OCCASION

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

DISCLAIMER

FAIR USE POLICY

CONTACT

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

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

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

21304

Vol. 2, Nos. 1 and 2, 1995

GENETIC ENGINEETING AND BIOTECHNOLOGY MONITOR

Vol. 2, Nos. 1 and 2, 1995 (Double issue)

CONTENTS

UNIDO s *Genetic Engineering and Biotechnology Monitor* is established as a mechanism of current awareness to monitor developments in the genetic engineering and biotechnology sector and inform governments industry and academia primarily in developing countries

The *Monitor* is issued four times a year and distributed free of charge to readers in developing countries It is not a formal document and has been reproduced without formal editing Opinions expressed here do not necessarily reflect the views of UNIDO Mention of the names of firms and commercial products does not imply an endorsement by UNIDO

Scientific editor Virginia Campbell
Compiled and edited Diana Rhind
Editorial Board V Podshibyakin G Tzotzos G Ramsey B Sugavanam Z Cziser

Published in 1995 by the United Nations Industrial Development Organization (UNIDO)
Vienna International Centre
P O Box 300
A 1400 Vienna
Austria

Tel (43 1)21131 0
Fax (43 1)230 7355

ISSN [illegible]
Printed in Austria

TO OUR READERS

While in the process of preparing the first Task Manager's Report on Chapter 16 of Agenda 21 Environmentally Sound Management of Biotechnology UNIDO became aware of a widely expressed need to establish a mechanism for information sharing on biotechnology that would keep pace with the extremely rapid rate of global biotechnological development The aim of this mechanism would be to periodically review, examine, assess and report on the current status of biotechnology, and on new trends and emerging issues in biotechnology development and its applications In addition, a consultative process would bring together a general body of comprehensive and well-balanced information on the ways biotechnology interacts with other factors in achieving the goal of sustainable development

UNIDO is now resuming its work of gathering information for the Second Task Manager's Report, focusing on more recent developments and trends in biotechnology This Second Report will seek to place a stronger emphasis, and include more information and proposals on financing biotechnology initiatives and on the ecological, safety, health, socio-economic and ethical aspects of the applications of biotechnology, as well as the commercialization of biotechnology products In addition, this second report will serve as an important resource in keeping developing countries informed of new developments and trends in this rapidly changing technology, as well as enhance public awareness of strategic issues, and hopefully promote an accurate understanding of the technology

This Second Task Manager's Report will provide key information for a related event, an interagency and governmental Round Table on Biosafety to be held by UNIDO in 1996 as a follow-up to the discussions of the Third Session of the Commission on Sustainable Development

One of the most noteworthy projects to evolve in recent years has been the FARM programme (Farmer-centred Agricultural Resource Management) with the support of UNDP and FAO This is a unique Asian initiative for sustainable agriculture to support the implementation of Agenda 21 in eight countries, with the purpose of eliminating the degradation of natural resources, increase production and eradicate poverty in rainfed areas Working linkages between demonstration sites have been set up, as well as national and regional networks, including training activities

As many readers will be aware, UNIDO is going through a major reform process, which we call UNIDO 2000, our programme for managed change and improvement This programme is approaching its final phase It is not always easy to perceive improvements in the midst of major change, resource reduction, shifting funding sources, modified processes and uncertain political support, but nonetheless some tangible results can be seen For instance, we are advancing in marketing and competitors' analysis so that for the first time we will be able to design sound strategies vis-à-vis our sister organizations and bilateral agencies We are also developing a select number of focused programmes showcasing our expertise and integrated services The use of electronic mail has registered dramatic growth, allowing us to make a quantum leap over tiers of communication, which combined with other tools, is speeding up our decision-making On a less visible, more conceptual and indeed more complex plane, work on priority-setting for the next two years is proceeding apace

Virginia Campbell
Scientific Editor

GENETIC ENGINEERING AND BIOTECHNOLOGY MONITOR

Vol. 2, Nos. 1 and 2, 1995
(Double issue)

UNITED NATIONS INDUSTRIAL DEVELOPMENT ORGANIZATION
Vienna, 1995

CONTENTS

CONTENTS (continued)

CONTENTS *(continued)*

CONTENTS *(continued)*

A. SPECIAL ARTICLE

FINANCING BIOTECHNOLOGY FOR SUSTAINABLE DEVELOPMENT

by Malee Suwana-adth and Virginia W. Campbell*

I. Introduction

The concept of sustainable development is based on the conviction that it should be possible to increase the basic standard of living of the world's population without unnecessarily depleting our finite natural resources and further degrading the environment in which we live. Technology can be the key to a more effective utilization of the world's limited resources that help at the same time to achieve sustainable development. The rapid global changes in technology are significant factors in setting the pattern and rate of industrial and subsequently the rate of economic growth; thus they significantly affect the development of society as a whole.

Agenda 21, a participatory plan of action jointly formulated and agreed upon by the world community at the Earth Summit in Brazil in June 1992, addresses many pressing problems of the world, including the concept of sustainable development, and focuses on addressing the challenges of the next century. Agenda 21 proposes a number of interrelated programmes and programme actions for implementation that are to be carried out by various key players according to the different capacities, situations and priorities of countries, taking into account all the principles contained in the Rio Declaration on Environment and Development.

Among the several proposed programmes of Agenda 21 are the transfer of environmentally sound technology (Chapter 34) and the environmentally sound management of biotechnology (Chapter 16), which reflects the necessity to properly manage technological and environmental changes resulting from new, rapidly advancing and sophisticated biotechnologies, in particular the changes brought about by the applications of genetic engineering.

Countries require appropriate infrastructures that permit them to acquire, absorb and develop technology, to manage it properly and systematically, and to build up local scientific and technological competence. The resultant ability of any country and of a developing country, in particular, to discern, choose and adapt an environmentally sound technology can serve as a measurement of sustainable self-reliance that will allow it to fully participate in world-wide efforts to achieve sustainable development.

Biotechnology, especially the modern version being developed on the basis of modern scientific research, is widely regarded to be a new technological tool because of its perceived potential impact on economies and on society. It is applied at increasing levels of sophistication in more and more sectors, improving the effectiveness of the way in which products and services are provided. However, theeffective transfer and development of biotechnology in an environmentally sound manner requires a variety of conditions, the most important of which are capital inputs that, in the case of many developing countries, are not readily available. The financing of biotechnology poses new challenges that must be addressed to enable developing countries to realize its potential benefits, to minimize any possibly adverse socio-economic effects, and for the donor community to properly plan and mobilize its funding in support of developing countries.

This paper attempts to provide a broad overview of the rationale and justification for new and additional sources of financial support, the financing currently available, the requirements for future funding, and a discussion of some future financial policy options that include an increase in active participation by developing countries in the development and applications of biotechnology focused towards sustainable development.

II. Assessment of biotechnology development: A general overview

It is now widely recognized that biotechnology can play an essential role in fostering the economic and social progress in developed and in developing countries as well, if properly managed. In the industrialized world, biotechnology research, development and applications are growing at a very rapid rate, leading to an expanding range of products and processes across several sectors, a range that began with pharmaceuticals and health care, and extended into agriculture and, more recently, into the environmental sector. At present, more than 2,000 clinical trials of biotechnology-related products are in progress, primarily in more advanced countries. Other new products and technologies include improved seeds, new vaccines, novel food ingredients, biotechnology-based techniques for the rapid detection and identification of toxic materials and several bioprocessing technologies. The tendency of most developing countries is to acquire biotechnologies aimed at improving agriculture, food and pharmaceutical production, and in converting low-cost or marginalized raw materials into high value-added products and marginalized lands into more productive areas.

In addition to traditional technologies, many kinds of biotechnology are appropriate and accessible to developing countries. Tissue culture and some new diagnostics that demand a relatively low level of resources and technological capacity are currently available for immediate transfer to developing countries. However, many biotechnologies appropriate to and required by developing countries are proprietary in nature. Therefore, biotechnological

* Technology Promotion Section, Technology Service, Investment and Technology Promotion Division, UNIDO, January 1995

solutions to problems in developing countries must be assessed and selected on the basis of priority and effectiveness. New and additional management skills are urgently needed. Along with the continued use of conventional technologies as appropriate, developing countries can seek to integrate more advanced biotechnologies into national development plans and programmes.

III. Economic impact of biotechnology

Economic analysts agree in the prediction that biotechnology will have significant impacts on health care, on agriculture and on environmental management. Biotechnology in its broad sense ranges from traditional biotechnology to the most advanced modern biotechnology. Commercial biotechnology consists of a growing range of interrelated techniques, procedures and processes that apply in practical ways to the health care, agricultural and industrial sectors. The effective commercialization of biotechnology links basic research to concrete products and services.

Because there has been a very rapid rate in biotechnological research as well as a wide technological gap between developed and developing countries, advanced genetic engineering techniques are more widely used in industrialized countries. Moreover, the current popular public understanding of biotechnology's impact tends to be confined mainly to the impact of modern biotechnology products and services. In this connection, data concerning the USA biotechnology industry show that world-wide annual sales of biotechnology-derived products have grown from zero in 1980 to US$ 5.9 billion in 1992; these sales are projected to reach US$ 50 billion by the year 2000 in the United States alone (Ernst and Young: *Biotechnology Series*). The 1994 report in the series indicates that the biotechnology industry as a whole continued to grow steadily. The total annual revenue of the industry increased in this period to US$ 10 billion. More than US$ 5.7 billion was spent on research and development by the private sector alone; more than US$ 4 billion was spent by the public sector.

As commercial biotechnology applications gradually increase in scope, from pharmaceutical and health care to agriculture and environment, their economic impact will undoubtedly increase throughout the world, especially in response to an increasingly globalized economy. Pressure to decrease dependency on chemical pesticides, for instance, is expected to drive the growth of biopesticide sales world-wide. As an indication of this growth, sales in the USA for this newly emerging biopesticide industry are expected to reach over US$ 150 million by 1997, as compared to US$ 6.8 billion in sales of conventional pesticides.

Several reports on the United States commercial biotechnology industry have predicted that the coming decade will see a stabilizing of biotechnology activities, especially in the private sector, on the basis of an increasing number of products entering the market and a global tendency for more flexible government regulation of biotechnology products.

A similar trend in Europe, Japan and Canada has been reported. A 1994 report commissioned by the Senior Advisory Group on Biotechnology analyses the macroeconomic potential of biotechnology, on the basis of the current data, it estimates a market value of US$ 50 billion. Revenues are expected to double by the year 2000. Of special interest is information concerning the number of jobs directly related to biotechnology, estimated to be 184,000. With respect to investment in biotechnology, US$ 1.2 billion a year was reported.

In contrast to industrialized countries, most developing countries have very little, if any, modern industrial biotechnology. Programmes in biotechnology deal mainly with traditional and with intermediate biotechnology, some exceptions being in a few of the more advanced Asian and Latin American developing countries. Nevertheless, an increasing number of developing countries have steadily invested, at a very low but significant level, in a broad version of biotechnology development. However, comparable figures on investment and sales are not readily available for developing countries. Nevertheless, there appears to be a positive trend in biotechnology development and in its impact. In the Republic of Korea, three major biotechnology-related companies in the pharmaceutical sector have a share of about 20 per cent of the total market. Moreover, the research investment in the area of biotechnology is growing at about 40 per cent. It has been estimated that the Republic of Korea will eventually produce about 2 per cent of the world's biotechnology-related pharmaceutical products. Major projections for the Taiwan Province of China are US$ 600 million in sales in the field of the more conventional tissue culture biotechnology and about US$ 60 million in sales of vaccines in 1996. An economic impact of similar intermediate biotechnologies in other biotechnology-advancing developing countries is also being noted.

