the brain.

If Epstein's hypothesis is correct, it could have dire consequences. The so called "blood-brain barrier" prevents the passage of most substances in the blood into the brain. This makes it very difficult to design drugs to fight the brain infection. The problem has worsened by the fact that the brain is not patrolled by the immune system. Secondly, even if a treatment were available tomorrow to treat AIDS successfully, it would eradicate the infection in blood but would do nothing for the viruses that have set up house in the brain tissue.

Epstein speculates that even if the immune system does recover as a result of the therapy, it would then begin to wage war on the brain cells - self-destruction at its most horrific. Finally, we have no idea how many people are at risk of developing encephalopathy. It could be that everyone who has antibodies to the AIDS virus (that is, who have been exposed to the virus at some time) will eventually suffer brain dysfunction.

Epstein freely admits that he is speculating. He has no evidence that the virus is responsible for the brain disease. Although he has isolated virus from diseased brains and shown that it elicits a response in the immune system of chimpanzees when transplanted into the brains, the chimpanzees have not developed any disease. The AIDS virus might happily replicate and live in the brain for the whole of an individual's life without causing any disease at all.

All of which makes it imperative that scientists learn about the early consequences of infection by the AIDS virus.

Scientists are suggesting that Kaposi's sarcoma, the cancer seen in the most severe cases of AIDS (acquired immune-deficiency syndrome), may be caused by an as yet unidentified virus.

Kaposi's sarcoma (KS) has baffled scientists since it was first diagnosed. Prior to AIDS this cancer was confined to a region of central Africa. It was also seen among people whose immune systems were suppressed for medical reasons - for example to prevent a transplanted kidney being rejected. In both cases the disease was indolent and would often regress when the immune system recovered.

But KS in AIDS patients is different; it is far more aggressive, invasive and life-threatening. There is also a similar, more virulent KS on the increase in central

Africa, and this "atypical" form is often unrelated to AIDS. Scientists have looked to the virus that causes AIDS as the possible culprit for KS - it does, after all, cause immunosuppression.

Scientists have found, for example, that people with "classical" KS in central Africa do not carry the AIDS virus, whereas those with the newer "atypical" KS do.

Professor Jan Desmyter, head of microbiology at the Catholic University of Louvain, in Belgium, told a meeting at the London School of Hygiene and Tropical Medicine why he thought this was unlikely. Desmyter mentioned two studies; one showing that 35 per cent of blood samples taken in 1970 from healthy mothers in Kinshasa in Zaire showed some reactivity with the AIDS virus, indicating that they have antibodies to the virus and so must have been in contact with it in the past. Because KS is increasing one would expect more reactivity in samples taken more recently, but the reverse is true.

In the second study, only 10 per cent of blood samples taken in 1980, from healthy Kinshasa mothers contained antibodies to the AIDS virus.

There are other reasons to suspect a novel virus in KS. The first is that haemophiliacs who develop AIDS through infected blood rarely develop KS even when they do develop the other symptoms of AIDS. Secondly, KS in AIDS was rare at the early stages of the disease but is increasing all the time.

New evidence from Denmark may dispel the idea that AIDS in the West will eventually affect men and women equally, as it now does in central Africa. Dr. Mads Melbye and others from the Cancer Research Institute at Aarhus investigated the families of 14 haemophiliacs who had all been infected by the AIDS virus from American clotting concentrate. Only one of the 35 individuals they examined had caught the virus from one of the haemophiliacs, and she was the only female sexual partner who practised anal intercourse.

The other wives or consorts, were unaffected. It seems, therefore, that rupture of the very thin lining of the rectum is the route by which the virus is spread perhaps by a blood-sucking insect vector for the disease.

New fears that children may catch AIDS

The number of infants suffering Acquired Immune-Deficiency Syndrome (AIDS) in the US may be grossly underestimated so claimed one of the 2400 scientists attending an international meeting on AIDS in Atlanta, Georgia. Dr. James Oleske of the New Jersey Medical School said there was "tremendous under-reporting" of paediatric AIDS in the US. The real number could lie anywhere between 400 and 800 cases.

Since the Centers for Disease Control (CDC), the US watchdog on communicable diseases, first began counting AIDS cases in 1981, 72 cases in children under 13 years of age have been reported. Of these, 46 have one or both parents who had AIDS or are members of groups recognised to be at high risk of contracting the disease. These groups include intravenous drug abusers, bisexual men, Haitians and haemophiliacs.

The disease in children differs from AIDS in adults. Whereas the majority of adult cases of AIDS affect white homosexual men, 74 per cent of the childhood cases are black or Hispanic, and only 58 per cent are male. Pneumonia caused by Pneumocystis carinii is the commonest infection and Kaposi's sarcoma in children is rare.

The virus is thought to be passed on from mother to child by one of three routes. The first is across the placenta. The second route could be via the amniotic sac, or the AIDS virus could infect the child by direct contact with the walls of the birth canal during birth.

The virus is known to insert its genetic material into that of the host and once a child is infected by the AIDS virus it is for life. This allows for the possibility of transmission of the virus from generation to generation, so long as germ cells have been infected. Two of the infants in Oleske's study were identical twins. One contracted AIDS and the other did not. Since identical twins have identical genetic complements, there must, at the very least, be other contributory factors. (Extracted from articles appearing in New Scientist, 18 and 25 April 1985)

AIDS in Central Africa

A meeting in Senegal enabled AIDS researchers to learn more of the possible African origin of the virus that causes AIDS and virus-associated cancers in Africa.

Because of growing evidence that the virus that causes acquired immune deficiency syndrome (AIDS) originated in Central Africa, AIDS researchers are turning to their atlases. What they were forcibly reminded of is that in African terms, AIDS is an insignificant problem, but that most common forms of cancer in Africa are caused in part by viruses.

At times the question of the origin of AIDS has seemed to be no more than a matter of geographical buck-passing - first between the United States and Haiti and then to and within Africa - but the issue is much more serious. At its worst, the argument is that the virus (HTLV-III or LAV) has only recently emerged in virulent form, has been able to do so as a result of changing socio-economic factors in Africa and may be followed by equivalent conversions to virulence of other relatively harmless viruses. More optimistically, the question becomes: can one learn anything from the origin of the virus that would help to contain the disease?

Geographically, the finger of suspicion points at Central Africa, possibly Zaire, as the location from which the virus has spread. The data, however, are sketchy and dependent on what historical and contemporary sera samples are available for analysis, and to whom. From one of the most extensive surveys so far, G. de Thé of the CNRS, Lyon, provisionally concluded that the virus emerged in Kenya only after 1970, that there are still very puzzling differences between adjacent countries, and that there may be evidence of change of viral form in some comparative data.

The evidence of change comes from the comparison of two tests, one of which (an enzyme-linked immunosorbent assay) is less sensitive to change than the other ("Western blotting" of proteins). That the current virus is very prone to change is clear. The sequences of viruses that came directly or indirectly from patients in New York in 1982-83 differ by only a few per cent, whereas the sequences of a virus from a Haitian taken in the same period and one from a resident of San Francisco isolated in 1984 show considerable differences. Most variation is in the mid-portion of the gene that encodes the envelope protein of the virus. Up to 25 per cent variation is recorded there, according to W. Haseltine of Harvard Medical School.

By definition, however, all of these isolates and the other hundred or so whose variation is fully documented in only a few cases, are from AIDS patients. All, therefore, have caused immunodeficiency, and no correlation has emerged between variation in viral structure and the precise manifestations of the immunodeficiency syndromes. The pressing question is whether such a correlation can be found and, in particular, whether the African population will yield variants that are less prone to cause AIDS and from which the "American" variants are descended.

Now the focus of attention has shifted to the African green monkey. Most of some recently collected specimens from the wild in Zaire contain serum proteins characteristic of HTLV-III/LAV and yet are healthy, according to M. Essex from Harvard School of Public Health. A comparative study of the monkey and human virus together with that which caused an outbreak of AIDS-like disease in a captive colony of Macaque monkeys in the New England Primate Center may help to clarify the origin and virulence of HTLV-III/LAV and suggest approaches to vaccination or therapy.

A separate reason for delving deeply into variants is to discover whether sequence changes are responsible for some of the human pathologies other than AIDS with which HTLV-III/LAV is coming to be associated. R. Gallo from the National Cancer Institute in Bethesda, Maryland, pointed in particular to an association with brain abnormalities in children without immune deficiency; evidence exists for the presence of replicating virus in the human brain, particularly in glial cells. Such evidence tends to strengthen the claims of both Gallo and S. Wain-Hobson, of the Institut Pasteur in Paris, that HTLV-III/LAV is related to the lentiviruses, of which the prototype is visna virus, which causes a slowly progressive demyelinating disease of the central nervous system of sheep. Gallo also tentatively suggested a new pathological involvement of the virus that would dispense with the first word of idiopathic thrombocytopaenic purpura.

While AIDS is a growing concern in the industrialized nations, African priorities lie elsewhere. In Senegal, for example, either there is no AIDS or it has not yet been recognized, whereas many die from a liver cancer caused in part by hepatitis B virus. In Africa generally this, and cervical cancer are major types of cancer. A third virus-associated cancer in Africa is Burkitt's lymphoma, an infrequent disease but responsible for many childhood tumours and causally linked to the Epstein-Barr virus.

Hopes, however thin, are pinned on the development of a vaccine against HTLV-III/LAV. For the hepatitis B virus, vaccines are already in trial but for the Epstein-Barr virus the first glimpse of a vaccine was provided in Senegal by M.A. Epstein of the University of

Bristol. The vaccine is composed of one of the major proteins of the virus and protects cotton-top tamarins against cancers induced by the virus. The tamarin disease does not altogether resemble the human disease and the frequency of Burkitt's lymphoma may never warrant mass vaccination in terms of cost. In Asian countries where the virus is a part cause of nasopharyngeal cancer, vaccination may be more realistic. Epstein foresees an initial trial of the vaccine against mononucleosis, the relatively mild result of infection by the virus after childhood. (Extracted from Nature, Vol. 315, 23 May 1985)

Anticlotting agent betrays its promise

One of the most exciting new agents made by genetic engineering for treating heart attacks may not be so promising after all. A major trial involving tissue plasminogen activator (TPA) as an anticlotting agent for opening blocked blood vessels, has revealed unexpected side effects such as uncontrolled bleeding which may limit the agent's usefulness. The company that developed TPA thinks that heparin, the blood thinner, used to administer the TPA, could be responsible for the side effects.

The report in The Lancet (13 April, p. 842) summarises the results from seven European centres participating in the European Co-operative Study Group for Recombinant Tissue-type Plasminogen Activator. The study compares genetically engineered TPA developed at Genentech, with streptokinase, another highly favoured natural agent extracted from bacteria by the German chemicals firm Hoechst.

One hundred and twenty-nine patients with blocked coronary arteries and in the throes of a heart attack were treated. Of the 64 receiving TPA the arteries of 70 per cent had opened 90 minutes later, as angiograms taken of the hearts revealed. In the streptokinase group this figure was only 55 per cent. These results confirm those of a large American trial published in the New England Journal of Medicine, in early March.

However, in the European study, the small rate of mortality was the same in both groups, and although, overall, bleeding episodes were less common in TPA patients, at least two required blood transfusions. This seems to contradict what is known about the role of TPA in the body. The new properties may limit TPA's usefulness as a treatment.

Tissue plasminogen activator is one of a group of plasminogen activators that break down blood clots. They work by converting an inactive precursor involved in clotting, plasminogen, to an active form (plasmin) which breaks up fibrin, the main component of blood clots.

Streptokinase is another activator widely used for eliminating blood clots in lungs and in heart attacks. Its use, however, does not have the full approval of the US Food and Drug Administration. Streptokinase attacks plasminogen anywhere in the blood and so may cause uncontrolled bleeding. Also the bacterially derived streptokinase causes some immunological disturbances in humans.

TPA, on the other hand, is a natural human enzyme, produced by the walls of human blood vessels near where the clot is formed. Scientists believe that, in order to act, TPA needs fibrin, and so it attacks only clots, and not other clotting factors in the blood. This behaviour eliminates the hazard of haemorrhaging. The European study did show that TPA had a much less damaging effect on fibrinogen, another blood clotting factor.