With respect to investments in biotechnology, a decision was recently made by the Islamic Development Bank to support the establishment of a Biosaline Agriculture Centre. The Centre will rely on accessing biotechnologies from other centres of excellence in order to make use of marginal lands and sea water irrigation. A feasibility study on the project estimates a minimum benefit and cost ratio at close to 2 and up to 5.

In spite of scanty information about the immediate economic impact of biotechnology in developing countries, the trend for development in developed and advanced developing countries, in particular in Asia, indicates a similar positive trend. It is reasonable to say that the economic impact of biotechnology in a given country is in correlation with the biotechnology capacity and related investment.

IV. Economic and institutional environment of biotechnology development

A brief overview of the economic and organizational nature of biotechnology development may be useful as a basis for funding considerations. This is especially important because the international community faces increasing difficulty in mobilizing funds for development assistance to developing countries. Key prerequisites for successful biotechnology development include:

(a) *A strong scientific and multidisciplinary base.* Undeniably the rapid evolution of molecular scientific knowledge in the last two decades is and will be the critical foundation for successful commercial biotechnology development. In developing countries, the role of universities and research institutions in building the necessary infrastructure for generic research into new biotechnologies has been widely recognized.

(b) *Public and private sector cooperation.* This cooperation ranges from the university-industry cooperation

in various forms, including science parks, to public financing of the private sector's research and development, to joint ventures. It is a key and critical requirement.

(c) *Active private sector participation.* Bringing scientific knowledge and basic research to development and from there to the market requires high resource inputs, especially in terms of investment, supporting engineering services, and management. The active participation of the private sector is crucial for success.

(d) *Enabling policy environment.* In addition, it is widely recognized that a positive policy environment is a critical prerequisite for the successful commercial development of biotechnology. Because of the scientific, social and economic implications of biotechnology, it is vital that an enabling policy environment be created through effective formulation, integration and coordination. The creation of science and technology policy based on biotechnology alone and in isolation is not enough. Of particular importance is the issue related to biosafety regulation that is currently under discussion at various fora and levels, most actively within the Convention on Biological Diversity.

Lessons learned from successful industrialized countries and from developing countries that enjoy a more advanced level of biotechnology development indicate that economic and institutional structures play very important roles in fostering biotechnology industrial development.

V. Financing and financial sources for biotechnology in developing countries

Most, if not all, developing countries are well aware of the potential of biotechnology to foster economic growth. Many countries have identified biotechnology as a key area for development. However, the basic and applied research activities are conducted primarily in the universities and are fragmented. A demand for practical goal-oriented research and development is largely beyond the technical and financial resources available to the scientific sector. With the exception of more advanced developing countries, funds for meaningful biotechnology R and D come from external sources. Financing for biotechnology is rarely supplied by the private business sector.

There have been no direct or comprehensive international surveys of financial expenditures concerning biotechnology programmes that address the challenges outlined in Chapter 16 of Agenda 21. However, a 1993 survey concerning international initiatives in agricultural biotechnology was conducted by Intermediary Biotechnology Services. It indicated that bilateral and multilateral aid agencies, international organizations, private foundations, universities, commercial companies and national governments are all involved in the financing of international biotechnology initiatives for developing countries.

Since 1985, the contribution in grant funds for biotechnology programmes in developing countries was over US$ 260 million, in comparison with World Bank loans and credits for national agricultural research and development at a level of about US$ 150 million. Compared to biotechnology research and development in industrialized countries, the total financial efforts devoted to international biotechnology initiatives are far from adequate.

The IBS survey provides an interesting profile of financial sources, as follows:

Foundations	40.9 per cent
Bilateral donors	31.6 per cent
Multilateral donors	16.5 per cent
National institutions (matching funds)	4.6 per cent
Miscellaneous research grants	3.9 per cent
Private commercial	2.3 per cent

These data indicate: (a) a significant participation by non-profit organizations (foundations) in biotechnology development; (b) a similarly significant role of bilateral donors; and (c) weak participation by the private business sector in contributing financially to the development of biotechnology in developing countries.

The active contribution and participation of non-profit organizations in biotechnology development is of particular importance in view of the social implications of biotechnology and the concern on the part of developing countries about equity. In addition to the Rockefeller Foundation, that reportedly has contributed since 1985 more than US$ 50 million to the International Rice Biotechnology Programme alone, there are biotechnology support activities of other non-profit foundations. The Biofocus Foundation in Sweden and the M.S. Swaminathan Foundation in India are examples of social organizations created to help direct the benefits of biotechnology towards less privileged target groups in developing countries.

Bilateral donors and related bilateral cooperative programmes in biotechnology have been instrumental in strengthening the biotechnological capability and capacity of developing countries. Many developed countries such as Japan, France, the United States of America, Australia and the Netherlands have actively supported biotechnology programmes, including collaborative research and training. In addition to the financial contribution through the conventional Official Development Assistance Programme, other channelling of funds have also been created. Examples include the Japanese Society for the Promotion of Science (JSPS) which has been carrying out special bilateral exchange programmes in biotechnology with several South-East Asian countries, and Australia's Crawford Fund for International Agricultural Research.

Important lessons learned from these assistance cooperation programmes include the following:

(a) Long-term commitment is vital to achieving sustainable capacity building and to enable a country to reach a critical level in self-reliance for further biotechnological development. The Indo-Swiss project initiated in 1974 has led to pilot commercial production of biopesticides.

(b) A networking arrangement among institutions within the country and region is one of the most cost-effective means to maximize limited resources.

(c) Access to or provision of modern scientific equipment and key biomaterials for research are important components for successful and equitable strategies for collaborative research.

(d) Most importantly, the financial commitment of a developing recipient country Government is critical to successful collaboration. This commitment can include in-kind contributions.

The Asian Development Bank, in cooperation with the German Government, is funding the Asian Rice Biotechnology Network. The network is a new major initiative of the International Rice Research Institute (IRRI). The

programme aims to transfer advanced biotechnology in rice to national agricultural research systems (NARS). The fund will provide for joint NARS-IRRI biotechnology programme, a biotechnology training laboratory at IRRI and equipment and supplies for NARS laboratories, leading to biotechnology products to be shared with NARS in Asia. The newly launched UNDP FAO UNIDO Farmer-Centred Agricultural Resources Management project (FARM) has an important biotechnology component; it actively involves NGOs.

As part of the Children's Vaccine Initiative (CVI), UNDP, along with UNICEF, WHO, the World Bank and the Rockefeller Foundation, is establishing an autonomous institute in the Republic of Korea. The institute is to be committed to developing, testing and delivering affordable new and improved vaccines for the world's children. It is a partnership of public and private sector institutions, agencies and companies. It will assist vaccine producers in developing countries to improve vaccine production and quality control systems. The institute will attempt to enhance vaccine research on diseases of particular importance to low income countries. This new initiative addresses a very serious gap in protecting the health of children, especially those living in less developed countries.

The World Bank and the United Nations agencies that include UNDP, FAO, UNEP, UNIDO and WHO have been and continue to be a significant, although relatively small, source of funding and/or technical assistance for biotechnology development in the developing countries, due mainly to the continuity and coverage, technological and geographical. Examples include support to various international agricultural resource centres (IARCs) and, more recently, to the International Centre for Genetic Engineering and Biotechnology (ICGEB). Approximately 10 per cent of the total core budget of IARCs (US$ 23.6 million of the total US$ 236 million in 1993) is spent on biotechnology.

The ICGEB, established by UNIDO, spends approximately US$ 15 million annually to support its biotechnology programme for developing countries. Currently, ICGEB receives its funding mainly from its host countries, i.e. Italy and India, and voluntary contributions from its member States.

Within developing countries, the government's financial support for biotechnology is in general far below what is normally required to provide the adequate scientific and technical infrastructure necessary for meaningful biotechnology development. However, the trend is encouraging. This is indicated, for example, by the plan in Viet Nam to seek US$ 30 million to re-equip the country's biotechnology-related research and development facilities, and by the significant increase from less than US$ 1 million in 1985 to US$ 18 million in 1995 for biotechnology programmes in Thailand.

Bio-based micro-enterprises and small bioindustries in developing countries play a significant role in income generation for rural populations in providing markets for agricultural produce and providing employment. They benefit from improved biotechnology and related support technologies if given opportunities along with technical and management assistance. The small industries and enterprises involved in traditional biotechnologies is also a subject of bilateral assistance. The technical assistance project, Training and Technology Transfer Project on Application for Small Bioindustries Development, funded by the Carl Duisberg Gesellschaft-South East Asia Programme, is a classic illustration of support leading to benefits derived from biotechnology applied in a holistic and sustainable manner. The project uses a fund of less than DM 3 million to provide technical and management training, support services, an information database and a networking arrangement between South-South institutions and with South-North cooperation. The project is largely built upon existing resources and the potential for capacity building in the developing countries themselves. As a result, mechanisms are being developed that apply to a number of small bioindustries and can serve as models for other small bioindustries and in other developing countries. The project evolves around strengthening local technology institutions, R and D capability, and on technology transfer. It includes resource mobilization through networking arrangements. The biotechnology promotion model is based on the institutionalization of a vital quality control and training programme for bio-based small-scale industries that include biofertilizers, food fermentations and mushroom cultivation.

Currently, financing contributions from the private sector for commercial biotechnology development is still low, mainly due to the high business risk involved with modern biotechnology enterprises and partly due to unfavourable policy environments. Experience from developed countries indicates the importance of the private sector's participation. Limited but successful experiences in developing countries such as the Republic of Korea and Singapore could lead to an increase in the next decade in the private sector's financing in biotechnology, especially in Asia where the economy has been continuously growing at a significant rate.

In developing countries, the formation of partnerships between the private sector and government enabling institutions, notably science and technology parks, is an approach being increasingly adopted for promoting biotechnology development and commercialization. Venture capital funds, such as the Transtech Venture Fund in Singapore, are few but they can serve as successful models for fund mobilization from banking institutions and industrial subscribers, and also – and more importantly – in the fund's financing operation. The Transtech Venture Fund operates both within and outside the country, and includes investments in overseas technology companies that provide access to technologies and to management support.

In view of the relatively high risk associated with biotechnology product development and commercialization, more risk capital must be found. Cross-country strategic alliances have been particularly successful between USA and European companies and between USA and Japanese firms. Strategic alliances with and in developing countries, although not common in biotechnology development, have been known and are being promoted by a number of international programmes and venture capital firms. The role of such enabling mechanisms and institutions should be encouraged to foster biotechnology development.

VI. Assessment of financial resource requirements for biotechnology under Agenda 21

The implementation of the various programmes as set out in the Agenda 21 will undoubtedly require the provision of substantial new and additional financial resources to developing countries. These new and additional financial resources are needed to supplement financing from a country's own public and private sectors. In principle, industrialized countries reaffirm, through Agenda 21,

commitments to reach the United Nations target of 0.7 per cent of the Gross National Product (GNP) for official development assistance.

Chapter 16 of the Agenda 21: The Environmentally Sound Management of Biotechnology identifies five programme areas for action. These are:

A. Increasing the availability of food, feed and renewable raw materials;
B. Improving human health;
C. Enhancing protection of the environment;
D. Enhancing safety and developing international mechanisms for cooperation;
E. Establishing enabling mechanisms for the development and the environmentally sound application of biotechnology.

For each of the programme areas, objectives are established and a number of activities are proposed for implementation. Cost estimates are also given to indicate the financial resource requirements, during the period 1993-2000, necessary for achieving the agreed-upon objectives. These are briefly outlined in the table below.

The total annual requirement for financial resources from the international community for the period 1993-2000 is estimated to be US$ 197 million for the five programme areas. Needs are highest in the area of human health, at US$ 130 million, followed by US$ 50 million for agricultural improvement. However, the overall total financial cost estimate from all sources is US$ 20 billion per year during the same period. The cost estimates for biosafety (Programme Area D) and endogenous capacity building (Programme Area E) are much lower, at US$ 2 million and US$ 5 million respectively, and are based on support to be provided by the international community alone.

VII. Key implications for policy and plans

- In view of the different economic and institutional requirements for the environmentally sound management of biotechnology and the limited amount of funds expected to be mobilized from the international community, emphasis must be given to ensure "quality" financing of biotechnology programmes and initiatives. Moreover, it is essential to ensure a continuity in financial support in achieving clearly defined objectives and practical biotechnological solutions.
- Biotechnology is considered to be a cross-sectoral issue: biotechnological solutions can be found for many problems addressed in other programmes of Agenda 21. New and additional resources facilities within the framework of Agenda 21 should be structured with sufficient flexibility that expands their scope and coverage, where appropriate and feasible, and accommodates the integration of the relevant biotechnological components.
- Successful lessons from the still limited investments by regional banks in biotechnology projects indicate a large potential for expanding the role of financial institutions at various levels in promoting biotechnology programmes. Regional banks should be encouraged to participate more actively, directly or indirectly, in the development and, especially, in the commercialization of biotechnology in developing countries.

VIII. Financing arrangements for consideration

1. New Financial Resources and Mechanisms

1.1. Establishment of an International Biosafety Trust Fund

Of urgency is a rapid solution to the controversy surrounding the biosafety issue. Concerted efforts must be applied ensuring that biosafety will not become a constraint against the development, transfer and applications of biotechnology in the global drive to achieve sustainable development.

An International Biosafety Trust Fund would provide funds to strengthen capacity building in biosafety regulation in developing countries and to facilitate the effective

Programme Area	Objectives	Annual Cost Estimate (US$)
A. Agriculture	Increase productivity and nutritional and storage quality Eliminate overdependence on agrochemicals Evaluate potential of marginal lands	5 billion (50 million from international community)
B. Human Health	Combat major communicable diseases Create enhanced R&D capabilities Promote good health	14 billion (130 million from international community)
C. Environmental protection	To adopt environment-friendly production processes To promote bioremediation	1 billion (10 million from international community)
D. Biosafety and international cooperation	To ensure safety in biotechnology through international agreement on risk assessment and management	2 million from international community
E. Endogenous capacity building	To promote biotechnology development and application To identify and develop effective strategies To establish mechanisms for risk assessment	5 million from international community

participation of developing countries in a participatory process on biosafety. The objective of this process would be to bring into agreement a set of internationally agreed-upon principles facilitating the development and transfer of biotechnology that benefits the world community.

In this connection, the International Bioindustry Forum has called for the establishment of a Task Force to examine common principles and practical approaches to biosafety issues. It has further suggested that UNIDO, as Task Manager and lead UN agency for biotechnology and Chapter 16 of Agenda 21, be asked to bring such a Task Force together and to provide its Secretariat. The suggestion is particularly appropriate in view of the fact that UNIDO is cooperating closely with the Interim Secretariat of the Convention on Biological Diversity on the issue of biosafety in biotechnology in matters related to scientific and technological issues.

The proposed International Biosafety Trust Fund could be executed by UNIDO, on behalf of the UNIDO UNEP FAO WHO Informal Working Group on Biosafety, in cooperation with other UN agencies that have programmes in biosafety, including the Interim Secretariat of the Convention on Biological Diversity.

The biotechnology business community should be encouraged to contribute to the Fund.

1.2. Establishment of an International Venture Capital Fund for Biotechnology

The rapid rate of biotechnology development, the increasingly widening economic and technological gap between developed and developing countries, and the major role of the private sector in commercial biotechnology development are causes for concern about equity in biotechnology transfer agreements among countries. Developing countries are genuinely concerned that developed countries will be able to use new proprietary biological tools in producing high-value products that displace materials currently produced by developing countries, negatively affecting the already weak position of most developing countries in the highly competitive and increasingly globalized markets. At the same time, developing countries are concerned about their weak technological and financial capacity to access the new, effective biotechnologies developed by the private sector in developed countries that provide new opportunities for improvement and diversification in agricultural and industrial production.

Lessons learned from various biotechnology venture funds indicate that these are the most effective means to rapidly transfer commercial biotechnologies. Venture capital funds can be used to facilitate transfer of biotechnologies specifically serving common needs of developing countries and at the same time facilitating the process of capacity building in biotechnological development. Examples include biotechnologies for new vaccine development for major communicable diseases, biotechnologies for marginal lands and biotechnologies for pollution abatement (bioremediation).

The International Venture Capital Fund could be initiated by the World Bank International Monetary Fund and implemented by the International Finance Corporation. Part of the Fund could be used to conduct feasibility studies on potential commercial biotechnology projects in order to promote joint ventures and attract additional funding sources.

In parallel to the operation of the Venture Capital Fund for Biotechnology, it would be worthwhile to consider the establishment of a programme for an Expert Volunteer Corps in Biotechnology, based on the model of the successful programme of the (Business) Executive Volunteer Corps. Under such a programme, retired biotechnology experts' service would be made available to developing countries to augment the limited biotechnology management expertise available within the developing countries.

1.3. Increase in Official Development Assistance (ODA) for Biotechnology

Within the framework of the general commitment by Governments to increase the ODA to the level of 0.7 per cent of GNP by the year 2000, Governments supporting biotechnology development in developing countries should be encouraged to expand and or extend their financial assistance to more developing countries. Similarly, Governments that have no ODA programme in biotechnology are encouraged to consider including biotechnology for future ODA financial assistance. Contributing to the newly proposed International Biosafety Trust Fund is a response to the commitment to increase ODA funding. Such contributions to the International Biosafety Trust Fund would create a significant window for broader and coordinated participation in implementing the action plan of Chapter 16 of Agenda 21: the Environmentally Sound Management of Biotechnology.

2. New Improved Financing Strategies

2.1. Financial Support from the International Community for Biotechnology-Related Local Initiatives in Developing Countries

In view of the increase in biotechnology-related initiatives being undertaken by developing countries, additional financial support from the international community should be encouraged to facilitate the integration of strategic biotechnologies that enhance biotechnological solutions to local problems, especially those having potential benefits for other developing countries. Examples of appropriate problem-oriented biotechnology-related initiatives include a Petroleum Microbiology (Bioremediation) Project in Viet Nam, a Sustainable Development Training Centre Project in China, a Traditional Medicine for AIDS Project in Thailand, and a Biosaline Agricultural Centre in the United Arab Emirates. Financial support from the international community can be used to effectively mobilize international experts and access appropriate biotechnologies that augment national efforts. Such financial support strategies allow maximum cost effectiveness of the limited resources provided by the international community and also provide opportunities for a more active participation of developing countries in implementing the Agenda 21 work plan. The sharing of developing countries' financial resources and of their valuable indigenous knowledge are positive contributions that can be highlighted.

2.2. Third-Country Financing in Cooperation with New Small Donor Countries

Despite the declining official development assistance from traditional donors for developing countries, there is an encouraging sign of emergence and increasing participation of small new donors in the international community. These donors are advancing developing nations seeking gradually

to increase their role in the international community. Many of these countries give high priority to biotechnology development and seek to further advance their biotechnological capacity. On the other hand, they are in a position to provide training and resources that promote the "intermediate" biotechnologies often required by less developing countries.

Third-country financing through tripartite cooperation should be actively encouraged and promoted in order to consolidate and maximize limited resources and to actively pursue commonly shared objectives and goals. These cooperative activities will help to ensure that efforts to implement Agenda 21 are globally integrated among countries.

IX. Conclusion

Because biotechnology is a key and rapidly evolving technology and can be widely applied in efforts to achieve globally sustainable development, innovative mechanisms should be adopted to ensure that developing countries participate as full partners in global and integrated efforts to implement the various programmes set out in Agenda 21. To meet this challenge, three new financial resource mechanisms are suggested for consideration by the international community. These include:

- The establishment of an International Biosafety Trust Fund
- The establishment of an International Venture Capital Fund for Biotechnology
- An increase in Official Development Assistance for biotechnology.

In addition, new and improved financing strategies suggested for consideration include:

- Financial support from the international community for biotechnology-related local initiatives in developing countries
- Third-country financing in cooperation with new small donor countries.

B. NEWS AND EVENTS

UNIDO News

ICGEB moves forward

The resumed first session of the Board of Governors of the International Centre for Genetic Engineering and Biotechnology (ICGEB) took place at Trieste, Italy from 3-5 October 1994 where several issues outstanding from its first meeting held at Vienna during April 1994 were deliberated and important decisions taken.

At the time of the meeting of the Board the new premises of the Centre at Trieste comprising 7,000 square metres was inaugurated in a meeting addressed by representatives of the Italian Government and local authorities and the President of the Research Area of Trieste (Professor Romeo) which has provided the facilities.

Addressing the distinguished gathering present at the inauguration, the Director-General of UNIDO, Mr. Mauricio de Maria y Campos, commended the Governments of Italy and India and the Research Area of Trieste in building the infrastructure and facilities for the ICGEB at New Delhi and Trieste respectively.

Mr. de Maria y Campos observed that the generous support of the Government of Italy, together with the visionary role played by Professor Abdus Salam resulted in Trieste becoming a leading international city for science and technology and a meeting ground for scientists of North and South. At the opening of the meeting of the Board of Governors, Mr. de Maria y Campos underlined the importance of providing assured support on a long-term basis by the Member Governments to the ICGEB to enable the Centre to maintain and accelerate the excellent progress already made in the short span of its existence. Mr. de Maria y Campos observed that competitive research in the field of modern biotechnology is expensive and sufficient resources should be made available to the Centre to enable it to pursue its critical mass of activities essential for achieving its objectives.

Mr. de Maria y Campos further noted that it is timely to initiate a long-term collaborative programme between UNIDO and ICGEB in areas including biosafety, commercialization and conservation of biodiversity at the molecular level and its sustainable utilization.

Opening this meeting of the Board of Governors, Mr. Adolfo R. Taylhardat, President of the Board, urged those countries who have not yet joined the Centre to become members, particularly in view of the fine progress made by the Centre in research and product development and in providing training to the developing country scientists.

Among the decisions taken by the Board at the meeting are approval of membership of the Republic of Slovenia, approval of staff regulations and adoption of rules of procedure for the Board, and election of the Council of Scientific Advisers (CSA). The CSA consists of: Professor L. L. Cavalli-Sforza, Professor A. Chakrabarty, Professor G. Georgiev, Professor X. Gu, Professor A. Kornberg, Professor J. Lederberg, Professor N. Okafor, Professor G. Padmanabhan, Professor H. Torres, Professor P. Valenzuela, Professor R. Wu, which includes two nobel laureates.

The meeting of the Board of Governors was followed by a two-day (6-7 October 1994) scientific conference on "Emerging biotechnologies and industrialized opportunities", which was attended by over 40 delegates representing academia, industry and Governments.

UN and other organizations' news

The International Plant Genetic Resources Institute

Following the ratification of its Headquarters Agreement and the publication of the Agreement in the *Gazzetta Ufficiale* of the Republic of Italy, the International Plant Genetic Resources Institute (IPGRI) has started to function as an independent institution of the Consultative Group on International Agricultural Research and as the successor to the International Board for Plant Genetic Resources (IBPGR). To ensure an orderly transition, IBPGR will continue to operate alongside IPGRI until April/May 1994.

While IPGRI will operate as an independent international institution, its long association with the Food and Agriculture Organization of the United Nations on programme matters will be maintained under a Memorandum of Understanding on Programme Cooperation, signed on 21 September 1990.

IPGRI was established as a legal entity under international law more than two years ago under the terms of an agreement signed by the Governments of China, Denmark, Italy, Kenya and Switzerland. The agreement has since been signed by an additional 20 countries: Belgium, Bolivia, Cameroon, Chile, Cyprus, Egypt, Greece, Hungary, India, Iran, Jordan, Pakistan, Poland, Portugal, Romania, Russia, Senegal, Syria, Uganda and Turkey.