So it comes as a surprise that both studies show that TPA also causes massive internal bleeding in a significant number of patients. It is uncertain whether TPA or heparin [a blood thinner conventionally used to administer drugs] is causing the problems. The bleeding problems could be resolved by adjusting the dosage of TPA, and the more appropriate use of heparin. (Extracted from New Scientist, 25 April 1985)

Probes to distinguish protozoa species

DNA probes that can distinguish several species of similar protozoa have been developed by researchers at Codon (Brisbane, CA) and the Walter Reed Army Institute of Research (Washington, DC). The probes use DNA from an accessory body called the kinetoplast or micronucleus found in many protozoa. The probes can be useful for diagnosing leishmaniasis, which is caused by about 12 species of protozoa. Depending on which species causes the infection, the disease can produce self-healing lesions or fatal infections of internal organs. Gen-Probe (San Diego, CA) has also developed a probe to detect nucleic acids outside the nucleus of mycoplasma. Mycoplasma contamination is a frequent problem in laboratories, and it can also infect the human respiratory tract. (Extracted from Science News, 2 March 1985)

Cell surface receptor sequenced to recognise human insulin

Genentech has sequenced the cell surface receptor that recognizes human insulin and directs the cells' response to it. The isolation and characterization of the insulin receptor may provide an important aid to the study of insulin's interaction with normal cells and to the abnormal interactions that characterize some forms of diabetes. The receptor is first produced as a single protein of 1,370 amino acids and later cleaved into alpha and beta subunits. Thus, the entire receptor is the product of a single gene. The receptor has some similarities to the epidermal growth factor (EGF) receptor and to the products of the src family of oncogenes. However, the insulin receptor appears to be related equally to each of the src family members, suggesting either that it differs from the EGF receptor and is not a cellular protooncogene or that its oncogene counterpart has not yet been identified. Genentech's researchers worked on the project with researchers from Memorial Sloan-Kettering Cancer Center and the VA Medical Center (San Francisco, CA). (Extracted with permission from Chemical and Engineering News, 11 March 1985, Vol. 63, No. 10, p.18 copyright 1985, American Chemical Society)

Leukemias diagnosis

Definitive diagnosis of leukemias may be possible now that the gene for the alpha chain of the T cell receptor has been cloned, according to Dr. J. Kappler of the National Jewish Hospital & Research Center (Denver, CO). The gene that codes for the alpha chain has segments homologous to regions of the beta chain and immunoglobulin chains. Investigators can now use the cloned alpha gene to expand leukemia and lymphoma analyses that nad previously used only the Beta chain gene. The genes will help determine if a patient's lymphocyte proliferation is composed of B or T cells, clonal or polyclonal cells. The information should help distinguish between malignant and benign disease. Gene probes could also be used to link rearrangements of the T cell receptor genes with cellular oncogenes. (Extracted from Medical World, 11 February 1985)

Research on animal genes

Gene-blues for the cheetah

Biochemical analysis of enzymes and other proteins shows that the cheetah has 10-100 times less genetic variation, or polymorphism, than is normally found in mammals. This causes a number of problems, all of which are important if the cheetah is not to become extinct.

Cheetahs have poor reproductive success, both in the wild and in captivity. Infant mortality in the wild is estimated to be as high as 70 per cent, and data from breeding programmes worldwide show that, on average, 29 per cent of cheetahs born in captivity die before the age of six months.

The genetic constitution of the species resembles that of highly inbred livestock, probably due to a severe reduction in numbers - a population bottleneck - in its evolutionary past. The implications for conservation are particularly serious, because the cheetah is already one of the most endangered of all the cats.

Research by a joint team of scientists in the US and South Africa, led by Stephen O'Brien of the National Cancer Institute in Maryland, has produced further evidence of the cheetah's genetic malaise and its vulnerability to disease. (Science, vol. 227, p. 1428).

The time taken for skin grafts between unrelated cheetahs (allografts) to be rejected provided researchers with an estimate of genetic variability in the cheetah's immune system. All mammals produce antigens responsible for allograft rejection. These antigens are genetically determined by one particular chromosomal segment known as the major histo-compatibility complex (MHC). The MHC normally shows more polymorphism than any other genetic locus of vertibrates, and so allografts between domestic cats are rejected suddenly and rapidly, 7-13 days after grafting.

Allografts between 12 South African cheetahs showed no rapid rejection. Three individuals rejected slowly, at 39-70 days, but all other grafts were apparently accepted. So there was a high degree of shared MHC antigens in the group tested.

The main function of the MHC, however, is in immune defence against infection organisms. Lack of genetic variability in the MHC may explain why an outbreak of feline infectious peritonitis (FIP) killed 18 of 42 cheetahs at a wildlife park in Oregon in 1983. FIP is caused by a virus and is seldom fatal in domestic cats. African lions exposed to the disease also failed to develop symptoms.

Some genes at the MHC are known to vary in how much they control the ability to develop antibodies to viruses, and others play a major role in the ability of defensive T-cells to recognise and destroy cells infected with viruses.

The researchers suggest that lack of polymorphism in the MHC might limit the variety of viral antigens that T-cells are able to recognise.

The outlook is not entirely bleak, however. The development of effective breeding programmes has helped other inbred species, such as Père David's deer, survive. In the wild, the northern elephant seal suffered a population bottleneck in the last century due to overhunting. It too has critically low genetic variation, but has nevertheless made a successful comeback on the Californian coast.

Also, cheetahs in East Africa which have not yet been investigated may provide some much needed genetic variety. (Source: New Scientist, 16 May 1985)

Abalone research: implications for aquaculture and human medicine

Biotechnology is finding its way into the laboratories of marine biologists and chemists who are trying to improve the yield of marine organisms like oysters, abalone, clams, fish and seaweeds. Dr. Daniel Morse, a researcher from the University of California at Santa Barbara has chosen to work with abalone because this shellfish provides an excellent model system for studying the biological "bottlenecks" - such as an animal's growth rate - that limit commercial aquaculture. Dr. Morse has discovered some surprisingly simple means to overcome some of these limitations, and his findings also have unexpected implications for human medicine.

Various species of abalone (Haliotis) occur in coastal waters from the British Channel Islands, the Mediterranean, Japan, China, and Australia to the Pacific Coast of America. Because of its scarcity, abalone fetches $20 to $30 a pound in California, with worldwide sales at $400 million last year.

Until recently, it was not profitable to grow abalone in aquaculture. Now several enterprises are using Dr. Morse's findings to raise abalone successfully. First, the UC researchers discovered that prostaglandin regulates reproduction in abalone, as it does in other animals and man. Once a gravid abalone starts spawning, it releases the hormone, which triggers nearby individuals of the gregarious shellfish to spawn too, thus increasing the chance for successful fertilization of the sperm and egg cells released into the water.

Dr. Morse then found that a trace of hydrogen peroxide added to the breeding tank stimulates prostaglandin release, resulting in simultaneous and copious spawning. Morse adds that this simple stimulus also works on oysters, clams, scallops, and mussels. He thinks that the rate-limiting enzyme in the biosynthesis of the hormone, the prostaglandin endoperoxide synthetase, needs free oxygen radicals, which the hydrogen peroxide provides.

The poor survival rate of the tiny, free-floating larvae presents the second bottleneck in cultivation. The larvae die by the thousands or even millions if they do not find a suitable substrate upon which to settle and grow into adult abalone.

Dr. Morse screened many rock surfaces, looking for a clue to the abalone's preference. He eventually isolated a chemical signal, a close relative of the neurotransmitter gamma amino butyric acid (GABA), from a red algae that colonizes rocks. The relative mimics GABA so well that GABA itself - an amino acid easily isolated from plant matter - can exert the stimulus.

"Without the use of GABA," Morse says, "only one per cent of the abalone larvae survive; when GABA is added, 95 per cent attach themselves to a substrate and begin metamorphosis."

Morse is now employing genetic engineering techniques to produce and characterize chemicals which mimic GABA because they have great potential in human therapy. GABA controls about 40 per cent of all brain nerve transmissions, involving muscle tone, sleep and wakefulness and a range of psychological states. Morse hopes that GABA mimetics, which bind a hundred times more tightly to the GABA receptors, could one day replace commonly used medications, which often have undesirable side effects.

"We have now isolated several classes of GABA-mimetics, also from marine bacteria," Dr. Morse says, "and we have been able to clone the bacteria, which are a much easier system to work with than the red algae." His goal is to transfer the GABA-genes into E. coli for a more convenient study and production system.

Dr. Morse is also trying to overcome the third bottleneck, abalone's slow and uneven growth rate. The marine biologist showed that exogenous peptide hormones, such as mammalian insulin and growth hormone, accelerate metamorphosis by 25 per cent and promote synchronous growth of the abalone culture. Recently his group has started to accumulte a gene bank from abalone species - DNA cloned in microbial plasmids. With this amplification technique the researchers hope to study the growth-regulating hormones, their receptors and enzyme targets. (Extracted from Genetic Engineering News, April 1985)

Illinois scientists seek drugs from the sea

Several chemical compounds isolated from marine organisms during the past decade by University of Illinois researchers have been shown to have potent antiviral, antitumor, immunosuppressive and antimicrobial activities.

Among the most bioactive of these compounds are the didemnins (10 related depsipeptides) and eudistomins (17 β-carbolines), which are found in certain species of tunicates, said Dr. Kenneth L. Rinehart Jr., professor in the University of Illinois School of Chemical Sciences and leader of frequent expeditions to collect marine plants and animals.

Tunicates - the highest form of invertebrates - have a primitive backbone in the larval stage and grow in discernible colonies or as solitary individuals. More commonly called sea squirts, these small filter feeders spout water when squeezed or otherwise disturbed. They live in all the oceans and often form a thin layer attached to rocks or coral, sometimes at great depths.

One of the compounds isolated from tunicates - didemnin B - recently became the first marine-derived drug to enter clinical trials for cancer, Dr. Rinehart said. The trials are being conducted at the University of Texas Health Science Center at San Antonio, under the direction of Dr. Daniel D. Von Hoff. Meanwhile, David W. Montgomery and Dr. Charles F. Zukoski of the Veterans Administration Medical Center, Tucson, Ariz., have shown in laboratory tests that the immunosuppressive activity of didemnin B resembles that of the widely used cyclosporin A. In addition, didemnin B has been found effective in vitro against several serious tropical viruses such as Rift Valley Fever Virus, found in Ethiopia, and a picninde virus (related to lassa fever virus), largely confined to West Africa.

Work on the eudistomins also is progressing. Dr. Rinehart and his colleagues reported last spring that the eudistomins are extremely potent in killing several viruses, including Herpes simplex, types 1 and 2; equine rhinovirus; and parainfluenza virus. Late last year, Dr. Harold Renis of the Upjohn Co., Kalamazoo, Mich., demonstrated the in vivo activity of eudistomins.

The way tunicates make eudistomins and didemnins also is under investigation. The University of Illinois scientists want to find out what part of the animal is involved and what raw materials are used. This research is made difficult because of the fragile nature of the tunicates, which die soon after being removed from their natural habitat, Dr. Rinehart said. But thus far, the research hasn't been significantly hindered as a result. (Extracted from Genetic Technology News, April 1985)

Genex seeks to clone mussel glue protein

Fathoming the secrets of the glue that binds marine mussels to rocks and ships is leading to a biotechnology product.

Genex (Rockville, Md.) is trying to clone synthetic analogues of the unique biological glue. After years of effort, the mussel protein was recently isolated and characterized by Dr. J. Herbert Waite, a marine biologist and assistant professor in the orthopedic surgery laboratory at the University of Connecticut, Farmington.

The biological glue is a valuable property because it is strong, it hardens in a wet environment, and it is water resistant.

Orthopedic surgeons are interested in the possibilities of a glue that bonds to bones, prosthetic devices and soft tissue. The cement that is currently used to bond hip joint prostheses, for example, typically lasts only 10 years and often loosens more rapidly. Currently available adhesives bond only by mechanical forces, whereas the mussel glue forms strong, long lasting chemical bonds even to wet surfaces.

In addition, the glue may replace casts. Surgeons would like to temporarily rejoin bones with a glue, while bones heal; this would prevent muscle atrophy and bone mineral loss, such as occurs with the use of immobilizing casts.

The glue also may be useful in repairing tendons, nerves, and blood vessels.

Dentists are also interested in the potential of a new, nontoxic and long lasting adhesive that can be used in the mouth. They have a sealant that prevents tooth decay when it is painted on teeth, but it requires painstaking application. The top of each tooth must be etched with acid and thoroughly dried before adhesive is applied. Being able to apply the sealant to wet teeth would improve the technique and make it more practical.

The U.S. Navy is interested in the possibility of using the glue to make underwater repairs and as a protective surface coating.

The glue also may have uses as a heavy metal sequestrant to monitor nuclear waste leakage. The natural mussel glue has been used for this purpose; a weak discharge of Plutonium 238 into the marine waters adjacent to a nuclear reactor was detected in the glue from harvested mussels, Waite said.

With its natural properties, the protein appears to be an adhesive marvel, but like many natural products, its application has had to wait for a biotechnological approach.

The biological glue should be safer than existing fossil fuel-based synthetic adhesives which can produce cytotoxic effects. Such compounds can alter the structure of a cell's membrane which then leads to a cascade of problems involving cell leakage.

However, because the mussel glue is a protein, scientists are concerned about its antigenic effects. Dr. Waite has begun testing its immune reactivity in animals. The mussel protein is antigenic in rabbits, but not when it is crosslinked. Also, Dr. Waite has found that the protein is not cytotoxic in cell culture. Furthermore, when crosslinked, the glue passes undigested through animals, a good indicator that it is safe, according to Dr. Waite.

Because of FDA requirements, getting the glue into the biomedical market will take some time. The glue protein may find a place in dentistry sooner, however, because it appears to be less toxic than some compounds now used by dentists.

Nonmedical applications should come more rapidly, Dr. Waite predicted. (Extracted from Genetic Technology News, April 1985)

Research on plant genes

Light activated genes

Some genes activated by light are active in specific plant tissues, according to Dr. N.H. Chua of Rockefeller University (New York, NY). Signals for light activation and those for tissue specificity are recognized even after the genes are moved to another species of plant. A gene from wheat was properly turned on by light and expressed in the appropriate tissues in tobacco. A sequence only 35 nucleotides long is at least in part responsible for light activation of the gene. (Extracted from Science News, 9 March 1985)

Gene splicing for herbicide resistance

For the first time a commercially useful gene has been transplanted and shown to be active in an important crop plant. After a bacterial gene was introduced into tobacco plants, the plants showed an increased tolerance to the widely used herbicide glyphosate. A problem currently limiting the usefulness of herbicides is that they must distinguish between the crop and the pest. Genetic engineering has made more practical another approach - the tailoring of the crop plant to make it less susceptible to a particular herbicide.