IPGRI has four major objectives. First, it will assist countries, particularly in the developing world, to assess and meet their needs for the conservation of plant genetic resources and to strengthen links to users of those resources. Second, it will build international collaboration in the conservation and use of plant genetic resources, mainly through the support of networks on both a crop and a geographical basis. Third, it will work to develop and promote improved strategies and technologies for the conservation of plant genetic resources. Finally, the Institute will provide an information service to inform the world's genetic resources community of both practical and scientific developments in the field. (Source: *News Release*, 1994)

Forestry information network

The Forestry Research Network Information System (FORNIS) is accumulating information on institutions with projects and capabilities of potential interest to the Center for International Forestry Research (CIFOR). The FORNIS team is collaborating with the European Tropical Forest Research Network in developing and testing a forestry "front end" which may be suitable as a global standard for summaries of forestry research projects for AGREP, the principal database on agricultural research projects in the European Community. For additional information contact: Dr. Jeffrey Sayer, Director General, CIFOR,

P.O. Box 6596, JKPWB, Jakarta 10065, Indonesia. Tel.: 62-251-31-9423, Fax: 62-251-32-6433. (Source: *Diversity*, Vol. 10, No. 2, 1994)

PAHO

The Pan American Health Organization (PAHO), a regional office of the World Health Organization (WHO), has initiated a biodiversity initiative to explore connections between biotechnology and biodiversity and to strengthen scientific research in member countries. "The identification and evaluation of biodiversity in [member States] can be used as a method of fostering scientific and technological development, particularly in biotechnology, cellular and molecular biology, biochemistry, phytochemistry, phytopharmacology, mycology, pharmacognosy, pharmacology and ethnobotany, with resulting benefits in resolving both old and new health problems through the development of new pharmaceuticals", said PAHO Consultant Dr. Julie M. Feinsilver. Part of PAHO's mission is technical cooperation with member countries to create clear analyses of biodiversity conservation, sustainable use, and health research and their interrelationships. For more information contact: Dr. Julie N. Feinsilver, PAHO, 525 23rd Street, NW, Washington, DC 20037-2895, USA. Tel.: 1-202-861-4303 430. Fax: 1-202-861-8472. (Source: *Diversity*, Vol. 10, No. 2, 1994)

OECD looks at the "green face" of biotechnology

At a time when some biotechnologists are promising considerable environmental benefits from the use of modern biotechnology, the views of the Organization for Economic Cooperation and Development (OECD) are worth considering. In the August September 1994 edition of the *OECD Observer*, Saloman Wald of the OECD Biotechnology Unit discusses the "green face" of biotechnology. In the wake of health care and agriculture, he suggests, biotechnology is now turning to a third application - careof the environment. "Many commentators believe that biotechnology is on the way to becoming one of the main 'generic' technologies of the next century", he says, "modifying economic and social conditions in major ways, as information technology has been doing for the last few decades". The successful diffusion of any new technology, he suggests, depends on the satisfaction of five criteria:

- A new range of technically improved products and processes;
- Cost reduction for many of them;
- Social and political acceptability;
- Environmental acceptability;
- Pervasive effects throughout the economic system.

Attention is focused on environmental biotechnology. Information technology satisfies all five criteria. Environmental biotechnology appears to satisfy at least the first criterion, with a growing range of products and services on offer over the last five years. For the second criterion, one of the most critical assets of biotechnology compared to other environmental technologies "could be its clear, sometimes massive cost advantage in every sector of environmental remediation: air, water and soil. Data collected in the Netherlands in 1993 [indicate] that biotechnology is the least expensive method in all three". Biological clean-up methods are much more "sustainable" than competing methods. Wald concludes, which include extraction, thermal treatment and incineration, steam-stripping, chemical scrubbing (air) and oxidation (water), ultra-filtration and so on. Major advantages are seen under both the third and fourth criteria. In terms of the fifth criterion, pervasiveness, Wald suggests that the potential market for environmental biotechnology could reach "$75 billion or more" by the year 2000. Details: OECD Publications Service, Chateau de la Muette, 2 rue Andre-Pascal, F 75775 PARIS CEDEX 16, France or on +33 1 45 2' 82 00. (Source: *Biotechnology Bulletin*, August 1994)

Study released by UNDP charges compensation to developing countries is inadequate

Developing countries would be owed as much as $5.4 billion if they were compensated only 2 per cent in royalties for global seed industry sales of $15 billion and 20 per cent for pharmaceutical products derived from indigenous plants and knowledge, according to a recent report commissioned by the United Nations Development Programme (UNDP).

The study, *Conserving Indigenous Knowledge: Integrating Two Systems of Innovation*, conducted by the Rural Advancement Foundation International (RAFI) for UNDP, focuses on forming linkages between indus-trialization and environmental protection as an integral part of the merging concept of sustainable human development, mandated by Agenda 21 of the 1992 United Nations Conference on Environment and Development (UNCED). Agenda 21 calls for "recognizing and strengthening the role of indigenous people and their communities ... with a view to promoting environmentally sound and sustainable development."

The report recommends specific steps towards the "establishment ... of arrangements to strengthen active participation of indigenous people and their communities in the national formulation of policies, laws, and programmes relating to resource management and other development processes, that may affect them." The new "intellectual integrity framework" suggested by the report includes:

- Consultation with indigenous communities to learn their preferences;
- Identification of biological "inventions", including their origin, names of the discoverers, when they are deposited in genebanks, and when patent application is made;
- Protection of germplasm in genebanks by refusing patents to applicants other than those by the developing countries;
- Investigation of complaints from indigenous communities and their Governments;
- Dispute resolution; and
- A fee structure to cover expenses by source countries.

The report claims that an estimated 80 per cent of the world's population depends on indigenous knowledge to meet their food and medicinal needs. However, the recipients of these benefits, the report further charges, do not provide adequate compensation, involvement in decision-making, or recognition of this indigenous knowledge.

The widely acknowledged use of raw materials and indigenous knowledge by industry is exacerbated by the growing use of patents which grant exclusive protection to

Northern corporations and researchers for material or knowledge which originated in the South, according to a RAFI statement. One trend noted in the current management of biodiversity is that developed country corporations are increasingly using medicinal plants in the development of their products without paying royalties to the source country.

The report includes a wide-ranging list of over 100 instances of the North benefiting from the South's resources and several dozen examples of "potentially patentable" products or processes developed by indigenous communities themselves. For example, RAFI says that "farmer-derived Ethiopian barley is worth $150 million in the United States each year. The annual value of the American crop is more than $670 million."

In calling for changes in governing the ownership of biological materials and local knowledge about them, RAFI cites a particularly inequitable example: "Industrialized countries patent material wholly or partially derived from farmers' varieties. [Then] as private companies move into the developing countries' seed markets, indigenous farmers are finding themselves paying for the end product of their own genius."

Indigenous knowledge has not been simple accumulation, the report contends, but rather the result of a "dynamic cooperative innovation system which continues to work ... and offer hope for planetary survival. To destroy or ignore this system would ... deprive the world of one of its main sources of innovation and diversity."

"The real challenge for science and technology in the decades ahead is to find mechanisms to allow these two separate, but highly complementary, systems to work together", the report states, while "the challenge for the cooperative system is to recognize the potential merits of the other side". To this end, the report warns that recent trends in intellectual property rights suggest that "the 'rules of the game' have shifted in the last few years and the scope of the patent system is becoming limitless".

Issues and trends in the management and use of biodiversity and economic and social contributions of indigenous rural communities in nurturing biological products and processes are also reviewed.

Based on this study, UNDP plans to consult with indigenous peoples' organizations in Latin and Central America, Asia and the Pacific, and possibly Africa to learn their views of the most appropriate strategies for preserving traditional knowledge and their innovations and contributions.

"As a first step, indigenous communities should meet to discuss their policy choices at least at the regional level", the report suggests, and "two- and three-day workshops in each region of the world could help establish a realistic understanding of the current situation and the real opportunities".

The report urges multilateral organizations, Governments, non-governmental organizations, and other involved to

- Consider further study of inventors' certificates and material transfer agreements;
- Encourage establishment of the appropriate national legislation and an international convention;
- Evaluate the possibility of a trust fund for remuneration of indigenous knowledge;
- Establish model agreements for Governments, corporations, and indigenous communities;
- Discuss the role of indigenous communities regarding *in situ* conservation;
- Provide key information to indigenous people; and
- Convene a meeting with indigenous organizations and information experts to discuss needs and means for safeguarding the development and exchange of indigenous knowledge.

For further information on the UNDP report, contact: United Nations Development Programme, Bureau for Policy and Programme Support, One United Nations Plaza, New York, NY 10017, USA. Tel.: 1-212-906-5312. (Source: *Diversity*, Vol. 10, No. 4, 1994)

International genebanks come under United Nations FAO control

An agreement signed at the 1994 annual meeting of the Consultative Group on International Agricultural Research (CGIAR) in Washington DC, places some of the world's most important collections of plant genetic resources under the authority of the United Nations Food and Agriculture Organization. Signed in October 1994, the contract covers genebanks housed in CGIAR-sponsored research centres in Africa, Asia and Latin America. The agreement allows the research centres to become legal trustees of the collections they house and could pave the way for other international and national collections of plant samples to be placed under a similar arrangement.

The agreement moved forward after all 112 Governments attending the Intergovernmental Committee on the Convention on Biological Diversity in June 1994 in Nairobi called for the establishment of intergovernmental control over the genetic resources held in the genebanks. Countries that donate samples feared that they might not benefit from any breeding improvements to their samples. The new agreement legally brings the genebanks under the Biodiversity Convention and puts donors of seed stock in a position where they could benefit in the future.

Together the genebanks covered by the agreement hold 500,000 different samples of the world's most important staple foods, such as rice, wheat, maize and other cereals, which are vital for breeding crops of the future. This accounts for approximately 40 per cent of all unique samples held world-wide, including 80,000 rice samples at the International Rice Research Institute in the Philippines and 35,000 wheat samples at the International Maize and Wheat Improvement Center in Mexico. For further information contact: RAFI, 71 Bank Street, Suite 504, Ottawa, Ontario K1P 5N2, Canada. Tel.: (613) 567-6889, Fax: (613) 567-6884, E-mail: rafican@web.apc.org (Source: *Global Pesticide Campaigner*, Vol. 4, No. 4, 1994)

Key provisions of the FAO-CGIAR Agreement

The CGIAR Centres will

- Place the international germplasm collections under the auspices of FAO as part of the International Network of *Ex Situ* Germplasm Collections;
- Not claim ownership or seek intellectual property rights over designated germplasm accessions but will

hold them in trust for the benefit of the international community;
- Not seek any intellectual property rights over designated germplasm or related information;
- Manage and administer the designated germplasm according to international standards;
- Provide FAO with access to their premises to monitor adherence to these standards;
- Recognize the international authority of the FAO Commission on Plant Genetic Resources in setting policies for the International Network;
- Make the designated germplasm and related information available without restriction to users; and
- Ensure that the recipients of the designated germplasm are bound to the same conditions as the Centres regarding access and intellectual property protection.

FAO will:

- Operate the International Network of *Ex Situ* Germplasm Collections within the framework of the International Undertaking on Plant Genetic Resources;
- Recommend action required to enable the Centres to adhere to the agreed standards;
- Assist Centres in evacuating and or transferring collections in case of emergencies;
- Provide the international forum to set policy for the International Network and to provide policy advice to the Centres;
- Assist Centres through the provision of expertise, if so requested; and
- Assist Centres in making germplasm available to users.