The gene that scientists of Calgene, Inc. have transplanted into tobacco originally arose in mutagenized bacteria. A form of the gene aroA, it encodes an enzyme in which one amino acid is different from its natural counterpart. The mutant enzyme has a lower affinity for the herbicide glyphosate than either the plant or normal bacterial enzyme. In the leaves of tobacco plants containing the transplanted gene, the mutant gene provides 25 per cent of the total activity of the enzyme that normally is inhibited by glyphosate.

Calgene scientists have already introduced the mutant aroA gene into soybean, tomato and oilseed rape cells in laboratory culture and are currently working on corn cells. They also plan to develop and market glyphosate-tolerant varieties of corn, in collaboration with Phytogen of Pasadena, California, and forest trees, in collaboration with the U.S. Forest Service. (Extracted from Science News, 2 March 1985)

The structure of sweetness

Chemists at the University of California at Berkeley have determined the three-dimensional structure of what they believe is the world's sweetest compound derived from thaumatin I. It is one of the first taste-bearing proteins to be found, is about 100,000 times sweeter than sugar, and tastes sweet at concentrations as small as 1 molecule in 100 million. With X-ray crystallography, Sung-Hou Kim and colleagues have determined the arrangement of the molecule's protein chain. It has two different features: a series of slats called a beta sheet (a structure commonly found in proteins) and regions of complicated loops.

The loops have attracted the scientists' speculation as they resemble parts of other proteins, such as snake venom toxins and ragweed pollen allergens, that bind to specific receptors. Kim and colleagues report that antibodies that bind to the looped regions eliminate the sweetness of the proteins. They are now determining more specifically which loop areas are crucial in creating a sweet taste. (Extracted from Science News, 16 March 1985)

Seaweed's clue to a cure for cystic fibrosis

A chemical currently extracted from seaweeds and widely used in the manufacture of food may hold the clue to new treatments for cystic fibrosis. Genetic engineers at the University of Chicago have succeeded in making a microbe produce large quantities of alginic acid. Alginic acid occurs in high levels in the lungs of people suffering from cystic fibrosis. An understanding, achieved by experiments in genetic engineering, of how this chemical is produced by sufferers could lead to new treatments for the genetic disease which occurs in one out of 1,600 people born in the US. One in 20 people in Britain carry the recessive trait for the disease. The bacterium Pseudomonas aeriginosae produces alginic acid, but only under certain conditions, in cystic fibrosis, for example. The disease affects many organs, but patients usually die of a massive pseudomonas infection, and as the disease gets worse the bacteria produce more alginic acid. The gummy polysaccharide interferes with the normal function of the lungs and must be removed by painful slapping on the back several times a day.

The Chicago team lead by Ananda Chakrabarty postulates that manufacturing the polysaccharide presents an enormous energy burden to the normal cell, and that genetic controls usually keep the genes that produce alginic acid turned off. So the pseudomonas strains isolated from fibrotic lungs provide a unique and stable strain of bacteria, in which the alginic acid genes are permanently switched on. In the lungs some, as yet unknown, condition seems to favour the growth of these strains over the normal ones.

By studying the genes controlling the metabolism of alginic acid in these microbes, Chakrabarty's team isolated the characteristics which controlled stability in the bacterium. They produced a stable line of genetically engineered pseudomonas bacteria which also manufactured alginic acid continuously. It is this special line of pseudomonas bacteria which could provide unique insights into the disease of cystic fibrosis.

A closer study of the enzymes involved in the synthesis of alginic acid (phosphomannose isomerase, for example) could lead to the development of non-toxic inhibitors which could be inhaled from an aerosol spray to prevent alginic acid formation.

Chakrabarty's team also studied another biochemical pathway which could benefit the food industry. Alginic acid is a substance widely used as a thickener in the food industry. The genetic engineers in Chicago think they have found a way of varying the properties of alginic acid almost to order. Alginic acid consists of varying quantities of two components, mannuronic acid and guluronic acid. The ratio of these two molecules governs the viscosity of alginic acid. The conversion of mannuronic acid to guluronic acid is controlled by an epimerase enzyme. The final viscosity of the polysaccharide depends how much enzyme is available to convert mannuronic acid to guluronic acid, and so vary the viscosity.

Chakrabarty's team plans to use a variety of genetic engineering techniques to insert a high number of copies of the gene coding for epimerase into the stable strain of Pseudomonas aeriginosae. Chakrabarty says that by controlling the number of epimerase genes it will be possible to get different degrees of polymerisation and thus a new range of polysaccharides. (Source: New Scientist, 11 April 1985)

Honen Oil clones enzyme to lyse plant cell walls

A Japanese oil company is planning to use a cloned enzyme instead of hot water to extract more flavour from tea leaves. At a recent plant pathology conference Honen Oil Co. Ltd., and assistant professor Shinji Tsuyuna of Shizuoka University's department of

agriculture announced they had expressed the genes for pectic acid lyase, an enzyme that breaks down pectin, a principal component of plant cell walls.

The catabolic-enzyme genes came from the bacterium, Erwinia carotovora subsp. carotovora, causative agent in root-rot disease of carrots and radishes. The research group initially achieved expression of the 35-kilodalton protein in Escherichia coli at only a quarter the concentration found in the original pathogen. But with the addition of a pectic-acid inducer, enzyme production increased 20-fold, 90 per cent of which was excreted into the growth medium. (Extracted from McGraw-Hills Biotechnology Newswatch, 6 May 1985)

Research on yeast and fungus genes

Cancer and the yeast

Malignancy arises from an abnormality in a select group of normal cellular genes or in their control, according to a major hypothesis among cancer researchers today. The gene called ras modulates the activity of a regulatory enzyme called adenylate cyclase.

The yeast Saccharomyces cerebisiae has two genes similar to the human gene, c-ras, which has been implicated in bladder cancer. The yeast genes, RAS1 and RAS2, appear to be involved in a yeast cell's decision about whether to reproduce by cell division or to form spores. A normal yeast chooses cell division when nutrients are plentiful, and sporulation when nutrients are scarce, but a yeast with reduced RAS activity sporulates even in the presence of excess nutrients, and yeast with no active RAS gene cannot survive. In experiments with genetically engineered yeast, however, a transplanted human c-ras gene can substitute for the yeast gene and the cell will grow normally.

The ras gene associated with human cancer is a mutant that produces a protein with one altered amino acid. Scientists have examined a yeast RAS gene with the corresponding mutation. They find that yeast cells carrying this mutant gene (called RAS-val19) are also impaired in the divide-or-sporulate decision. The mutant always enters into cell division even if there are insufficient nutrients. This might be considered the yeast equivalent of malignancy.

It was soon realized that the RAS mutants were similar to another set of yeast strains. Yeast lacking adenylate cyclase - the enzyme that makes cyclic AMP, a small regulatory molecule - cannot begin cell division. On the other hand, strains that bypass the need for adenylate cyclase always begin cell division, even under inappropriate conditions. By putting different combinations of the genes into yeast, the researchers determined that the RAS gene products regulate growth in yeast solely by modulating adenylate cyclase activity. (Extracted from Science News, 9 March 1985)

Research on bacterial genes

Bacteria against pesticide contamination

Genetically engineered bacteria may one day help to clean up land contaminated with pesticides. A microbiologist with the US Department of Agriculture reported he had identified genes in two bacteria responsible for regulating enzymes which break down pesticides. If the genes could be cloned the bacteria could produce a lot more enzymes for safer, more thorough pesticide disposal, especially on farms.

The type of place where bacteria could help, are tanks in which farmers dump pesticides left in spray tanks. Normally, they put the pesticides into pits lined with concrete or plastic, and wait for natural microorganisms to break the chemicals down. However this process is slow and leaking pits can allow pesticides to contaminate ground water.

What the researchers still have to do is to clone the gene, and splice it back into bacteria so they produce more enzymes. So far, no products of genetic engineering are in routine use on American farms. (Source: New Scientist, 16 May 1985)

Bacterium with ore affinity

The spore-forming bacterium Bacillus cereus is said to have an affinity for gold, copper and other ores. Concentrations of the bacteria were much higher in a copper deposit in Montana than in surrounding soils. Most bacteria do not live in metal deposits as they would be killed either by the metal or by the penicillin and other antibiotics produced by metal-tolerant fungi in the soil. B cereus takes a water molecule from each penicillin

molecule, leaving a gap in the penicillin that traps copper before it can hurt the bacterium. In this way, the bacteria detoxify the copper molecules. Penicillin is also used to treat copper toxicity in humans. The bacteria also feed on the metal-tolerant fungi. (Extracted from Science News, 16 February 1985)

Research instrumentation

Positrons picture genetic disorders

In five years' time, a technique that identifies biochemical anomalies in the body could predict which people are at risk of developing Huntington's chorea. The technique, positron emission tomography (PET), picks out metabolic irregularities in cells long before there is gross structural damage in tissues. PET could also detect other genetic diseases, such as some forms of senile dementia.

A PET scan builds up cross sectional pictures of the chemical processes in the cells of tissues. It can locate very accurately certain radioactively labelled compounds. Such compounds emit positrons - particles that destroy electrons. In this way, PET can spot irregular chemical reactions that indicate the presence of a defective gene.

In 100 per cent of the cases studied with PET, Dr. Richard Phelps of the University of California School of Medicine at Los Angeles has pinpointed the altered chemical processes in the brains of the parents with symptoms even before it is detectable with other imaging procedures.

Huntington's chorea usually strikes in middle age, or later. It is caused by a single, defective version of a gene lying on chromosome four. The children of a man or woman with the disease appear perfectly healthy, even though 50 per cent of them carry abnormal genes and will develop the symptoms in later years.

Phelps sampled just over 40 young people whose parents had the symptoms of Huntington's chorea. Of those, 50 per cent had biochemical irregularities as shown in PET scans. So far, Phelps has followed these people for six years, and has found that about half of those with the biochemical anomalies eventually developed the disease. The other half may also eventually develop the disease. Phelps said that it will take about five years to see whether enough of them develop the disease to show that PET is predictive and accurate.

Researchers in the US and Britain already are working on a predictive test for Huntington's, but based on a gene probe. This test identifies the defective gene rather than the chemical irregularities caused by it. In the long term, a gene probe will be more useful because it would find the defective gene in the fetus, giving pregnant women the option of having an abortion.

PET may prove a useful cross check on the accuracy of the gene probe and, more important, it could help scientists to understand what goes wrong in the brains of people carrying the gene that causes Huntington's chorea. When they know what goes wrong, they would be in a better position to develop a cure for the disease. (Extracted from New Scientist, 30 May 1985)

D. APPLICATIONS

Pharmaceutical and Medical Applications

Hoffman-La Roche gets alpha-interferon patent

Hoffman-La Roche's US subsidiary has received a fundamental product patent for its alpha interferon from the US patent office. The patent covers all highly pure, human alpha-interferons irrespective of the method of manufacture, the company says.

Just over a year ago, Biogen received a European patent for its alpha interferon. This patent, which holds in the 11 countries of the European patent convention, covers gene-spliced alpha-interferons made in bacteria, yeast and animal cells. The patent is licensed to the US drug major Schering-Plough, which hopes to introduce its version of the drug, Intron, to the market this year. Alpha interferons have shown some effect in treating rarer forms of cancer and in preventing viral diseases.

The basis of the Roche patent, according to the company, is the discovery by Dr. Sidney Pestka and Dr. Menachem Rubinstein, working at the Roche Institute of Molecular

Biology in Nutley, New Jersey, of an entire family of structurally distinct leukocyte interferons.

Applications have been filed for registration of the product in Sweden, Switzerland, the US and Japan under the brand name Roferon A. (Extracted from European Chemical News, 18 March 1985)

Diagnostic assay for Legionella

Gen-Probe (San Diego, CA) has developed a rapid diagnostic assay for Legionella, the bacterium that causes Legionnaire's disease. The assay reduces disease diagnosis time from 48 hours to 45 minutes and can be performed on a patient's serum, blood, sputum, feces, or liver cells. David Kohne, chief scientist at Gen-Probe, developed the assay with DNA probes specific for ribosomal RNA. Because rRNA is an abundant cellular species, the assay is very sensitive: it can detect 400 organisms in 0.4 milligrams of liver tissue, and as rRNA is already single-stranded, it will hybridize immediately with a complementary DNA probe: this eliminates the time-consuming step of denaturing the sample DNA. Don Brenner's group at the Biotechnology Branch of the Centers for Disease Control (Atlanta, GA) is one of several laboratories evaluating the Gen-Probe Legionella assay. Brenner says that he readily identified all 22 Legionella species and could distinguish them from many non-Legionella species. Moreover, he used the Legionella-specific probe to confirm his identification of ten new species. (Extracted from Biotechnology, Vol.3, May 1985)

New perspectives on cholera

Though cholera epidemics have plagued mankind since ancient times, the cholera bacterium is not a human pathogen requiring a human-infecting phase in its life cycle, instead it is an integral component of the indigenous flora and fauna of estuarine environments, where it lives in commensal or symbiotic relationships with zooplankton and invertebrates.

This theory has evolved from research conducted by Rita Colwell, president of the American Society of Microbiology, and many others over the last decade. Cholera is transmitted by contaminated food and water. Vibrio cholerae, first isolated in 1884 by Robert Koch, is always found associated with estuarine environments. The organism is widespread in the United States, and, in fact, has been detected in all estuaries. The seasonality of cholera outbreaks is associated with phytoplankton blooms. An increase in the zooplankton population is invariably followed by epidemic cholera. In Bangladesh, this occurs at about the same time every year.

Vibrio cholerae microorganisms play an important role in the estuarine ecosystem. They play a role in their symbiotes' nutrition, osmoregulation, urea homeostasis, and larval morphogenesis. Vibrio lives in the oral region and gut of copepods - chitinous zooplankton. The copepods cast their eggs into the water in the spring and cholera organisms attach to the egg cases. In fact, it is likely that they aid in breaking the egg case during larval release. Vibrio are also found associated with oysters, clams, and crabs. Oysters - filter-feeding molluscs - ingest copepods regularly. Colwell says that Vibrio might help the crab in its migration from sea water to the upper bay, a journey which involves changes in temperature and salinity. The human, on the other hand, is an imperfect host for this microbe.

Vibrio can survive in its estuarine environment in a viable but "nonrecoverable" state. Colwell and others have collected samples which would not plate out on conventional agar but which did contain the organisms. To detect them, she had to add nalidixic acid, which prevents cell division. The inhibited cells elongated, and, after staining with acridine orange, were detected by epifluorescence. Normal concentrations of Vibrio cholerae in the environment are low: Colwell has never isolated more than 46 cells per litre from the Chesapeake Bay. Concentration of the microorganism in the copepod gut starts an increase in total population size which ultimately causes epidemics. (Source. Biotechnology, Vol.3, May 1985)

First genetically engineered protein A available

The world's first genetically engineered protein A is being marketed by Repligen (Cambridge, Mass.). Protein A binds tightly to antibodies and thus is useful for their rapid purification and concentration. The protein also may be useful for the treatment of autoimmune diseases and cancer, according to a company spokesman. Current treatment for autoimmune diseases, such as rheumatoid arthritis, includes therapeutic plasma exchange (TPE), whereby plasma that contains autoantibodies is separated from the cellular fraction of

the blood, discarded and then replaced with normal plasma not containing autoantibodies. Protein A, however, could replace TPE. A patient's own plasma could be regenerated by filtering it through a column containing immobilized protein A. The protein would latch onto and remove autoantibodies. The plasma would then be returned to the patient. As a cancer drug, protein A is undergoing clinical trials. Reports indicate tumor regression in skin, breast and colon cancers. (Extracted from Chemical Week, 24 April 1985)

Black market forces legalisation of AIDS drug

Desperate victims of AIDS in the US are flocking across the border into Mexico to buy experimental drugs that are not approved for sale at home. The two drugs they seek are isoprinosine tablets and ribavirin capsules.

Chemists' shops in Tijuana on the border with California and in Juarez, across the Rio Grande from Texas, are selling out of the drugs as soon as they stock them. In El Paso in Texas, meanwhile, individual tablets of isoprinosine are selling for $2 each on the black market. Across the border a 20-tablet box costs $2.50. The prices in the US are inflated because the drugs are being confiscated by customs officials.

In mid-May - partly in response to the publicity surrounding these desperate trips to Mexico - the US Food and Drug Administration (FDA) eased restrictions on the availability of isoprinosine. A policy called "compassionate-use protocol" would be introduced, the agency said. It means that doctors can contact the American manufacturers of the drug, Newport Pharmaceuticals International of Newport Beach, California, to request supplies for individual AIDS patients. The agency is now viewing isoprinosine much like an experimental cancer drug.

A good deal of confusion and controversy surrounds the use of isoprinosine. Newport Pharmaceuticals said it had not agreed to the FDA's plan. The company is concerned it will not recoup manufacturing and distribution costs. Drugs made available under the "compassionate-use" policy cannot be sold for profit. The company says it may not be able to meet demand for the drug and says that the FDA in effect is inviting every AIDS patient in the country to call up and ask for the drug. Ironically, there is no guarantee that the drug will be of any use to AIDS victims. It gained its reputation in the community, following publicity in homosexual magazines about the drug being used to fight the AIDS virus in laboratory experiments. But both the company and researchers agree that it is unlikely to be effective against full-blown AIDS.

There is some early evidence that isoprinosine may help against what is called "AIDS-related complex", however. Sufferers from the complex show early symptoms of a depressed immune system and may have been infected by the AIDS virus. But they have not developed the full-blown version of the disease.

Isoprinosine, an anti-viral drug, has long been controversial in the US. It was discovered in 1968 by Newport Pharmaceuticals. Since then, the company has been trying to obtain permission from the FDA to market the drug to fight disorders such as herpes, upper respiratory conditions, encephalitis and viral hepatitis, but the FDA has not been satisfied with the research documentation supplied by the company. Nevertheless, Newport Pharmaceuticals has licensed companies overseas to manufacture the drug. It is marketed in 70 countries, including Mexico.

Widespread clinical trials of the other drug being sought by AIDS victims, ribavirin, are expected to start in September. It is also an anti-viral drug that has not won general FDA approval. It is manufactured by ICN Pharmaceuticals of Costa Mesa, California and became highly sought after in Mexico earlier this year when the drug was tested at Cornell University Medical Center in New York. (Extracted from New Scientist, 16 May 1985)

Sharper tests for AIDS

At least two biotechnology companies have overcome a technical obstacle to accurate tests for AIDS. The work should lead to a test for the disease that is free of false positives and negatives.

The US Food and Drug Administration has licensed five companies to develop a screening test for the disease. Eight weeks ago, it granted a product licence to Abbot Laboratories. Now two more companies, Electro-Nucleonics and Litton-Bionetics, have won licenses. The other two have licences pending.

The kits available now are called ELISA (enzyme-linked immunosorbent assay) tests. The test is carried out in three stages. In the first stage, particles of AIDS virus are

disrupted and attached to a plastic sheet. Human serum is added in the second stage. If the subject has been infected with the virus, the serum will contain antibodies which will bind to the antigen now attached to the plastic sheet (the solid phase). Unbound antibody is washed away. In the final stage, an anti-antibody is added as a marker. The anti-antibody is usually made by injecting a goat with human immunoglobulin (the basic "antibody protein"). This goat anti-human antibody is labelled with an enzyme which produces a colour reaction if it is allowed to react with a specific chemical. The labelled goat antibody is added to the solid phase, and excess is again washed away. If the serum contains human antibodies against the AIDS virus, it will have bound to the virus on the plastic sheet. This, in turn, will have bound the goat antibody. If, when the substrate is added, a colour forms, it means that the subject has at some time been infected with the AIDS virus. He or she is said to be seropositive. These are first-generation kits. They can produce false positives and false negatives. (Extracted from New Scientist, 2 May 1985)

New AIDS test in Japan

A Japanese researcher claims to have developed a cheaper and more reliable method of detecting AIDS. Takeshi Kurimura of Tottori University says that his technique is 100 per cent accurate in screening samples of blood for the presence of antibodies to the AIDS virus. The test can be taught within a week and one hospital technician can check 200 samples a day - 10 times more than a method that is currently in use.

Kurimura says that his technique, which uses a fluorescence microscope to spot antibodies to the AIDS virus, is cheaper and faster than the Western Blot method of detecting antibodies, and more relisble than the alternative, called ELISA, which has won official approval in the US as a test for AIDS antibodies and is now being evaluated by Britain's Department of Health.

Kurimura has developed a technique in which a cell infected with the AIDS virus is fixed to glass and covered with the sample of blood that is to be tested. If the blood contains antibodies to the AIDS virus, then the antibodies will stick to the infected cell.

The next step is to see whether this binding has occurred. Kurimura does this by adding to the blood sample a stained antibody to the AIDS-virus antibody, a so-called anti-antibody. These are made by injecting into rabbits the human antibody to the AIDS virus. The rabbit then makes an anti-antibody, which will stick to the AIDS antibody on the infected cell. Kurimura stains these anti-antibodies with a fluorescent dye so that when the blood sample is irradiated with ultraviolet light, blood samples containing antibodies to the AIDS virus will show up under a fluorescence microscope.

Kurimura believes he is the first person to have applied immunofluorescence in this way. (Extracted from New Scientist, 18 April 1985)

New technology in AIDS test

Diagnostics Pasteur is launching a test capable of detecting the antibodies of the AIDS virus or LAV in blood donors. The test, called Elavia, is said to be both specific and sensitive because of the "two-solid-phase" technology used and is claimed to differ from rival kits on both those points.

The first two phases of a three-stage evaluation process have been successfully completed on 2,300 people in France and Belgium. The third phase is being conducted at six blood transfusion centres in France. An application for marketing was submitted to France's Laboratoire National de la Santé at the beginning of April.

Diagnostics Pasteur has formed a joint venture, Blood Virus Diagnostic Corp, with Genetic Systems to produce and market the kit in the US. In March, this company obtained a provisional licence from the FDA to test Elavia in the US. The French company is also negotiating a marketing agreement for Japan with Immunis, and hopes to capture 15 per cent of the Japanese market. (Extracted from European Chemical News, 29 April 1985)

Japanese procedure isolates blood plasma faster

Toyobo Co., in co-operation with Tohoku University, has developed a new blood-collecting procedure whereby plasma is extracted during collection to enable the rest of the blood to be returned to the donor's system.

Modifying the cellulose-type hollow-fibre membrane used in the filter of artificial kidney machines, the unique method enables plasma separation, which normally takes 2 hours, by centrifugalization carried out in just 20 minutes.

By passing the donor's blood through this special membrane, plasma can be extracted by means of the porous wall structure which allows only the low molecular weight component to seep through. Thus, the hollow-fibre membrane acts as a molecular sieve to separate blood corpuscle and plasma. (Extracted from The Japan Economic Journal, 29 January 1985)

Interferon fights Hepatitis B

Scientists believe interferon may offer the first hope of stopping carriers of Hepatitis B from being infectious. The treatment also appears to end their risk of catching cirrhosis and liver cancer.

The doctors' newspaper General Practitioner reported on research at the Royal Free Hospital in north London, which found that up to 70 per cent of male homosexual carriers of the virus can be "cured" by interferon.

Professor Howard Thomas and Dr. Andrew Lever at the Royal Free found that interferon inhibited replication of the virus in two-thirds of the patients treated. This halt to replication ends infectiousness and liver damage.

One risk is that some viral DNA may remain incorporated in the patient's own DNA. If the patient later becomes immunosuppressed the viral DNA may again start to produce replicating virus. (Extracted from New Scientist, 25 April 1985)

Safer vaccine developed in UK for whooping cough

A safer whooping cough vaccine is due to undergo clinical trials in the UK next year. The vaccine, developed by scientists at the Centre for Applied Microbiology and Research at Porton Down, Wiltshire, consists of a number of purified antigens extracted from the bacterium Bordetella pertussis.

Several antigens have been incorporated into the vaccine as researchers believe more than one is involved in conferring immunity to susceptible individuals. Bacterial toxins have been removed.

The new vaccine is similar to a Japanese whooping cough vaccine which has been on the market in Japan since 1981. However, the Japanese vaccine is apparently less well defined chemically than the UK version.

The Centre intends to negotiate with a drug company over production and marketing rights for the new vaccine, although it is not likely to be marketed in the UK for at least another two years. (Extracted from Manufacturing Chemist, May 1985)

New cholera vaccine

A new cholera vaccine is being investigated at the Center for Vaccine Development, University of Maryland, Baltimore. Researchers hope it may confer life-long protection against the disease. Initial clinical trials of the vaccine have shown a significant rise in serum antibodies to cholera in all recipients. When the volunteers were innoculated with the virulent bacteria six weeks later, the vaccine protected 90 per cent of them.

The current cholera vaccine uses a preparation of whole killed bacteria, but the vaccine is very ineffective.

However, the new vaccine has been made by constructing a mutant of the cholera-causing bacteria, Vibrio cholera. This mutant is unable to produce the toxin which normally causes the rapid fluid loss that characterises cholera. (Extracted from Manufacturing Chemist, May 1985)

Tumour necrosis factor

In an unusual move, the US Food and Drug Administration (FDA) has allowed human tumour necrosis factor (TNF) produced by recombinant DNA technology to be given to a cancer patient. FDA had previously maintained that there are insufficient animal data on the effects of TNF to approve clinical trials, but it has now allowed Dr. Herbert Oettgen of Memorial Sloan-Kettering Cancer Center in New York to treat a gravely ill patient with TNF manufactured by the Asahi Chemical Industry company of Japan on compassionate grounds. FDA allowed a compassionate exemption for the Sloan-Kettering patient on condition that Sloan-Kettering's institutional review board accepts full responsibility for the case, since FDA had no prior information on the TNF used, and the data submitted with the compassionate exemption request covered only basic safety requirements such as pyrogenicity and sterility.

Dr. Lloyd Olds, associate director of scientific development at Sloan-Kettering, is one of the original researchers on TNF, first produced from mouse serum. Dr. Olds is being supplied with genetically engineered human TNF for research purposes by Genentech Inc.