(Source: *Diversity*, Vol. 10, No. 4, 1994)

Sprouting up: the CSD and biodiversity

The United Nations Commission on Sustainable Development (CSD) reviewed during its third session in April 1995 a wide range of matters dealing with land, desertification, sustainable agriculture, biodiversity and biotechnology. The CSD was set up to follow up on the implementation of Agenda 21 – the non-binding document signed by all nations during the UNCED Earth Summit in 1992 – at national and international levels.

The CSD has requested the Convention on Biological Diversity to input into its coming session. At the second session of the Intergovernmental Committee for the Convention on Biological Diversity (CBD), held in June 1994 in Nairobi, it was agreed that the First Conference of the Parties to the Convention (COP-1) – which met in Nassau between 28 November and 9 December 1994 – should consider the CSD request. The CBD Interim Secretariat prepared a working paper on the subject for COP-1, based on country submissions and the report of an expert workshop, held in Madrid, 11-14 October 1994.

Although the request from the CSD came basically because it will be dealing with Agenda 21's chapter 15 on biodiversity, the Interim Secretariat made it clear in its paper that the conservation of biological diversity is a cross-cutting issue and that therefore the provisions and mechanisms of the Convention are relevant to many of the issues included in Agenda 21, not just one specific chapter. Actually, chapter 15 was modelled after the CBD. One of the main recommendations to the CSD would be that it consider the Convention as the legally-binding international mechanism to implement its recommendations dealing with biodiversity. Specific areas in which the CSD and the CBD should link their agendas are, among others: forests management, genetic resources conservation and use, promotion of sustainable agriculture and rural development, the FAO process in adjusting the Plant Genetic Resources Global System to the Convention, indigenous peoples' and farmers' rights, sustainable and safe use of biotechnology, and furthering a protocol on biosafety. This would entail that both international bodies develop effective mechanisms for cooperation.

The CSD's Ad Hoc Inter-Sessional Working Group on sectoral issues met in New York from 27 February to 3 March 1995. The third session met in April 1995, also in New York.

Those interested in following CSD developments can receive the *CSD Update*, a bi-monthly newsletter from the Secretariat. Contact: Zehra Aydin, CSD Update Coordinator, Division for Sustainable Development, One United Nations Plaza, Room 1044, New York, NY 10017, USA. Tel.: (1-212) 963 88 11, Fax (1-212) 963 12 67, E-mail: dpesd@igc.apc.org. (Source: *Nature*, December 1994)

Darwin initiative projects help conserve crop biodiversity around the globe

At the end of the 1992 landmark United Nations Conference on Environment and Development (UNCED) in Rio de Janeiro, Prime Minister John Major of the United Kingdom announced a special Darwin Initiative through which funds would be earmarked for follow-up to Agenda 21. By supporting numerous activities to aid improving preservation and conservation around the world, the Darwin Initiative is responding to Principle 9 of the Rio Declaration on Environment and Development which declared:

> "States should cooperate to strengthen endogenous capacity-building for sustainable development by improving scientific understanding through exchanges of scientific and technological knowledge, and by enhancing the development, adaptation, diffusion, and transfer of technologies, including new and innovative technologies."

The three Darwin Initiative projects described below focus specifically on work involving crop genetic resources.

Building institutions to conserve Latin American Indigenous Crops

The World Conservation Monitoring Centre (WCMC) is undertaking a study of the *in situ* plant genetic resources of Central America, focusing particularly on wild progenitors and relatives of some priority indigenous crops. The project will establish a Darwin Initiative broad-based consortium of developing-country and developed-country agencies that strongly emphasize building the capacity of the institutions within the region.

The goal of the four phase Darwin Initiative is to test and refine a methodology for the assessment, collation of data and [illegible] national and regional priorities. Early in 1994, the first phase, a feasibility assessment, was completed and was followed by a planning workshop at WCMC headquarters. The final phase, which will initiate action, was discussed at a workshop held in October 1994 in Costa Rica.

Discussions in Costa Rica focused on extent and coverage of information on plant genetic resources *in situ*; availability of experts within the region on the taxa identified as priority by the Mesoamerican Network for Plant Genetic Resources (REMERFI); assessment as to the representation of these taxa in *ex situ* collections; extent to which data show the taxa are present in protected areas, the details of the information, and the needs for further data gathering on populations; need to integrate data sets with Geographic Information Service (GIS); need for data transfer formats applicable to *in situ* conservation; and identification of a number of high priority taxa so that action plans can be developed.

Participants noted that while priority taxa are inventoried in protected areas, there is inadequate information on the populations. Attendees agreed that as far as possible there should be a focus on perpetuating much of the genetic resources in protected areas. Though they concluded that only in a few special cases would there be the need to establish specific reserves, they agreed there will clearly be a need to set up some target genetic reserves within the protected areas, and in all cases management protocols are likely to be needed.

Participants agreed that there is great merit in standardizing data transfer formats. Whereas genebanks have tended to deal with the needs to transfer specific data related to accessions of cultivars, wild plants have to be thoroughly documented. Botanic Gardens Conservation International (BGCI) has developed an international standard transfer format which seems to be a useful tool to merge data on both collections in botanic gardens and those in field genebanks of genetic resources institutes. Use of such a technique would go far in efforts to bridge interdisciplinary interests.

The meeting limited the discussions to wild species which are closely related to important agricultural and horticultural crops. Documentation for the meeting had provided an assessment of "what we know" about the genepools of those crops accorded priority by REMERFI. These priorities were analysed and discussed in detail on the basis of availability of institutes and expertise in the region, degree of threat to segments of the wild genepools, the need for focus on certain environments, and economic importance.

As a result, the target taxa for cooperative action were identified as follows:

- **High priority**: Sapotaceous fruits, avocado (*Persea*), yams (*Dioscorea*), cucurbitaceae, and cassava (*Manihot*).
- **Priority**: *Xanthosoma*, *Hylocereus*, *Pachyrhizus*, *Inga*, *Annona*, *Physalis*, *Jacobsia* and *Capsicum*.

WCMC will now develop plans for future action in consultation with donors. For further information contact: Ms. Harriet Gillett, World Conservation Monitoring Centre, 219 Huntingdon Road, Cambridge, CB30DL, UK. Fax: 44-0223-277136, E-mail: plants@wcmc.org.uk

Studying the genetic diversity of wild rice in India

Another Darwin Initiative Project shows promise of shedding light on several aspects of the genetic basis of salt tolerance of a perennial wild rice, *Porteresia coarctata* (*Oryza coarctata*). The result of this research, undertaken by the M.S. Swaminathan Research Foundation in Madras, India, is expected to help rice breeders locate sources of salt-tolerant genes and genes for submergence tolerance.

The focus of this project, coordinated by Mr. P. Balakrishna, is on the collection, maintenance, and genetic characterization of *Porteresia coarctata*, a tetraploid species of tribe Oryzeae. *P. coarctata* is important because it is the only known salt-tolerant relative of rice that has inherited tolerance to coastal salinity. Occurring along the halophytic belt of brackish waters and deltas as an associate species of mangroves in South-East Asia, this wild rice grows vegetatively and produces seeds that are very highly recalcitrant. It also survives longer times of submergence in sea water.

After several previous research initiatives had not yielded considerable results either on the micropropagation aspects or on protoplast fusion experiments aimed at transferring this salt-tolerant character into other rice varieties, researchers decided that the basic problems were due to the lack of genetic diversity in the material. During subsequent collection visits to the coasts of Goa, Maharashtra and Orissa the presence of diversity in *Porteresia coarctata* was observed even at the morphological level.

These findings prompted an investigation at the M.S. Swaminathan Research Foundation, led by Balakrishna, to collect and document the variations present in this species. Initial results on the morphological and physiological characteristics showed the presence of diversity. Studies were then carried out on the genetic diversity using the PCR-based marker system, RAPD (Random Amplified Polymorphic DNA).

Preliminary observations revealed the presence of vast genetic diversity and the possibility that the nature of crossability and alteration in flowering and seed-setting characters may be genotype specific. Based on these results, the Darwin Initiative has funded a long-term research project at the Swaminathan Foundation on the collection, maintenance, and characterization of *P. coarctata* by using morphological, biochemical and genetic markers. The work will be carried out in collaboration with the Scottish Agricultural College in the United Kingdom.

For additional information, contact: Mr. P. Balakrishna, Coordinator for India, Darwin Initiative Project, M.S. Swaminathan Research Foundation, 3rd Cross St., Taramani Institutional Area, Madras 600113, India. Tel.: 91-44-235-1229; Fax: 91-44-235-1319.

Birmingham University trains Darwin Fellows in Africa

The first of a series of three specialist courses sponsored by the Darwin Initiative began last September at the University of Birmingham. The University has gained world-wide recognition for its 25 years of specialized training for developing-countries scientists in the theory and practise of plant genetic resources conservation. The International Plant Genetic Resources Institute and the Southern Africa Development Community are also participating in the project entitled "Plant conservation and sustained utilization training in Southern Africa".

The Darwin Fellows attending the three courses will receive training in plant exploration and conservation strategies. According to the training coordinator, Dr. Nigel Maxted, the course will be divided into 40 units which will cover relevant aspects of ecogeography, *ex situ*

in situ, and *in vitro* conservation; botanical inventories and plant identification; post-collection seed conservation; seed handling and storage techniques; and conservation data management and analysis. Maxted says that the project will provide students from the southern African countries, which are rich in biodiversity, but poor in financial and technical resources, with the skill and experience necessary for them to order, collect, conserve and utilize their native botanical diversity.

For additional information, contact: Dr. N. Maxted, Training Course Coordinator, School of Biological Sciences, University of Birmingham, Edgbaston, Birmingham B15 2TT, UK. Tel.: 44-21-414-5924, Fax: 44-21-414-5925, E-mail: maxted*a*bham.ac.uk. (Source: *Diversity*, Vol. 10, No. 4, 1994)

Japanese, Swiss, Germans collaborate with CIP to save endangered biodiversity of Andean roots and tubers

"The genetic biodiversity that exists in edible Andean root and tuber germplasm, and that has been maintained by native highland communities over the centuries, is now in danger of being lost", warns Carlos Arbizu, a Peruvian agronomist who has 20 years of experience working with the oddly-shaped, colourful vegetables.

The Biodiversity of Andean Roots and Tubers (ART) is a collaborative programme addressing this situation. Funded by the Swiss Agency for Technical Cooperation, the International Potato Centre (CIP), the German Agency for International Cooperation, and the Japanese International Centre for Agricultural Research, the programme forms an important part of CIP's Andean Natural Resources Initiative, undertaken in 1992, and of the centre's Genetic Resources Program.

Arbizu describes the critical nature of the situation in Peru, for instance, where population growth, lack of arable land, over-grazing, soil erosion, environmental contamination (specifically by mining operations), and replacement of native varieties resulting from the official promotion of modern, high-input agriculture "are destroying the existing Andean ecosystems of which the roots and tubers formed a part". Introduced foods are changing dietary habits and poor soil management is causing soil erosion. Deforestation is also a serious problem.

More than 25 species of edible roots and tubers were being cultivated on the American continent at the time of its discovery by Europeans in the 15th century. Seventeen of these were domesticated in the Andes. Today, Peru is in the forefront of the Andean countries in terms of genetic diversity, production, and area given to cultivation of Andean roots and tubers, followed by Bolivia and Ecuador.

After the potato, three tubers (oca, ulloco and mashua) and six roots (arracacha, yacon, achira, maca, mauka and ahipa) are considered most important in terms of area cultivated. Ulluco, oca, mashua and arracacha are the most popular.

This highland agriculture has developed at elevations between 1,500 and 4,200 metres, mostly on sloping, often inhospitable land. In general, roots and tubers are separated altitudinally, with tubers becoming more important at the higher elevations and colder temperatures. Roots, except maca, are generally adapted to the lower elevations and warmer temperatures.