Although this material is being used only for animal and in vitro studies, according to Genentech, Asahi's TNF is undergoing clinical trials in Japan. It is still unclear how soon organized clinical trials of TNF will start in the United States, or whether the Sloan-Kettering case will serve as a precedent for future compassionate exemptions in similar cases. (Extracted from Nature, Vol.315, 16 May 1985)

Mass production technology for TNF

Asahi Chemical Industry (Japan) and City of Hope Medical Center & Research Inst (US) have jointly developed mass production technology for human tumour necrosis factor, which kills cancer cells without affecting normal cells. Asahi Chemical previously synthesized TNF using rabbit chromosomes. Human TNF is more effective, however, and has been proven effective against a variety of cancers, including leukemia, breast and lung cancers. Asahi Chemical will soon begin clinical trials of human TNF, and will seek patent rights for the substance and production technology. (Extracted from The Japan Economic Journal, 12 March 1985)

Livestock Applications

Amgen tests interferon in US cattle trials

Amgen has started field trials of its alpha consensus interferon against shipping fever in cattle, following a go-ahead from the US Food & Drug Administration. The Californian biotech company is currently conducting preclinical trials of consensus interferon as a human therapeutic - its originally planned application - and is poised to begin clinical evaluation of the substance.

Amgen estimates that shipping fever, which affects up to half of all US feed cattle (12m. head a year), kills as many as 500,000 young cattle, at an annual cost of $500m. The company adds that animals which survive the pneumonia-like condition can succumb to a lingering condition, which drastically reduces their weight-gain-to-feed ratio, resulting in higher costs and lost revenue. The condition is triggered by the stress of being moved perhaps 1,000 miles from farm to the feedlot.

Amgen says its consensus interferon has a unique amino acid sequence which results in high antiviral potency in animal tests. Studies in vitro have turned up higher activity in bovine cells than bovine interferon. The field trials, involving some 500 animals, will test this further. (Extracted from European Chemical News, 8 April 1985)

Increasing shellfish production through marine biotech

Genetic engineering methods are now being applied to improving the production of marine animals such as oysters, clams and mussels. Researchers and shellfish fanciers hope these techniques will increase the yield - size and weight - of the bivalves just as aquaculture has dramatically improved the yield of carp in China and of other fish in hatcheries around the world.

A major centre of marine biotechnology research on the East Coast is the University of Maryland at College Park, where Dr. Rita Colwell and colleagues Dale Bonar and Ronald Weiner are studying the life cycle and colonization of the American oyster, Crassostrea virginica.

In both the natural environment and in mariculture, successful oyster development is critically dependent upon the "settling" process. During settling, the planktonic oyster larvae land on an oyster shell or plastic sheet and undergo metamorphosis to form attached oyster spat. A number of investigators have shown that microbes secrete products that mediate the colonization of marine surfaces by macroorganisms. Dr. Colwell's group has discovered that a unique bacterium, called LST, is associated with the induction of settlement and metamorphosis of the oyster larva.

The LST bacterium was originally isolated from oysters and from holding tanks for oyster spat at the Mariculture Unit at Lewes, Del. Isolated LST were then grown in synthetic medium and genetic analyses revealed that a new genus of marine bacterium had been discovered.

LST adheres to a variety of surfaces, including glass, plastic and oyster shell, by producing two viscous capsular exopolymers. Since this adhesive polysaccharide polymer has commercial potential, the Maryland group is cloning the genes for the polymers.

Following adhesion, during its later stationary and decline phases of growth, LST synthesizes a brown-black pigment which researchers isolated and identified as melanin. The investigators at the University of Maryland have shown that the melanin and melanin precursors, such as the neurotransmitter dihydroxyphenylalanine (DOPA), specifically attract the oyster larvae and promote their settlement and subsequent development.

The research thus has two commercial outcomes: increasing the output of oyster hatcheries and obtaining a new polymeric adhesive from the sea.

Shellfish diseases

Unfortunately, other species of bacteria cause diseases in bivalve molluscs. Dr. Colwell and others have shown that several antigenically different strains of Vibrio are pathogens of the American oyster as well as of hard shell clams (Mercenaria mercinaria). These bacteria were isolated from dead and dying oyster larvae and juveniles in which they had induced a disease called bacillary necrosis. Phenotypically similar bacterial strains were isolated by V.E. Jeffries in England, where they were found to be pathogenic to the larvae of the local oyster species.

In view of the potential economic importance of the vibrios in the cultivation of bivalve molluscs, Dr. Colwell's laboratory has explored the genetic and phenotypic properties of six strains of these pathogens. With this information it should be possible, using recombinant DNA techniques, to develop vaccines against these pathogens.

The Maryland researchers also are currently attempting to clone genes that code for characteristics such as disease resistance and growth hormone production in the oysters. Success in these endeavors will greatly increase the yield of oysters in aquaculture.

Hybrid vigor

"Hybrid vigor," a well-known phenomenon, is associated with heterozygosity (which occurs when parent organisms contribute different genes - alleles - at a specific locus). Researchers have correlated multiple locus heterozygosity with increasing growth rate and metabolic efficiency in a variety of species, ranging from aspens to humans.

Researchers are examining the effects of genetic heterozygosity in a variety of marine bivalves, both in natural populations and in laboratory environments. For example, oysters growing in a sea bed or in culture display considerable variation in growth. Correlation of the size and growth rate with heterozygous alleles may elucidate adaptive mechanisms which are important in aquaculture.

Researchers at the Bodega Marine Laboratory of the University of California (Bodega Bay, Calif.) made a survey of the gene-enzyme variation in population samples of several species of oysters (Crassostrea). Using electrophoretic gels to visualize the products of the different alleles, many karyotypic and morphological similarities were found among three sub-species of C. virginica, suggesting evolutionary conservation of a basic developmental gene regulatory program. Two other species of oysters studied showed clearly evolved protein differences characteristic of old and well-separated biological species. Like other bivalves that have been surveyed for genetic variation, the Crassostrea show significant heterozygosity.

Using a different experimental design, E. Souros of Dalhousie University, (Halifax, Nova Scotia) and R. K. Koehn and S. E. Shumway of the State University of New York at Stony Brook showed that the fastest growing eastern oysters are also the most heterozygous. Y. Fujito of Japan determined this to be true of the Pacific oyster as well. When the effects of single loci were determined, researchers found that in general (with only one exception), all gene loci contributed to the relationship between heterozygosity and growth rate.

In addition, researchers at Stony Brook determined that heterozygosity is linked with metabolic efficiency. As reflected by rates of oxygen consumption, the ratio of energy available for growth to total energy absorbed increased with individual heterozygosity.

Heterozygosity involving multiple loci also influences the response of oysters to starvation. Both the basal oxygen uptake and the rate of weight loss decreased significantly with increasing heterozygosity. Scientists thus attribute the link between such genetic variability and metabolic efficiency as the key to the positive correlation between heterozygosity and growth rate and survival.

Other studies on natural populations of oysters, quahogs, mussels, coot clams and oyster drills have shown a positive correlation between heterozygosity and measures of fitness such as growth rate, tissue weight and fecundity. Animals collected from the field cannot yield definitive genetic data since their parentage is unknown; however, the use of pure-bred stock makes it possible to define and isolate specific alleles which are responsible for different traits.

Dr. Laura Adamkewicz and colleagues at George Mason University (Fairfax, Va.) have studied the specific effects of genes that code for different forms of the same enzyme (allozymes) in a laboratory population of clams. They discovered that two genes, LAP and PGM-3, are associated with shell size.

The LAP allele not only affects size, but is also a key to the ability of some bivalves to acclimate to changing salinities in estuaries. Depending on tides and rainfall, the water in an estuary varies from nearly fresh to quite salty. Mussels adapt to this changing environment by changing their internal osmolarity. This response to changes in salinity is under the control of the enzyme leucine aminopeptidase, which breaks down the proteins to free amino acids in order to adjust the internal osmolarity. The mussels thus maintain a "normal" cell volume by keeping constant the difference in osmotic pressure between inside and outside the cell.

The enzyme is controlled by a gene with multiple alleles. Dr. R. Garthwaite of the Marine Biological Laboratory at Woods Hole, Mass., has determined that there are three LAP alleles in the mussel Geukensia demissa. The frequency of two of these alleles, LAP^1 and LAP^2, is correlated with environmental salinity: LAP^1 increases in frequency and LAP^2 decreases in frequency in low salinity environments.

By analyzing shell size and by direct measurements of growth rates, researchers found in low salinity environments, mussels with the LAP^1 allele grow faster and have heavier tissue weights than those with LAP^2. The reverse is true in high salinity environments. Dr. Garthwaite also has shown that mussels possessing the LAP^1 allele survive better under low salinity conditions.

In addition, Dr. Garthwaite is investigating the genetic structure of a pure-bred strain of M. mercenaria using quahogs supplied by the Aquacultural Research Corporation, a hatchery in Dennis, Mass. which has been selecting and breeding marketable size quahogs for more than ten years. His studies should shed new light on the evolution of adaptive mechanisms in this species. This research also has important implications for aquaculture, Garthwaite said, "especially when [as is usually the case] laboratory reared juveniles are transplanted to natural field environments to complete their growth to marketable size."

Advances in marine biotechnology are making it possible to breed shellfish that are optimally suited for the environment in which they are to be grown. Strains developed in this way generally should grow faster and heavier than organisms collected in the natural environment - to the delight of aquaculturists and consumers alike. (Reprinted with permission from Genetic Engineering News, Mary Ann Liebert, Inc., Publishers, April 1985)

Planning an aquabusiness

Since World War II, intensified research in marine science and engineering has fostered a number of advances in mariculture technology. Such studies have generated baseline data about behavior, nutrition, reproductive physiology, control of diseases and parasites, and various ecological parameters. High populations of fish and shellfish can now be confined in culture systems in ponds, cages or raceways through which water may flow or be recycled.

More recently, scientists have been employing the tools of molecular biology to modify marine organisms, to make them grow faster, reproduce more efficiently, resist disease and so on. However, translating such research from the R&D stage into a business requires an understanding of the particular problems inherent in scaling up an aquabusiness to a commercially viable enterprise.

The greater availability of public and private R&D funding, combined with wider recognition of the need and prospects for commercialization of mariculture, have spurred the development of aquaculture technology. Mariculture is becoming a more attractive proposition, partly as a consequence of the increasing costs in the capture fishery and the declining costs of culture fishery as productivity improves.

However, results of recent R&D in biotechnology and aquaculture have not yet been incorporated into the broader context of operations which can be referred to as "vertically integrated aquaculture (VIA)" - a commercial fish farming system where the grower has control over production, processing and marketing from the initial seeding of the culture to final sale.

VIA requires integrating a number of variables. Some of these variables (such as predation, disease, and other environmental perturbations) are difficult to control but may be predictable; other variables (such as food supply and breed of fish) are controllable but are not yet well enough understood in terms of systems engineering criteria. Although a great deal of baseline data have been accumulated about desirable species, much of this information has not yet been translated through critical scale-up trials into commercial enterprises. A frequent scenario is that of the experimentalist who has been encouraged by entrepreneurs into attempting full-scale application of concepts and techniques only recently developed and practiced in the research laboratory.

Mariculture requires crucial ecosystems management; thus, it is extremely site-sensitive and dependent on both specific characteristics of an organism's ecosystem and the society which will consume the "product". Mariculture has long been practiced as an art in Southeast Asia, China and the Mediterranean area. However, we have only recently gained the necessary technical knowledge and an appreciation of the social and institutional influences on biobusiness to translate the art of mariculture into practical commercial technologies.

These technologies may be transferred from the organism's native ecosystem to others around the world - particularly within the same latitudinal limits, where the characteristics of ecosystems are similar enough to permit technology transfer with relatively little adaptation to accommodate variability of sites. However, any plan for a mariculture venture must also take into account the many social, cultural and economic characteristics of the different societies that share a latitude.

Criteria for investment

The components of marine aquaculture production systems are designed to fulfill the goals of national as well as corporate planners. Thus, their criteria for investment may involve social considerations such as job creation, political considerations such as foreign exchange improvement and infrastructure development, or solely economic (profit-making) considerations. Planners, however, are uncertain about the degree of risk and the extent of potential rewards - the investibility - of marine aquaculture.

Traditional subsistence aquafarming yielded 200 to 500 kilograms of biomass per hectare - a harvest which reflects the natural carrying capacity of a crop species in most coastal ecosystems in the tropics. The aquafarm was either seeded by natural "recruitment" (opening a gate to a pond, letting the tide bring some fish in, and then closing the gate) or by actively gathering young from the wild.

In contrast, large scale industrial mariculture requires much greater productivity. The best way to increase productivity is to provide high stocking densities by seeding with juveniles bred in a hatchery. However, such increases in animal crop densities create special demands on the system. Energy "subsidies" - feed, water exchanges, aeration, and (in some cases) heat - must be provided. High water quality must be maintained, which requires precise monitoring of the chemistry of saline waters as well as the overall water condition.

In addition, a highly responsive automated-feedback controlling mechanism - to monitor oxygen, levels of nitrites, temperature and other physical or chemical parameters - is needed to ensure a healthy environment for growth and survival. Problems created by other organisms in the system - pathogens, parasites, predators or competitors - must be quickly resolved. The "unnatural" conditions of amended aquacultural ecosystems necessitate greater technical sophistication than was required for subsistence farming operations in the natural ecosystems of traditional coastal zone aquaculture.

Special management skills are required to shepherd the aquabusiness venture through its various stages: from spawning in a hatchery through larviculture, nursery and grow-out in the production phase to harvesting, processing, packaging and distribution in the marketing phase. Great efficiency and economy can yield higher productivity.

VIAs are usually capital-intensive ventures. Because they generally require three to five years to get in the black, they demand capital resources that can sustain the losses normally anticipated during start-up, as well as the unexpected perturbations which frequently plague high risk bio-industries. Undercapitalization has hastened many failures in aquabusinesses.

Selecting a species

Since the primary motivation for a mariculture enterprise is to put food on the table, market parameters should guide the design and management of the venture. First, traditional

food habits and taboos in the market should be considered. Only a few preferred species - out of the thousands of aquatic plants and animals that inhabit both fresh and salt waters - are being investigated as candidates for domestication. These species enjoy high acceptance among consumers which contributes to high market values and makes palatable the risk to investors.

Other important criteria include ease of preservation and preparation and nutritional qualities. In addition, subjectively judged attributes such as flavour, texture, colour, luster and form will often induce the consumer to embrace or reject an aquafood. The validity of relying on these subjective factors has been borne out by consumer tests involving taste, odor and appearance.

Aquacultural conditions can alter some of these subjective factors, so the culturist should be alert to changes such as off-flavours or soft textures that would render the product less appealing. Management must consider other market criteria related to problems of manufacturing efficiency, such as dressout percentages (that portion of the whole animal that is marketable as food, or the ratio of meat to bone).

Saltwater vs. freshwater farming

Although people frequently draw an analogy between terrestrial and aquatic animal husbandry practices, the analogy is not always an apt one. Moreover, such an analogy applies much better to freshwater farming (such as for catfish and carp) than to marine species which are managed in more hostile environments. For example, saltwater farmers must contend with salt-induced corrosion, predator and competitor species. These factors and others - such as ill-advised attempts to locate an operation on coastal areas that are subject to high energy wave action, storm and erosion - make it unreasonable to compare such a venture with poultry, swine and cattle husbandry.

Unless control over the reproductive cycle of the crop species is guaranteed (so as to ensure an adequate seed supply for stocking the next generation and perpetuation of the operation), culture technology carries a high risk. Marine fish are more of a problem in this regard than freshwater fish, due in large part to a lack of baseline information of fish behavior, reproductive physiology, diseases, and basic nutritional requirements for saltwater species. For example, commercial mariculture development has been severely constrained by a bottleneck in the larval stage of fish development, created by problems of feeding small-mouth fish larvae and achieving high survival in larviculture of marine species.

Another limiting factor in an aquaculture operation is nutrition during the crop species' growout phases. The cost of feed and feeding is the largest single item in an operating budget. Thus, any gains in efficiency through improved nutrition and feeding technology (or perhaps through genetic manipulations which will enable a species to grow larger and faster) can help to significantly increase profits.

To ensure the growth, health and survival of high density populations confined in ponds, cages, raceways or elsewhere, a feed supplement, or even a complete ration, may be required. Such rations are usually formulated from agricultural residues, various food processing wastes, oilseed cakes, and fishmeal. The latter not only supplies essential amino acids and lipids, but apparently growth-promoting substances and attractants as well. However, very little classical nutrition research has been conducted on the marine species that are the most likely candidates for aquaculture - and it will be impossible to optimize the system for profitability until better information about the essential components and proportions of diets is available.

Large scale operations are also limited by diseases and parasites in hatchery operations and in the nursery and growout stages in the crop animal's life cycle. Predation and poaching are problems which have occasionally limited an aquabusiness. In some environments, institutional constraints have made it difficult and expensive to operate the business.

Site location

Once a crop species has been selected which will satisfy a particular market and the most suitable culture technology has been worked out, one must select an appropriate site. This decision is crucial for the success of the venture. Ecological requirements (such as water quality, soils, and meteriological criteria) and economic, political, cultural and sociological factors must be considered. All of these issues can be limiting factors in the successful application of a business plan.

A number of enterprises in the United States have collapsed due to poor site selection. Site-related causes of failure of aquabusinesses have included hurricanes, water quality and supply, pollution, regulatory constraints, and opposition to the venture by the indigenous fishing community.

Scaling-up

Scale-up of an experimental laboratory operation to larger size is needed to generate enough sales to justify the high investment cost of research, development and start-up, as well as to gain the advantages of economy of scale. However, because of the complexity of the systems (particularly in vertically integrated operations), the nature of the development process and the magnitude of the problems involved in the transition from lab to full-scale operations are often misunderstood.

A pilot farm must function as part of an ordered sequence of development steps in order to adapt the highly site-sensitive production technology to the specific environmental conditions in which it must operate. Before the goal of high productivity can be realized, the interactions of such controllable variables as stocking rate, ration composition, feeding amounts and frequencies, pond fertilization, water exchange rate and aeration must be understood and optimized.

The decision to invest in aquafarming should be predicated on an in-depth analysis of the size and nature of the market and a determination of the elasticities of demand for and price of the crop species under consideration. The probable need for product and market development programs should be evaluated. At the same time, the state-of-the-art of the technological components must be assessed to determine the degree of risk being assumed and the site selection criteria that must be satisfied.

Bank financing

Bank financing is more attainable after completion of at least two crop cycles in the pilot facility. The experience and data accumulated from a pilot operation will help provide a more propitious debt/equity ratio to facilitate early expansion to a full scale facility.

The private sector justifies investment in mariculture by measuring the potential for sales revenue and profitability; the public sector justifies such investments by projecting rural employment and the generation of wealth in the form of high protein foods. However, before we can make vertically integrated aquaculture a significant source of food for people, individuals from government, industry and the university community need to understand more about the technical problems that relate to this commercial fish farming system. (Reprinted with permission from Genetic Engineering News, Mary Ann Liebert, Inc., Publishers, April 1985)

Agricultural Applications

New hybrid canola joint venture formed

Dr. John Evans, Chairman and Chief Executive Officer of Allelix Inc., of Mississauga, Ontario and Lorne Hehn, President of United Grain Growers of Winnipeg, announced that both companies had formed a joint venture to develop and subsequently market hybrid canola varieties suitable for Western Canada. Canola is Canada's most widely planted oilseed and an important cash crop for Canadian farmers.

The objective of the joint venture is to develop commercially useful hybrids with improved yield and quality characteristics. In 1984 Canadian farmers received more than $1 billion from canola sales and it is expected that yield increases due to hybridization could add 25 to 30 per cent to that.

Basic research and plant breeding will take place at Allelix, which has an 8,400 square-metre laboratory in Mississauga and a 40-hectare research farm, complete with 2,000 square-metre greenhouse, near Georgetown, Ontario. Allelix's breeding programme is reinforced by sophisticated research capabilities in cell fusion, plant tissue culture, anther culture, molecular biology and biochemistry. In addition, somatic cell fusion work, involving co-operation between Allelix and the University of Guelph, has been partially supported by a grant from the National Research Council through the PILP programme.

United Grain Growers will assist in the selection and operation of test locations in Western Canada. In future years, as hybrids are developed and commercialized, UGG will have primary responsibility on behalf of the joint venture for the production and marketing of sufficient quantities of seed to meet the needs of Western Canadian farmers and the seed industry. (Source: Company News Release, 24 April 1985)

Automating plant cloning with a bioreactor

An agreement to develop commercial applications jointly for large-scale, automated plant-cloning systems has been signed by Arthur D. Little (Cambridge, Mass.) and DNA Plant Technology (Cinnaminson, N.J.). The cloning systems could permit the commercial production of unlimited, identical copies of economically important crop plants. The companies previously completed a feasibility study that led to the development of a prototype bioreactor system using spin-filter technology. They report that they are now talking to major corporations about developing customized systems for specific crops. (Source: Chemical Week, 10 April 1985)

Microbes retain moisture

Nordic microbes will now turn sterile deserts into fertile fields. Biotech Inc. has developed a method for doing this which is now under study by the Nordic department for development aid. The method calls for spraying microbes on the desert following the planting of fast-growing trees and bushes. The microbes form a viscous layer that prevents the ground from drying out. It normally takes only days or hours for the desert to dry out after even the hardest rain. (Extracted from Svenska Dagbladet, 8 February 1985)

Plant that makes its own pesticide

Plant Genetic Systems has developed a tobacco plant that makes its own pesticide through genetic engineering techniques. The plant produces bacterial toxin that kills insects by destroying the lining of their guts. The gene was isolated from Bacillus thuringiensis and inserted into a Ti plasmid to carry the gene into the plant cells. Tobacco stems were treated with preparations containing the genetically altered plasmid, and the damaged tissue was then scraped off and grown into a callus. The calluses can then be grown into mature plants. Tests confirm that the tobacco plants do produce the toxin, but further studies will be needed to determine if the genes are passed onto future generations and whether the plant produces enough toxin to kill insects. (Source: New Scientist, 14 February 1985)

Food Production and Food Processing

Instant beer

Kirin Beer, Japan's biggest brewery, says that it can now brew beer in a day instead of a week in an experimental bioreactor at its Tasaki research centre. When Kirin's "biobeer" comes to market it will be among the first of a spate of modern bioreactor products emerging from Japanese industry.

Bioreactors are a fancy name for an old idea. In ancient times, milk was stored in calf stomachs so that rennin, an enzyme in the stomach, could act as a catalyst which helped milk proteins coagulate into cheese. Modern bioreactors work much more efficiently, mainly because of the new technique known as immobilisation. Instead of leaving the catalysts and other chemicals to mingle freely in a tank, the enzymes or cells can be bonded on to fixed structures inside it. In principle, the catalyst can then keep working without being washed away. Bioreactors have other advantages. By hooking immobilised cells to transducers they can form biosensors which keep close control of chemical reactions. Their extra efficiency means there is less need to juggle with temperatures and pressures to make processing cost-effective. Kirin's bioreactor immobilises yeast in a basket of beads made from calcium alginate which forms a fast-reacting core to churn out alcohol when the grain mixture flows past it. (Extracted from The Economist, 18 May 1985)

Chemical Applications

Enzyme growth seen

Real annual growth of 6.5 per cent will push US industrial enzyme demand to $255m. by 1988, according to US consultant, Frost & Sullivan.

Food preparations are the leading use, accounting in 1983 for three-quarters of total demand of $185m. Enzyme use in food preparations will rise from $140m. in 1983 to some $190m. in 1988, the consultants predict. Corn processing accounts for over half the enzymes used in the food sector; dairy applications for a fifth.

The second biggest sector, pharmaceuticals and medical applications, is predicted to grow from $30m. in 1983 to $40m. by 1988, thus maintaining a steady market share of 16 per cent. Enzymes for chemical synthesis, worth $10m. in 1983 or 5 per cent of the market, will grow slightly to $15m. or 6 per cent of the market, Frost & Sullivan predicts. The consultant envisages enzymatic production of ethylene oxide in the 1990s.

Glucose amylase and isomerase are predicted to grow at an annual rate of over 9 per cent, while rennin will grow at only 3 per cent a year over the next few years. (Source: European Chemical News, 20 May 1985)

Biopolymers in medicine and packaging

Biological polymers can now be designed with specific physical properties, thanks to biotechnology. The most promising area for biopolymers is the biomedical sector, according to a new study from BioInformation Associates (BIA) and the US consultant, Charles H. Kline.

Although most biopolymers are obtained from plant and animal sources, microbial products obtained by fermentation are potential substitutes when cost-effective new technologies are eventually developed. Improved fermenter design and process control and more efficient recovery systems currently on the drawing-board should lower costs, BIA predicts.

The most widely used biopolymers are starches, cellulose derivatives and algal polysaccharides like agar, carrageenan and alginic acid. The paper industry is the leading industrial end-user of biopolymers, and the food industry the biggest user in the consumer sector. The use of polysaccharides such as xanthan gum in enhanced oil recovery is also of growing importance.

Professor Tony Sinskey of Massachusetts Institute of Technology, who co-authored the report, predicts that biological polymers will find a place in bulk packaging applications where bio-degradability is at a premium. Italy is pushing for a ban on non-biodegradable plastic packaging by the end of the decade for environmental reasons, although there are strong doubts as to whether this can be achieved.

Sinskey reckons that current developments in biotechnology, including genetic engineering, could bring down the price of a biological thermoplastic like polyhydroxybutyrate (PHB) to economic levels to permit its use in plastic bags by the Italian deadline. Sinskey and his colleages at BIA are currently studying the production of PHB from bacteria. ICI has been developing this biopolymer for a number of years with a view to using it in biomedical and electronic applications. Its monomer, hydroxybutyric acid, could prove to be a valuable intermediate for stereo-specific synthesis of drugs and fine chemicals due to its stereoisomeric purity.

A biological polymer which is finding increasing commercial success is hyaluronic acid. This is sold for use as a buffer agent in eye operations by the Swedish company Pharmacia, and has great potential for a wide variety of uses in human and animal health care. Applications exist in the treatment of joint problems in humans and, longer term, in drug-delivery systems. Hyaluronic acid may find other uses because of its great optical clarity.

Pharmacia obtains high molecular weight hyaluronic acid by extraction from cockscombs and plans to continue doing so for the time being. Its technological edge lies in its separation and purification expertise, which enables the production of very pure material. The company is developing a bacterial route to the polymer in conjunction with BioTechnology General of Israel and is thought to be close to commercialization. It is also working on second-generation cross-linked hyaluronic acid polymers for applications in human joints. (Source: European Chemical News, 25 March 1985)

Biotechnology's webbed development

Spiders' webs could stimulate exciting advances in biotechnology during the next decade. Trevor Jarman from PA Technology in Cambridge told a conference in Geneva that the biotechnology industry could provide spiders' webs, with their unusual structural properties, to the materials industry.