Until recently, the genetic conservation of these species has been due exclusively to selection and preservation by the smallholders since no Government or private entity has been interested in them. They are, therefore, adapted to the ecologies where they are grown, mostly in association with other crops. Conservation over the centuries has been *in situ* and it is only in the last decade that *ex situ* and *in vitro* conservation methods have become important.

While the main thrust of the ART programme is conservation of Andean root and tuber genetic resources, it includes work with native potato varieties as well. Conservation efforts encompass three strategies: (1) *in situ* conservation at the farmers' level in the highland communities; (2) conservation *ex situ* at research stations; (3) conservation in field genebanks and *in vitro* culture.

The ART collaborative programme is a forum for information exchange. Reciprocity is one of the most common features of Andean culture, and the programme takes into account this way of living and allows researchers to exchange information on the different national experiences. For instance, Peru is advanced in *in situ* conservation. Ecuador has good experience in genetic *ex situ* conservation but wants to help farmers conserve biodiversity of their food crops *in situ*.

Some of the highland crops have moved out of the Andean ecoregion to become economically important elsewhere. Achira is now grown in Viet Nam, where it is processed into starch used to produce transparent noodles. It is consumed as a luxury food throughout East Asia and sells at premium prices, making starch extraction and noodle processing major sources of income for people with as little as 500 square metres of arable land.

Arracacha is very much appreciated by resource-poor farmers in Southern Brazil because of its low input and the high prices obtained for the storage roots. They are processed into baby food by Nestle and other companies. Oca (also called New Zealand yam) has been grown in New Zealand for the past 20 years.

Andean women have been and continue to be a key factor in conserving and increasing the biodiversity of Andean crops. Men may out-migrate temporarily in search of jobs, especially after harvest, but the women and children stay behind to watch the farm and care for the animals.

Weekly agricultural fairs and markets have been an important means of exchanging genetic material and increasing genetic biodiversity in highland communities. Seed tubers and roots are sold, traded, bartered or exchanged as gifts. Seed fairs are now being promoted by non-governmental organizations (NGOs) and government extension agents as ways of increasing the genetic diversity of Andean crops. Contests are being held to see which farmer or village can display the greatest diversity of agricultural crops.

Experts agree that documentation of the agricultural systems and indigenous knowledge in the highland communities should be undertaken with great haste because of the pressure on the Andean genetic resources and traditional knowledge. There is much work to do, including research, breeding and characterization.

Very little of the Andean root and tuber germplasm is conserved in genebanks as botanical seed since the flowers rarely produce viable seeds. Scientists working in the ART programme are examining whether the work done at CIP on true potato seed is useful for understanding seed production in other roots and tubers.

Andean root and tuber crops: altitudes grown and uses

Crop	Common local names	Scientific name	Altitudes commonly grown (metres)	Uses
Ulloco (T)	ulloco, melloco papalisa	*Ullucus tuberosus*	2500-4000	Boiled in soups and stews, dried, medical uses
Oca (T)	oca, oga, apilla, ibia	*Oxalis tuberosa*	2500-4000	Boiled in soups and stews, dried
Mashua (T)	mashua, añu, maswa, isaño	*Tropaeloum tuberosum*	2500-4000	Used in stews, soups, medical uses
Yacon (R)	jicama, llak'on, yacon, jiquama, aricoma	*Polymnia sonchifolia*	1000-3000	Eaten raw, source of insulin, rejuvenating properties
Arracacha (R)	arracacha, racacha, zanahoria, blanca	*Arracacia xanthorrhiza*	1500-3000	Baked or boiled, used in stews and soups, baby food, can be dehydrated
Mauka (R)	chago, mauka, miso	*Mirabilis expansa*	2000-3200	Boiled in soups, stews
Achira (C)	achira	*Canna edulis*	0-2500	Baked, processed into high-value flour, leaves used to wrap food
Ahipa (R)	ajipa, ashipa	*Pachyrhizus ahipa*	1500-3000	Usually eaten raw, thirst quencher, leaves, stems, pods and seeds are a source of insecticide
Maca (R)	maca	*Lepidium meyenii*	3800-4200	Baked, dried and used to make a drink

R root T tuber C corm

The indigenous highland crops, generally grown in small areas in association with other plants, are mostly hardy and disease resistant. However, with increased movement and exchange of genetic material among Andean countries and even world-wide, it is essential to produce pathogen-free germplasm. Developing detection techniques for viruses in the storage organs or plant parts is an important area of research.

Characterization of collected accessions is also needed. At CIP, Carlos Arbizu is now working to prepare a list of descriptors for morphological characterization of Andean roots and tubers.

For additional information, contact Dr. Miguel Holle, c/o CIP, apartado 5969, Lima, Peru. Tel.: 51-14-366920. Fax: 51-14-351570. E-mail: mholle *at* virgo.cipa.org.pe. (Source: *Diversity*, Vol. 10, No. 4, 1994)

Social issues

Genetic engineering of coffee: biotechnology company brews genetically engineered java — gene altered java brewing

Genetic engineers at the California-based Escagenetics Corporation were the first to produce genetically transformed coffee plants, and recently received a patent covering genetically modified plants and seeds of *Coffea*, the most important commercial coffee species, accounting for 70 per cent of the estimated $12 billion world-wide market.

According to Escagenetics, bio-engineered coffee is in the long-term product pipeline. The industry's goal is to develop varieties that produce coffee beans with lower caffeine content, plants with increased pest resistance, and beans of improved flavour and aroma.

Recent advances in biotechnology offer new potentials for altering specific agronomic, processing and consumer qualities of the coffee plant and beverage. The release of a new coffee variety using conventional breeding requires 15 to 20 years. With new genetic technologies, scientists can drastically accelerate breeding programmes.

Large corporate coffee buyers and sellers in the industrialized world will reap the greatest benefits from advances in genetic engineering. The development of coffee varieties with lower caffeine content, for example, would undoubtedly result in substantial savings for major coffee processors who now use a chemical process for de-caffeination of beans. Consumers would also benefit from a naturally-decaffeinated coffee bean.

Coffee is the developing world's most valuable agricultural export commodity, produced by more than 50 nations in Latin America, Africa and Asia. With the exception of Brazil, Colombia, Kenya and Indonesia, coffee is not generally a plantation crop. In most areas of the world, coffee is grown by small farmers on diversified land holdings. Although genetic engineering of coffee is still in the early stages, some researchers are concerned about the social and economic impacts of coffee biotechnology on small farmers and rural communities in the developing

world. According to a study conducted by the Rural Advancement Foundation International (Pittsboro, NC, USA), the potential negative consequences include:

Genetic uniformity - Mass propagation of new coffee clones could exacerbate problems of genetic uniformity in commercial coffee production.

Overproduction and lower prices - Mass propagation of coffee plants may facilitate the growth of large-scale coffee plantations, leading to overproduction and a subsequent drop in coffee prices. It is usually the largest coffee producers who can afford to adopt new coffee varieties, and they will be the most likely to survive a restructuring in the coffee economy.

Transfer of production - Overall, the application of new biotechnologies to coffee could facilitate a fundamental shift to large-scale coffee growing plantations in the developing world. The largest coffee producing nations, Brazil and Colombia, will continue to dominate, while the small *robusta*-producing nations (principally African countries), where coffee is grown predominantly by peasant farmers, will suffer the greatest losses. (Source: *African Diversity*, No. 10, October 1994)

Attitudes

The public assesses risk in a much different way than the experts. In a classic study cited in the *New York Times*, Dr. Paul Slovic of Decision Research in Oregon, USA asked 40 members of the US League of Women Voters and 15 experts in risk assessment to rate 30 different activities and technologies (a rating of "1" would indicate the highest risk).

While estimates of risk were comparable for things like pesticides and construction work, they varied widely in other areas. For example, the experts rated nuclear power at "20", while the League members put it on the top of the danger list. In contrast, the experts put X-rays relatively high on their list, at "7", compared to the League, who rated them at "20".

According to Slovic, public perception to a given risk can be amplified by several factors, including adverse news media coverage or spectacular incidents like the Chernobyl nuclear reactor or the chemical plant in Bhopal, India.

Risks that are beyond people's control are viewed as the more dangerous. Hence, skiing is more acceptable than food preservatives. Risks that are unfairly shared are also more unacceptable (a manifestation of this is the "not in my back yard" syndrome).

Natural risks are more acceptable than the man-made variety. For example, naturally-occurring radon gas in your basement is more acceptable than radon gas from uranium mine tailings, even though they may pose identical risks.

New technologies are also viewed with more suspicion than older methods. A train wreck may barely pique the public interest, while an accident in a recombinant DNA laboratory might create a clamour for the Government to clamp down and tighten regulations.

Slovic says human psychology works against building trust. Negative events are remembered much more vividly and people are more apt to believe bad news and give it more weight. For example, if animal testing shows a substance is safe, the results are discounted, while if the same study indicates the substance causes cancer, it is cited as solid truth. (Source: *The 10C Biotech Bulletin*, Vol. 2, No. 5, September 1994)

Regulatory issues

Biosafety regulation

Whereas by now most industrialized countries have adopted regulations concerning the safe handling and use of genetically engineered organisms, most developing countries still lack any regulations in this field. This imbalance is already stimulating companies to test their biotechnology products in the South, rather than in the North. Faced with many examples of such testing, there is a clear need for a binding regulatory mechanism to rule the testing, release and trade of genetically modified organisms (GMOs). This is often due to the limited financial and technological capacities of the regulatory authorities in these countries. As a consequence, an increasing number of companies from the US and Europe prefer to conduct releases of GMOs in countries which have no regulations in place (see table).

This, as is the case with many other dangerous or risky substances and technologies, there is a regulatory imbalance between developing and developed countries. And strict regulations in one country or certain parts of the world may have the effect that operators flee to the countries whose regulations are less strict or who have no regulations in place and or no capacity to control compliance with regulations. This regulatory vacuum and imbalance is one of the major arguments used by many Governments and NGOs for a biosafety protocol under the Convention on Biological Diversity (CBD). (Source: *Nexus*, December 1994)

The need for biosafety protocol

The current regulatory imbalance serves no one, except perhaps those who are interested in quick and uncontrolled testing of GMOs. It endangers the human health and the environment in countries abused as testing fields. The UK Royal Commission on Environmental Pollution expressed this concern already in its 1989 Report on the Release of GMOs to the Environment: "If any country allows releases to be carried out without thorough scrutiny, control and monitoring there will be a consequent risk to the environment and to health in that country and more widely."

The recognition of the need for internationally harmonized safety regulations led to the inclusion of Article 19 (3) in the Biodiversity Convention. According to this provision:

> "The Parties shall consider the need for and modalities of a protocol setting out appropriate procedure, including, in particular, advance informed agreement, in the field of the safe transfer, handling and use of any living modified organism resulting from biotechnology that may have adverse effect on the conservation and sustainable use of biological diversity."