Jarman is not suggesting starting a spider farm, but genetically engineering the protein which constitutes a spider's web. These materials would be needed in large quantities and might provide the stimulus for researching ways to make bacteria provide large yields, says Jarman. So far biotechnology companies have concentrated on producing pharmaceuticals which are valuable in small quantities, because bacteria currently give small yields.

Genetically engineered materials will have to compete with existing fibres and plastics that are petroleum based. But Jarman believes uncertain petroleum prices may give biofibres the edge.

An exciting possibility with biomaterials could be to modify their structure to obtain specific physical characteristics. Even if the biotechnology industry is not ready yet to

exploit the idea of modifying structures found in nature, there is a wealth of natural products that could be genetically engineered. One is resilin, a protein which stores mechanical energy. It is found in insects' wings and fleas' legs. Another is elastin. Collagen and elastin are major components of blood vessels. Collagen can be extracted from tissue intact, but elastin cannot. Genetically engineered elastin plus extracted collagen, says Jarman, could be used to build new blood vessels. (Extracted from New Scientist, 30 May 1985)

Energy and Environmental Applications

Is bioenergy stalled?

"Can bioenergy deliver the development goods, or is it a developmental cul-de-sac?" The question, posed at a recent conference on biomass energy, reflects the unfortunate fact that despite years of talk and research, there has been little progress in harnessing bioenergy in the service of development.

Biomass - mainly wood, crop residues, and dung - is the primary source of energy in the developing world. But there are only a handful of instances where bioenergy is supplying a significant fraction of an area's power needs - such as Brazil's sugarcane-ethanol conversion scheme, the manufacture of biogas from dung in China's Szechwan Province, and tree plantations that supply feedstock for power plants in the Philippines.

At the conference, which was sponsored by the World Resources Institute and Rockefeller Brothers Fund, the assembled experts agreed that technological obstacles to efficient bioenergy systems were insignificant compared with social, economic, and institutional impediments.

Biomass energy systems, to be economic, must be multipurpose, combined with food, fodder, fuel, fibre, or fertilizer production. They rely on local raw materials, labour, and initiative. Bioenergy thus cuts across all sectors of the economy and is intimately involved with local patterns of domestic and economic activity. Even relatively simple technologies such as efficient cookstoves have not been widely adopted because of developers' failure to understand local needs and preferences.

Most conference participants seemed convinced that bioenergy systems have boundless potential for contributing to national self-sufficiency, spurring rural development, and slowing environmental erosion.

But prevailing forces are hostile. Economically, bioenergy development is being elbowed out by a vicious cycle. Government oil subsidies hold the price of biomass fuels far below their real value, and price controls on agricultural products prevent farmers from making long-term investments, and drive them further into marginal lands as prime agricultural lands are devoted to export crops - which in turn are used to buy oil.

Furthermore, most bioenergy systems are not now particularly economic unless social and environmental benefits are calibrated into the equation. Payoffs are long-term. Private investors are wary, particularly because of the thorny issues surrounding ownership of the resource base.

There are also powerful institutional impediments to bioenergy. It has no institutional focus within governments, where agriculture, energy, and forestry ministries pursue separate agendas. Research, focused in developed countries, is divorced from practice. And training in bioenergy systems, according to one participant, can only be had in two places - the University of Nancy in France, and the University of Hawaii.

The evidence to date indicates that change requires support from the highest levels of government. But biomass, the "poor peoples' fuel," is something developing countries want to get away from. Cornell biologist David Pimentel observed that as far as political sex appeal goes, agriculture has low status in most countries, forestry is lower, and biomass is "the pits".

The contrast between the visions of technologists and the grass-roots realities is probably as striking in the bioenergy field as in any other aspect of development. For example, Princeton physicist Robert Williams, of the Center for Energy and Environmental Studies, gave a presentation demonstrating that it is possible for the entire world to enjoy a standard of living comparable to Europe in 1975 while reducing per capita energy use by half. By 2020, he said, new wood-efficient cookstoves could be converted to gas; gas-turbine cogeneration could open the way to efficient, decentralized local industry; and biomass-derived fuels could supply energy for transportation.

But a hint of the political obstacles that plague even modest efforts at change was offered by Wangari Maathai, founder of Kenya's social forestry or "Greenbelt" movement. Maathai, a farmer's daughter who holds a master's degree in biology from the University of Pittsburgh, has tangled with the government and even spent time in jail. The Greenbelt organization has a simple function, which is to supply seedlings and advice to groups around the country who want to start tree nurseries. It has been an uphill struggle, particularly since a major goal, according to Maathai, is to provide women with income-producing activities without "threatening the men," who otherwise "will rise up against you". Maathai has gained an international reputation for her work, and said Kenyan president Daniel Arap Moi now "likes to be seen planting trees".

Although the conference supplied a good picture of the bioenergy landscape, several speakers expressed frustration at the continuing absence of prescriptions. "I have gotten no concrete guidance from this conference," cried the Israeli participant Uri Marchaim. People were skeptical that either national governments or private industry would take the lead in bioenergy development, and international aid is on the decline.

The consensus of the meeting appeared to be that the impetus for bioenergy must come from the grass roots, so a priority must be the promotion of information networks and strengthening of the technical expertise of nongovernmental organizations (NGOs). There are signs that a constituency of sorts is beginning to organize around bioenergy. Al Binger, director of the new "energy cane" project in Jamaica, is organizing a Bioenergy Users Network among less-developed countries, with some help from the Agency for International Development. The United Nations Development Programme has a new project to encourage NGOs, and the Rockefeller Brothers Fund has set up an agribusiness consortium to engage in joint agricultural projects, including biomass, with developing countries.

The prevailing assumption among policy-makers world-wide is that fossil fuels will continue to supply the engine for development. But, according to a recent paper from Worldwatch Institute, most global energy analysts project a rise in energy use of 125 per cent by 2025, which would include a requirement for two more Saudi Arabias' worth of oil. Assuming these resources become available, the environmental and economic costs will be so staggering that, as one conference participant said, "There is no competition [between bioenergy and conventional fuels] because there is no choice." (Science, Vol.227, p. 1018, 1 March 1985, author C. Holden, Copyright 1985)

Extraction Industry

Two bacteria for petrochemical industry

Scientists at Nitto Chemical Industry who were looking for a way to dispose of the toxic sludge produced in the treatment of effluent became interested in two bacteria, nocardia and corynebacterium, commonly found in the soil. The bacteria are rich in an enzyme which helps turn a common chemical called acrylonitrile and water into acrylamide, an agent used in the petrochemical industry to treat effluent and squeeze oil from tired wells.

While its competitors continue to manufacture acrylamide at high temperatures with such catalysts as copper and sulphuric acid, Nitto plans to immobilise its new bugs and put them to work in a small bioreactor. The company expects production costs to fall by up to 30 per cent. (Extracted from The Economist, 18 May 1985)

Industrial Microbiology

Biodegradable polymer

Marlborough Biopolymers has developed polyhydroxybutyrate (PHB), a biodegradable polymer with properties similar to polypropylene. The plastic breaks down completely in the human body or in soil. PHB might thus be suitable for use as surgical sutures, pins or plates for broken bones, drug-delivery implants and wound dressings. Marlborough says there will be a large market for PHB in SE Asia, the Caribbean and Brazil, where there are large surpluses of sugar that could be used to feed bacteria that make the polymer. PHB could be competitive with oil-based plastics such as polypropylene in those areas. (Extracted from New Scientist, 14 February 1985)

Biohazards

Genes can be infectious

It is possible for a genetically engineered gene to spread through a population of bacteria without the help of natural selection. Experiments at the University of

Massachusetts have shown that a gene that has been introduced into a bacterium can increase in frequency by infecting other bacteria, rather than by imparting a beneficial trait to the individual.

Bruce Levin, professor of zoology at Massachusetts, told a session on the risks of genetically engineered organisms that he had seen this phenomenon in a small number of experiments to investigate the infectious transfer of genes between bacteria. However, Levin said that this is not likely to happen, mainly because in many plasmids that he has studied, the gene did not increase in frequency without the help of selection. Those plasmids that increased in frequency without selection did so because the second time they were transferred from one bacterium to another, the rate of transfer was four times faster. (Extracted from New Scientist, 30 May 1985)

E. PATENTS AND INTELLECTUAL PROPERTY ISSUES

Selection of recent patents

	Patent No. Date issued; Date filed	Assignee Inventors
Lymph treatment to remove antibodies	4,508,819 April 2, 1985 May 21, 1982	Bio-Response, Inc., Wilton, Ct. Sam Rose
Stabilizing r-DNA hoste cells	4,506,013 March 19, 1985 June 18, 1981	Eli Lilly and Co. Indianapolis, Ind. Charles L. Hershberger, Anna I Radue, Paul R. Rosteck, Jr.
Enzymes coupled to silicon dioxide	WO 85/00380 July 6, 1984 DK 3174/83 July 8, 1983	Superfos A/S, Frydenlundsvej, Vedbaek, Denmark Jan J. Hansen, Jesper C. Thygesen, Margrethe Winther-Nielsen
Plasmids transferred by protoplast fusion	WO 85/00382 July 6, 1984 NL 832010 16.9 July 6, 1983	Gist-Brocades NV, Delft, The Netherlands Johan P.M. Sanders, et al.
Insulin-potentiating peptides	WO 85/00597 July 16, 1984 US 514,158 July 15, 1983	Whittier Institute for Diabetes and Endocrinology, La Jolla, Calif., USA James U. Lewis
Epidermal growth factor precursor cloned	WO 85/000369 July 2, 1984 US 511,372 July 5, 1983	Chiron Corp., Emeryville, Calif., USA Graeme I. Bell
TPA production in tissue culture	EPO 0 133 070 June 26, 1984 FR 8310736 June 29, 1983	Choay SA, Genefusion (S.A.R.L.), Paris, France Gerard Brouty Boye, Michel Maman, Patrick Choay, Michel Darmon
Biological reduction of sulfur oxides	GB 2 143 810 June 18, 1984 US 505940 June 20, 1983 US 607960 May 10, 1984	Duncan Lagnese and Assoc., Pittsburgh, Pa., USA Meint Olthof, Jan A. Oleszkiewicz, Harold G. Weinreb
Lipsomes used in Lactobacillus transformation	EPO 0 133 046 July 30, 1984 JP 140257/83 July 30, 1983	Kabushiki Kaisha Yakult Honsha, Tokyo, Japan Mariko Kadota, et al.

Copper chelating protein	4,511,652 April 16, 1985 June 3, 1982	University of California, Berkeley, Calif. Seymour Fogel, Juliet W. Welch, Michael Karin
Labeling with antigen-conjugated microspheres	4,501,244 April 9, 1985 Sept. 22, 1982	Stanford University, Stanford Calif. David R. Parks, et al.

(Extracted from Mcgraw-Hill's Biotechnology Newswatch, 6 May 1985)

F. BIO-INFORMATICS

Biotechnologies: Challenges and promises by Albert Sasson

The Sextant series is a new group of Unesco publications designed to provide, in clear language, easily comprehensible to the general reader, a state-of-the-art review of important topics of our times. Following the first title, More than Enough? An Optimistic Assessment of World Energy, the second volume in the series is Biotechnologies: Challenges and Promises, a comprehensive, scientific discussion of the practical applications of biology and the dominant role it is rapidly assuming for the survival of this planet.

Biotechnologies represent an approach, at once biological and economic, to the basic problems of health, food and energy. The book focuses on production of basic foodstuffs, microbial fermentations, the possibilities provided by a better understanding of cells and living beings and the potential of biotechnologies applied to plants. It does not, however, ignore the risks which these technologies entail. The possibilities, hazardous as they may be, of acting upon the very mechanisms of life, as well as the considerable financial and strategic interest involved, constitute significant challenges.

This work, which succeeds in being both clear and precise without losing any of its scientific value, provides a complete guide to the field, making it required reading for specialists and the uninitiated alike. BIOTECHNOLOGIES: CHALLENGES AND PROMISES by A. Sasson (Sextant 2), is also available in French and Spanish. 1984 315 pp. illustr., tabl. ISBN 92-3-102091-9 Price: 85 FF, available from The Unesco Press, 7, place de Fontenoy, 75700 Paris, France.

Genetic Engineering and Biotechnology Yearbook 1985

Edited by Alan G. Walton, President, University Genetics Company, Westport, CT and Sharon K. Hammer, President, "Verbatim", Mahopac, NY, U.S.A. and published by Elsevier Science Publishers B.V., P.O. Box 330, 1000 AH Amsterdam, The Netherlands 1985 vi + 1060 pages, price: US $750.00 ISBN 0-444-42461-X

The 1985 Yearbook is completely revised and is 50 per cent larger in size than the earlier edition. Other differences include, the expansion of all sections, with Japan now covered exhaustively;

* a model for predicting success in biotechnology
* a broader spectrum of companies analysed
* a broader focus (analysis expanded to incorporate the needs of the investment community, ranging from financial planners, through corporate venture carital groups, to the underwriter/investment broker and individual investor)
* much more data on financial performance of biotech companies
* the inclusion of summaries of R & D progress, press reports, and other general information

The book is unrivalled in both its ease of use and its complete, far-ranging coverage. Information is presented in an easy-to-read format. Each company profile includes not only the name, address, telephone number and contact person, but also in most cases the business history, structure, ownership/management, research update, status and availability of products, and financial information.