In order to facilitate the consideration of the need for and modalities of a biosafety protocol pursuant to Article 19 (3) the Executive Director of UNEP established in 1992 an Expert Panel which was requested to deliver a report on this issue. After reviewing existing international agreements and instruments on biosafety, the majority of the Panel members concluded that no effective international biosafety agreement existed as of yet and agreed that the purpose of strengthened international cooperation in the

RELEASE WITHOUT REGULATION
Field tests with transgenetic plants in Latin America
(1989–1992)

Year	Country	Company	Crop	No. of trials	Trait
1989	Guatemala	Asgrow (USA)	Squash	1	Virus resistance
	Puerto Rico	Monsanto (USA)	Soybean	1	Herbicide tolerance
1990	Mexico	Calgene (USA)	Tomato	1	Long shelf-life
	Puerto Rico	Monsanto (USA)	Soybean	1	Herbicide tolerance
1991	Mexico	Campbell Sinaloa (USA)	Tomato	1	Bt insect resistance
	Argentina	Calgene (USA)	Cotton	2	Herbicide tolerance and Bt insect resistance
		Ciba-Geigy (CH)	Maize	1	Marker gene
		Monsanto (USA)	Soybean	1	Herbicide tolerance
	Domin. Rep.	Monsanto (USA)	Soybean	1	Herbicide tolerance
	Costa Rica	Monsanto (USA)	Soybean	1	Herbicide tolerance
	Chile	Calgene (USA)	Tomato	1	Long shelf-life
		ICI PetoSeed (UK USA)	Tomato		
	Bolivia	Calgene (USA)	Cotton	2	Herbicide tolerance and Bt insect resistance
	Puerto Rico	Monsanto (USA)	Soybean	1	Herbicide tolerance
1992	Argentina	Calgene (USA)	Cotton	2	Herbicide tolerance and Bt insect resistance
		Monsanto (USA)	Soybean	1	Herbicide tolerance
		Ciba-Geigy (CH)	Maize	1	Marker gene
			Canola		
			Sugar beet		
	Mexico	Campbell Sinaloa (USA)	Tomato	2	Bt insect resistance and long shelf-life
		CINVESTAV	Potato	1	Virus resistance
		Calgene (USA)	Tomato	1	Long shelf-life
	Costa Rica	Monsanto (USA)	Soybean	1	Herbicide tolerance
			Cotton	1	Herbicide tolerance
			Maize	1	Herbicide tolerance
	Puerto Rico	Monsanto (USA)	Soybean	1	Herbicide tolerance
	Belize	Monsanto (USA)	Soybean	1	Herbicide tolerance
			Cotton	1	Herbicide tolerance
			Maize	1	Herbicide tolerance
	Bolivia	Univ of Venezuela CIP	Potato	1	Cold tolerance

Compiled by CLAT Clearinghouse & GRAIN from W.R. Jaffe, 1993

field of biotechnology and biosafety is best served by the adoption of a legally binding instrument.

During the last governmental meeting on the Convention, held in June 1994 at Nairobi, the discussion on the need for a protocol on biodiversity became one of the "hot" issues. A few developed country representatives, led by the US delegation, opposed any action that may lead to a protocol, assuming the industry position that any such action should be based on "sound scientific evidence" and not on what hard-line biotechnologists consider "misrepresentations and distortions". This position contrasted with concerned expressed by third world country representatives and NGOs about ethical, socio-economic, safety and regulatory considerations. Fortunately, the vast majority of delegates including a unanimous position from Group-77 and China, were of the view that immediate work on a Protocol on biosafety should begin. The Conference of the Parties to the Convention now has the responsibility and opportunity to take the internationallead in creating a safe environment for the handling of GMOs, including the following criteria:

- That a Protocol on Biosafety under Article 19 (3) of the Convention be set up;
- That such a Protocol should cover domestic handling and use of biotechnology as well as inter-state transfer of GMOs;
- That such a Protocol should include an Advance Informed Agreement procedure which should apply to all transfers of GMOs;
- That the Protocol should also deal with socio-economic impacts biotechnological products may have on developing as well as on industrialized countries;
- That in order to ensure international recognition of safety principles set out in the Protocol, States Party to the Protocol should ban import and export of GMOs or products containing or consisting of GMOs from, or to States not Party to the Protocol.

In the meantime, as requested by many NGOs and some Governments, a moratorium should be declared on any further field testing of GMOs. (Source: *Seedling*, December 1994)

Issues of biotechnology safety and regulation

Stigmatization over biotechnology's safety has caused a curious twist in public policy, says Mark Cantley of the Organization of Economic Cooperation and Development. Scientifically, it is safe, i.e., as safe as other genetic manipulations.

But opinion polls indicate the public does not perceive it as such. One response is to erect special regulations intended to reassure the public. The new regulations are intended to protect biotechnology from the public, rather that their proper role of protecting the public from biotechnology.

Cantley's comments concluded the *Third International Symposium on the Biosafety Results of Field Tests of Genetically Modified Plants and Micro-organisms*, held in Monterey, CA, USA during November 1994.

Mixed messages confuse the public, undermine rational and science-based regulation and choke off public access to the benefits of safe and effective biotechnologies.

Safety issues challenge teachers and communicators from universities and industry in several ways: defining safety, distinguishing between safety and the feeling of safety, accommodating people with profound concerns unfounded by the available data; clarifying criteria for assessing safety; and assessing public policies that would generally prohibit or specifically penalize the commercialization of safe and effective products.

There is another specific challenge for teachers: biotechnology is often cited as a vehicle for teaching about the role of ethics, morality and social obligation in science. While student interest and the availability of case-studies make biotechnology a good vehicle, it is not – and should not be presented as – the sole technology infused with such issues. Clearly biotechnology is a case-study for developing critical thinking in students, but to focus all "Science in Society" issues on biotechnology falsely implies that those issues are unique to biotechnology.

Assessing the safety of the field release of transgenic plants and microbes is a contentious task entangling principles of science, the pragmatism of commerce and the politics of government.

Being understandable to all requires being clear in the criteria used to define and assess safety. While scientists focus on risk measurable by experiments, policy makers also usually consider the public's feeling for safety. Accommodating profound concerns unfounded by the data taxes the wisdom of public officials and requires the vigilance of scientists to ensure that concerns about the feeling of safety are not confused with the actual assessment of risk.

If the conclusion that recombinant DNA poses no special risks is accepted, then the criteria used to evaluate the risk of products of recombinant DNA would be the same criteria used to evaluate products of traditional and familiar genetic modifications. The feeling of safety may not be the same, but the risk-assessment principles would be the same. Even if those principles are not clearly stated, one can ask a critical question: Are transgenic organisms tested with the same scrutiny as other genetically modified organisms? If not, why not?

An increase in the number of field tests world-wide and a spate of new products clearing the final hurdles to commercialization, have spiked interest in improving public understanding of biotechnology in the hope of increasing public acceptance of biotechnology products. Clearly, public understanding will not in itself cause public acceptance, which is a function of both information and values. An improved understanding of the science will not necessarily change values.

People choose to reject a new technology for several reasons, including misinformation that leads to misconceptions, as well as well-informed people rejecting a tool because it is inconsistent with their values. To some people, new technologies such as recombinant DNA are taboo. Taboos are real and can be profound, but they are capricious and not bounded by reason. One is left asking if taboos are sound principles on which to base public policies that restrict liberty or demand compulsory action against a person's will.

An informed public is less likely to reject biotechnology products because of misconceptions. An involved public is less likely to reject biotechnology products because of a feeling of exclusion from the process of assessing safety. An informed public also is more likely to participate effectively in the debate. Addressing safety issues and regulations is a key component of that debate. (Extracted from *Genetic Engineering News*, December 1994)

General

Tool-box therapy

Rhône-Poulenc Rorer (RPR) claims to have created the world's first biotechnology network to accelerate the discovery and development of cell and gene therapies.

The network consists of 14 companies and research organizations which will work with a new division of RPR called RPR Gencell. The company believes the network can be a world leader in cell and gene therapy, according to Josef Bossart, in business and market development at RPR Gencell. Gencell's mandate is to make gene therapy work, he adds. Although RPR will spend about $1 million per annum on the network, Bossart stresses that more funding is available if necessary to access new technologies.

The "tool-box" of technologies will mean RPR can bring products to market more rapidly, but it will not be free to pick and choose from its partners' portfolios, as the agreements cover only specific areas of research.

Network partners will have access to RPR's world-wide clinical, regulatory and manufacturing teams to decrease the time in getting products to market. RPR will fund all clinical trials. The contributing partners will share in any commercial success the products may have.

Together, the network members have six therapies in the clinic, aimed at HIV, leukaemias, bone marrow transfusion, renal cell carcinoma and cancer of the central nervous system. Three anti-lung cancer agents are following closely behind. (Extracted from *Chemistry & Industry* 21 November 1994)

Molecular Simulation Laboratory to open at RMIT

American, Japanese and Australian software companies have joined with RMIT to establish a Molecular Stimulation and Design Laboratory which will have a key role in Australian pharmaceutical, plastics, chemical and metals industries. The RMIT laboratory will provide facilities for industry-linked research into polymers, chemicals and bio-medical products. Seminars and training in molecular modelling will be provided to Australian industries, researchers and RMIT's own students.

Computational modelling of materials at the molecular and atomic scale is established as an important tool in research. The combination of high-powered graphical computers and computational chemistry makes it possible to simulate and predict how molecules might behave in laboratory tests before a material is synthesized or purified. (Extracted from *Australasian Biotechnology*, Vol. 4, No. 4, August 1994)

"Bio-piracy" puts pharma and food firms under fire

Pressure is mounting for pharma and food multinationals to compensate developing countries for the use of plant species. Hard on the heels of the recently agreed biodiversity treaty, a report* commissioned by the United Nations Development Programme (UNDP) claims that "bio-piracy" – the developing countries' lack of royalty payment for indigenous use of plant species – is cheating developing countries of $5.4 billion per year.

The report estimates the value of third world plant species to the pharma industry alone at more than $30 billion per year. "While more than 90 per cent of the Earth's remaining biological diversity is located in Africa, Asia and South America, indigenous communities that have developed and nurtured such diversity are not acknowledged – much less compensated – for the material and local knowledge that is taken from them", it points out.

The inequality is exacerbated, it says, by the growing use of patents which grant exclusive protection to Northern corporations and researchers for material or knowledge that originated in the South.

The report cites 100 specific examples of major agriculture and drug companies profiting from products derived wholly from plants, fungi or bacteria from developing countries.

Examples show up the "unofficial" collection methods employed by the multinationals.

In calculating the cost of "bio-piracy" to developing countries, the report acknowledges that there has also been uncompensated pirating of agricultural chemicals and pharma compounds from industrial countries by developing countries, which it estimates at losses to the North of as much as $2.7 billion per year.

The UNDP has already begun consulting with indigenous people's organizations on strategies for preserving traditional knowledge and gaining acknowledgement for their contributions. (Source: *European Chemical News*, 7 November 1994)

1995 ATCC Laboratory Training Workshops

The American Type Culture Collection (ATCC) is a non-profit organization set up as an international repository for biological cultures. Part of ATCC's mandate is to provide education in the field of microbiology. ATCC's Laboratory Workshop Programme is part of the fulfilment of this education mandate. They have been offering "hands-on" training programmes for the past 13 years. At least 50 per cent of each workshop involves hands-on training and the remainder of the programme is devoted to lectures.

Readers may be able to benefit from these programmes.

Basic techniques in molecular mycobacteriology, 18-21 April 1995;

In vitro toxicology: techniques and applications, 25-28 April 1995;

Cell culture and hybridomas: quality control and cryopreservation techniques, 10-12 May 1995;

Freezing and freeze-drying of micro-organisms, 17-19 May 1995;

Fermentation microbiology, 25-28 July 1995;

Thirteenth Annual Biotechnology Patent Forum, 24-25 August 1995;

Anaerobic bacteriology, 7-8 September 1995; and

Microscopy photomicrography, 20-22 September 1995.

For information on ATCC workshops contact: ATCC, Workshop Coordinator, 12301 Parklawn Drive, Rockville, MD 20852, USA. Tel: 301-231-5566, Fax: 301-816-4364.

French conference highlights controlled-release methods

Drug and vaccine developers have long recognized the potential of controlled-release technology for improving the

---

* *Conserving indigenous knowledge: integrating two systems of innovation*, compiled by the Rural Advancement Foundation International for the UNDP.

safety, efficacy and cost-effectiveness of their products. But such delivery technologies may be even more vital to the success of products designed for agricultural use, where consistent efficacy and ease of administration are critical concerns.