Biotechnology Industrial Directory and its companion U.S. Biotechnology Company Intelligence Report stand ready to supply the most comprehensive set of reference guides on over 1,500 biotechnology companies worldwide and detailed profiles of over 190 private and public U.S.

companies. These comprehensive information sources give a quick insight into company performance. The publications are available from: CTB International Publishing Co., P.O. Box 218, Maplewood, NJ 07040, USA. The price per set is $428.40, plus $42 for overseas delivery.

First principles of biotechnology

Setting Genes to Work: the Industrial Era of Biotechnology by Stephanie Yanchinski, Viking. pp. 157, £10.95

This book is destined for a wide readership. First of all the author sees biotechnology in its true historical perspective - as a logical extension of industrial microbiology, some branches of which go back 4000 years or so. What modern-day biotechnology can offer is the opportunity for industrial microbiologists to do more efficiently what they have been doing for years, sometimes centuries. It can also open up vast new horizons for manufacturing products that hitherto have been difficult to obtain. Far too many people who have jumped on the biotechnology bandwagon do not seem to appreciate this. Yanchinski introduces her subject by outlining this lineage. She goes on to provide simple, but most readable accounts, of genes and the development of modern-day genetics, and a painless (for non-scientists) description of the techniques now available for recombinant DNA.

The historical and biological accounts set the picture for an assessment of some actual, but mostly potential, applications of biotechnology, and a discussion of its economic, political and sociological implications. The "biotechnology sunrise", which Yanchinski believes has already arrived, presages, she thinks, the development of products, chiefly in the fields of health-care and agriculture. Concentrating on the application of biotechnology in probing for human disease, she reviews most of the ideas that have been floated in recent years, from the development of a whole armoury of diagnostic kits to the treatment of genetic disorders. However, Yanchinski never adopts a pie-in-the-sky approach to ideas, but discusses them all in a balanced manner and with scientific, political and sociological insight.

The economic prospects for biotechnology - today and in the future - are assessed in a chapter which gives an account of the setting up of the first companies and their subsequent growth or demise. Again, the account is balanced, but it reveals an author who carries a healthy dose of scepticism for the subject.

Commenting, as many have, on the expected explosive growth of biotechnology companies - and their achievements - even before 1999, Yanchinski sees a slow-growing tree, having arisen from a seed planted in the 1970s, but which will not bear fruit before the beginning of the next century.

The balanced and broad approach is evident again when Yanchinski asks "how safe is safe?", when handling genetically engineered microbes. Biotechnologists seem to have come to a sensible arrangement regarding containment of genetically engineered microbes, but only after a show of near panic. But Yanchinski reserves some of her most telling comments for national and international politicians who, on many occasions, have opted for national prestige and even personal gain at the expense of the human population worldwide when making judgements on politics in biotechnology.

Setting Genes to Work is one of the first biotechnology books to take a broad approach to the subject. It requires little scientific knowledge to follow the arguments put forward, and can be recommended to a very wide readership, from sixth-formers to bankers, sociologists, industrialists and politicians. It is an excellent read, despite the complete absence of photographs, line drawings or tables; and it has the slick, gripping prose style that New Scientist readers have come to expect from Yanchinski.

Professor Smith's book, Biotechnology Principles is a recent addition to the "Aspects of Microbiology" series. It is positively dripping with diagrams and tables, and is aimed at an altogether different audience. The author faced a formidable task when he agreed to write a such a short text on a very broad subject, but he has succeeded admirably. He, too, introduces his book by putting modern biotechnology in its proper historical perspective. He then outlines the principles of biotechnology in four chapters which considers applied genetics, fermentation technology, enzyme and immobilised cell technology, and downstream processing. Smith has to be commended for his balanced treatment, which could not have been easy to maintain when having to deal with microbiological principles on the one hand, and thermodynamics on the other. Biotechnology Principles should prove particularly useful to

undergraduate students studying a biotechnology option, and as an introductory text for post-graduate students doing courses in biotechnology. Biotechnology Principles, by J. E. Smith, is published by Van Nostraud Reinhold in paperback form, at £5.25. (Extracted from New Scientist, 30 May 1985)

New journal on biosensors

A new international journal entitled Biosensors is being published by Elsevier Applied Science Publishers, Crown House, Linton Road, Barking, Essex 1G11 8JU, England. In the US and Canada, free specimen copies are available from: Journal Information Center, Elsevier Science Publishing Co. Inc., 52 Vanderbilt Avenue, New York, NY 10017.

This new international journal presents authoritative reviews on research, technology, and application of biosensors. The scope includes both sensors that employ biological molecules or systems in the sensing elements and other devices that sense parameters in biological processes. Thus, many types of measuring devices are covered, including enzymes, whole organisms, and immunoelectrodes (both amperometric and potentiometric); piezoelectric crystal detectors; novel chemical sensors; optoelectronic devices; specialist applications of mass spectrometry and nuclear magnetic resonance; and types based on field-effect transistors and those which utilize the principles of biological fuel cells.

Since the biosensor field is multidisciplinary, spanning fundamental and applied aspects of biochemistry, electrochemistry, and electrons, some articles will be of an introductory nature, directed particularly at life scientists who are showing increasing interest in biosensors but might be new to the field. Others will concern end-user requirements.

In addition to reviews, publication of original papers is encouraged. There is also a news section covering important developments in industry, notes on new patents, product reviews and details of government funding. There will be four issues per year.

The managing editors are: (1) I.J. Higgins and A.P.F. Turner, Biotechnology Centre, Cranfield Institute of Technology, Cranfield, Bedford, MK43 0AL UK; (2) W.G. Potter, Biotechnology Directorate, Science and Engineering Research Council, Polaris House, North Star Avenue, Swindon SN2 1ET, UK. The editorial advisory board is international in scope: J. Janata, US; C.R. Lowe, UK; F. Scheller, West Germany; S. Suzuki, Japan; D. Thomas, France; and L.B. Wingard Jr., US. (Source: European Science News, 39-6 (1985))

UK Government Chemist to set up biotechnology database

A biotechnology database is to be established at the UK's Laboratory of the Government Chemist which will be available to subscribers from private industry. Following a one year feasibility study and consultation with industry, it has been decided to set up a service known as MiCIS - Microbial Culture Information Service.

It will provide information on some 50,000 micro-organisms including the holdings of the National Culture collections. Subscribers will be able to find the source and details of named organisms or find organisms which display properties of specific interest.

The range of information available includes names, source, hazards, morphology, metabolities, enzymes, culture conditions, maintenance requirements, genetic information, industrial uses and properties, references and availability.

The service is expected to be fully operational by early 1986 and will be available to on-line subscribers for an annual subscription and a charge relating to level of use.

Plans for expansion of the service are already being made and discussions are currently taking place about the possibility of adding data from collections in mainland Europe. (Source: Manufacturing Chemist, April 1985)

Data-Star's computerised database

Data-Star, a new European computer bureau service, has signed a contract with Celltech Ltd., making available a new online database of biotechnology business news. The new service is based on Abstracts in BioCommerce, published jointly by Celltech and IRL Press Ltd. Details from: Data-Star, Plaza Suite, 114 Jermyn Street, London SW1Y 6HJ or on 01-930 5503. (Source: Biotechnology Bulletin, Vol.4, No.?, April 1985)

LGC's database to cover microbial culture information

Following a feasibility study and consultation with industry, the Department of Trade and Industry's Laboratory of the Government Chemist is to establish a database known as MiCIS - standing for microbial culture information service. It will be available to subscribers from private industry and will provide information on some 50,000 micro-organisms, including those held by the national culture collections. It should be open by early 1986. Details from: Mrs. G.V. Alliston, Biotechnology Group, Laboratory of the Government Chemist, Cornwall House, Waterloo Road, London SE1 8XY or on 01-928 7900, ext. 478. (Source: Biotechnology Bulletin Vol. 4, No. 3, April 1985)

G. MEETINGS

22-25 July 1985
6th International Symposium on Mycotoxins and Phytotoxins
Pretoria, Republic of South Africa. Further information: The Symposium Secretariat S.351, CSIR - PO Box 395, Pretoria 0001, Republic of South Africa

21-23 August 1985
International Workshop on Molecular Biosciences and Biotechnology,
SPIC Centre, 97 Mount Road, Madras, India. Further information: R. Srinivasan, Southern Petrochemical Industries Corporation, 97 Mount Road, Madras, India.

18-24 August 1985
10th Northamerican Rhizobium Conference,
Wailea, Maui, Hawaii. Further information: Dr. Jake Haliday, NiFTAL Director, Department of Agronomy and Soil Science, University of Hawaii, PO Box 0, Paia, Hawaii 96779, USA

25-28 August 1985
International Symposium on Biohydrometallurgy,
Vancouver, BC, Canada. Further information: Ms. Judy Novlesky, Symposium Secretariat, BC-Research, 3650 Wesbrook Mall, Vancouver, British Columbia, Canada V6S 2L2

3-5 September 1985
International Symposium on Recycling of Organic Wastes for Fertilizer, Food, Feed and Fuel, Hong Kong. Further information: Dr. M. H. Wong, Department of Biology, The Chinese University of Hong Kong, Shatin, Hong Kong

22-27 September 1985
VIII International Enzyme Engineering Conference,
Helsingor, Denmark. Further information: Engineering Foundation Conferences, 345 East 47th Street, New York, New York 10017, USA

23 September 1985
DNA Probes - New Technologies in their Development and Application,
Royal Lancaster Hotel, Lancaster Gate, London W.2. Further information: Miss Helen Raquet, Oyez Scientific and Technical Services Ltd., Bath House (3rd Floor), 56 Holborn Viaduct, London, E.C.1.

24 September 1985
Monoclonal Antibodies - New Technologies in their Development and Application,
Royal Lancaster Hotel, Lancaster Gate, London W.2. Further information: Miss Helen Raquet, Oyez Scientific and Technical Services Ltd., Bath House (3rd Floor), 56 Holborn Viaduct, London, E.C.1.

23-25 September 1985
Advances in Fermentation,
London, U.K. Further information: Mr. Norman T. Shepher, Conference Director, AIF85/c/o Process Biochemistry, Turret-Wheatland Ltd., Penn-House, Penn Place, Rickmansworth, Herts, England WD3 1SH, United Kingdom

29 September - 1 October 1985
Southwest Industrial Biomass Conference,
Hotel Westcourt, 10220 North Metro Parkway East, Phoenix, AZ 85021, USA. Further information: Sinyan Shen, Energy and Environmental Systems Division, Bldg. 362, Argonne National Laboratory, Argonne, IL 60439 - Tel. 312/972-6276

3-5 October 1985
Annual Meeting of Biotechnologists
Frankfurt-am-Main, FRG. Further information: DECHEMA, Postfach 970146, D-6000 Frankfurt-am-Main 97, Federal Republic of Germany

7-9 October 1985
Nature Update in Molecular Biology 1985;
Genes and Systems in Development.
Presented in association with the University of California at San Francisco
Sheraton-Palace Hotel, San Francisco. Further information: Nature Update in Molecular Biology, Nature Publishing Company, 55 Bleecker Street, New York, N.Y. 10012, USA.

8-10 October 1985
BIO Technica 85
Hannover, FRG. Further information: Deutsche Messe und Ausstellings-AG, D-3000 Hannover 82, Federal Republic of Germany

17-18 October 1985
Second European Seminar and Exhibition on Computer-aided Molecular Design,
European World Trade and Convention Centre Basel, Messeplatz 22, CH-4021 Basel, Switzerland.
Further information: Miss Helen Raquet, Oyez Scientific and Technical Services Ltd., Bath House (3rd Floor), 56 Holborn Viaduct, London, E.C.1.

27 October-2 November 1985
First International Congress of Plant Molecular Biology,
Savannah, Georgia, USA. Further information: Congress Secretary, 1st ICPMB, The Georgia Center, Athens, Georgia 30602, USA

11-15 November 1985
4th International Symposium on Anaerobic Digestion
Guangzhou, China. Further information: General Secretary, 4th ISAD, Ministry of Agriculture, Animal Husbandry and Fishery, Beijing, People's Republic of China

21-22 November 1985
First International Conference on Protein Engineering,
The Gloucester Hotel, Harrington Gardens, London, SW7 4LH. Further information from: Miss Helen Raquet, Oyez Scientific and Technical Services Ltd., Bath House (3rd Floor), 56 Holborn Viaduct, London, E.C.1.

16-17 December 1985
5th International Symposium on Agricultural Wastes
Chicago, Illinois, USA. Further information: Dr. John M. Sweeten, Chairman, Program Committee of ISAW-85, 303 Scoates Hall, Texas A&M University, College Station, Texas 77843, USA

16-18 December 1985
Getting into biotech business
The Biotechnology Centre Wales as a European Business and Innovation Centre is organising a 3-day Conference/Workshop on behalf of the EEC to introduce Academics and Entrepreneurs in Wales to all the necessary aspects of commercialising Biotechnology ideas. The Workshop will also teach how to successfully form and run a company giving experience of Business Management, Financial Management, Marketing and Feasibility Studies. Information will be given to indicate the help and grants available to support this exercise from the concept to full-scale operation. The Conference will be run at the Taliesin Centre, University College Swansea. Numbers will be strictly limited as this Conference is being subsidised by the EEC. Details from Christine Roberts, at the Biotechnology Centre Wales, Singleton Park, Swansea. Tel: (0792) 296396.

20-22 January 1986
Biotechnology looks to the next decade
New Orleans, USA. Further information:

Genetic Engineering and Biotechnology Monitor

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