The need for better controlled-release systems for insect control and animal health was a key topic at the recent Controlled Release Society's Twenty-First International Symposium, held at the Acropolis Convention Center in Nice, France.

A growing interest was noted on the part of farmers in biorational pest-control products for several reasons. Biorational products offer a means to control insects that have developed resistance to conventional insecticides. Biorational products are often safer than conventional insecticides—typically, biorational products avoid restrictions on harvesting, cause no harm to beneficial insects or contamination of the environment and are not harmful to plants. With regulations restricting or eliminating the use of many conventional insecticides, biorational control may soon offer the only means available for subduing some insect pests.

Despite the technology's benefits, however, significant improvements are needed before biorational pest-control methods are likely to gain widespread use. For example, while pheromones that disrupt insect mating have been employed as successfully as chemical insecticides to control several important insect pests, their use is still confined primarily to niche applications. Pheromones must be applied prophylactically to crops before insects appear and then continually throughout the growing season. Thus, a year-long commitment to the technology is required.

Growers must also learn how to use pheromones properly in order to achieve control. This is in contrast to most traditional insecticides, which can be applied in response to an outbreak.

For pheromone technology to achieve widespread use, two key improvements must be made. First, the cost of pheromone treatments must be reduced so that their use is economically compelling rather than economically competitive. Second, more consistently effective long-lasting formulations must be developed so that the products can be applied using conventional agricultural equipment and practices.

Among the technologies being developed for pheromone delivery are protective coatings, microencapsulation and microporous beads of various sizes and release profiles.

Biological insecticides that use bacterial toxins, insect viruses, fungi or nematodes to control agricultural pests could also benefit significantly from controlled-release formulations. Most current products are easily degraded by light, heat and or desiccation. Therefore, new formulations that improve product stability and extend the length of time during which the product is effective are being actively sought by many companies.

Livestock breeders should also benefit significantly from controlled-release technologies that reduce the amount of handling required for vaccination or treatment of animals. Traditional veterinary vaccines involve an initial dose of antigen followed by one or more booster doses. A single-dose vaccination system could reduce both the time involved and the cost of animal vaccination.

Protecting animals from infections when they are shipped or kept in close proximity, as in feedlots, is also a challenge. Animals are affected by many agents that enter the host through the nasal passages or other mucosal surfaces.

While vaccines administered by injection stimulate circulating antibodies, these antibodies do not necessarily prevent the attachment and invasion of microbes. Vaccination at mucosal surfaces is the best way to stimulate effective local immunity. Orally active vaccines delivered to animals in feed or water provide a relatively easy, cost-effective way to accomplish such mucosal vaccination. Because the mucosal immune system is interconnected, stimulation of gut-associated mucosal lymphoid tissue (GALT) results in immunity at mucosal sites throughout the body. Controlled-release formulations also provide the means for improving nutrition in cattle and sheep by protecting fragile amino acids used as feed additives from degradation in the rumen. (Extracted from *Genetic Engineering News*, September 1994)

Gene therapy market predicted to top $2 billion by the year 2000

A new Frost & Sullivan (Mountain View, CA, USA) report predicts that the gene therapy market will emerge in 1997 and generate $2.6 billion in world-wide revenues by the turn of the century. By 2000, about 48 per cent of the market's revenues will be generated by cancer treatments, 30 per cent by treatments of genetic diseases, 11 per cent viral diseases and 7 per cent anaemias, forecasts the report, "World Gene Therapy Markets".

Although most experimentation thus far has focused on *ex vivo* procedures, a growing number of companies are developing *in vivo* gene therapy and pharmaceuticals, and the first *in vivo* treatments have entered clinical trials. The report points out than *in vivo* therapy promises to be less costly and cumbersome than *ex vivo* procedures, which require removal and treatment of patient cells, followed by their reintroduction into the patient.

Based on current developmental activities, there is a significant probability of gene therapy treatments reaching the world market by the year 2000 for, in addition to brain tumours, malignant melanoma, leukaemia and kidney, breast, colorectal, liver, prostate, ovarian, lung and bladder cancers, according to the study.

Viral disease research is concentrating on AIDS treatments. Gene therapy approaches to viral disease focus on inserting genes for viral antigens to increase immune response, genetically modifying lymphocytes to enhance their ability to direct and destroy viral particles and infected cells and implanting genes to confer resistance to certain viral infections. Besides AIDS, the therapy most likely to reach the market by the year 2000 addresses cytomegalovirus infection in immunocom-promised persons.

There are currently more than 60 gene therapy trials ongoing or planned world-wide, and this number will increase rapidly, predicts the report, which notes that the treatment of human disease by gene therapy moved from the theoretical to practical realm with the first trial in 1990. (Extracted from *Genetic Engineering News*, 15 September 1994)

Exchange changes to benefit bioscience

Plans for a pan-European Nasdaq-style stock exchange to focus on entrepreneurial companies and further relaxation of the London stock exchange listing rules could make it easier for the UK bioscience industry to raise finance in the future. The UK has the best climate in the world for

biosciences, delegates at the Business Issues for Bioscience Companies conference held in London heard, but the so-called "equity gap" remains a major concern.

The London stock exchange rules were amended in 1993 to allow research-based companies to raise finance through a listing while their products are still in development. However, many in the bioscience community—and particularly the venture capitalists—believe that relaxation, through the so-called Chapter 20, has not gone far enough or in some cases that the new qualifying requirements are inappropriate.

The only real alternative to the London stock exchange is widely regarded as the North American Nasdaq system. A third alternative could be a pan-European exchange of the quality and status of Nasdaq, which would have a separate identity as a higher risk higher returns market, with Nasdaq-type trading and market surveillance. Full disclosure of information, as required under the Nasdaq listing rules, would be a principal requirement. (Extracted from *European Chemical News*, 31 October 1994)

Germ warfare ban talks planned

Negotiations on measures to strengthen the 1972 treaty outlawing biological weapons started in January 1995. After two weeks of difficult talks in Geneva, some 80 Governments agreed to set up an ad hoc group to draft proposals on verification, anti-cheating measures and other compliance issues. According to the *Financial Times*, the industrialized countries are keen to see the group—which is open to all 131 country members—pushing ahead with a protocol for approval at the next treaty review conference in 1996. Some developing countries, on the other hand, want to proceed more cautiously. (Source: *Biotechnology Bulletin*, October 1994)

Saving endangered species

Scientists estimate that 50 plant and animal species are disappearing daily around the world: some of these species might never have been identified. As tropical forests are being destroyed rapidly, through timber exploitation and improper farming practices, some economically and ecologically important species are threatened with extinction. Some of the endangered forest species have, however, found a haven on the 1,000 ha campus of the International Institute of Tropical Agriculture (IITA) in Ibadan, Nigeria.

The founders of IITA were persons of unusual vision. They recognized nearly 30 years ago the need to make sustainability, and conservation of natural resources including biodiversity, a major goal of tropical agricultural research – a goal that has only recently become widely appreciated and accepted.

Thus, in 26 years of its existence, IITA has accumulated a wealth of scientific information on, and developed technologies for, sustainable land management, soil erosion prevention and control, and stable alternatives to the traditional system of shifting cultivation.

As regards conservation of biodiversity, the Institute's Genetic Resources Unit holds the most important genebank in Africa, and its collections of cowpea varieties and related wild species, and of Bambara groundnut are the largest in the entire world. The Unit also maintains large collections of rice species indigenous to Africa as well as of other major crop plants. This effort ensures that, regardless of desert encroachment, massive deforestation, forest fires, floods and droughts, useful crop genes will be available for use by scientists and farmers of future generations. (Source: *Development and Cooperation*, March 1994)

Boom times expected for agricultural biotechnology

Sales of agricultural biotechnology products in the USA will boom, from $108 million in 1993 to $1.8 billion by 2000, according to Frost & Sullivan (New York). The consulting firm says biopesticides—now about 94 per cent of the market—will make up only 16 per cent of the business in the year 2000. Frost & Sullivan says growth hormones will make up 45 per cent of the business, while transgenic organisms and tissue cultures will account for 28 per cent and 10 per cent respectively. (Source: *CHEMICALWEEK*, 17 August 1994)

Europe to lose biotech investment to USA/Japan

Europe is set to lose out to the USA and Japan on future biotechnology investments by European companies. Regulatory constraints and worries about public perception are driving investment away, concludes the first in-depth survey* of the economic impact of biotechnology in Europe. Yet the survey also suggests that the application of biotechnology is more widespread in Europe than has been evident from previous surveys, with dependent sales estimated at Ecu 38 billion – some 1 per cent of European GDP.

According to the survey, only just over 40 per cent of companies' future investment is destined for Europe, compared with 58 per cent of previous investment. The main gainers are the USA – which will take some 45 per cent of investment – and Japan which will increase from just under 10 per cent to 15 per cent.

Perhaps not surprisingly, the survey concludes that the main factors influencing the location of investment are the availability of skilled staff and regulatory constraints, as well as the proximity of appropriate scientific institutes. Particularly in Germany, regulatory constraints and public opposition were found to deter new investment.

Factors cited as the main regulatory constraints included product approval delays (which were mentioned by 70 per cent of respondent companies) and lack of adequate patent protection (mentioned by almost 60 per cent). Difficulties with planning site approval and product liability also featured strongly.

According to the survey, the European market for goods and services which are dependent on biotechnology is currently Ecu 38 billion.

Overall growth estimates vary widely; a large proportion of firms view sales as being essentially flat to the year 2000 while, at the other extreme, some 20 per cent of companies expect sales to more than double over the same period.

Given the economic significance of biotechnology, the survey sets out a challenge to European policy-makers. Many of the areas of regulatory constraint can be changed by government action, it notes. "Industry can play its role

---

* *Biotechnology's economic impact in Europe: a survey of its future role in competitiveness*, published by London-based consultancy Ernst & Young with support from the Senior Advisory Group on Biotechnology (SAGB).

in improving the image and knowledge of applications of biotechnology, but the creation of an embracing climate in areas such as training, support activities, central funding of basic research and providing innovative means for accessto capital are the prerogative of government". (Source: *European Chemical News*, 10 October 1994)

IICA's policies for the development of agro-biotechnology

The Support Project for the Formulation of Policies for Agro-biotechnology Development is part of the Programme for Technology Generation and Transfer of the Inter-American Institute for Cooperation in Agriculture (IICA). One of the project's first steps was to generate basic information on the region's state-of-the-art agro-biotechnology. The outcome was the creation of a biotechnology programme coordinated by South American Southern Cone countries and the establishment of phytogenetic resource networks for the Middle American, Andean and Caribbean regions. Studies on the strategies of a significant number of the region's enterprises dedicated to agro-biotechnology was another achievement, and was followed by the publication of several volumes of the Latin American Biotechnological Industry Directory. In collaboration with the Pan American Health Organization, several guides on biosafety issues were released, as well as different activities of this nature undertaken by various countries. Another important step was taken through establishing a regional consensus concerning the need to introduce systems and mechanisms for protecting intellectual property rights in the field of agro-biotechnology. (Source: *Boletin de Biotecnologia*, Vol. 11, No. 1, July 1994)

REDBIO '95: Puerto Iguazú, Argentina

The Technical Cooperation Network on Plant Biotechnology (REDBIO), sponsored by FAO, was established and has operated since 1991. The main objective of the Network is to develop a mechanism for harmonizing and promoting knowledge for the application of plant biotechnology to the solution of production problems that affect Latin American agriculture.

Specifically, its objectives are:

- Promote the formulation of national policies;
- Encourage exchange of knowledge, technologies and biologic materials;
- Sponsor regional training activities;
- Develop cooperative projects between laboratories of the region and centres of excellence at the world level;
- Promote preparation of a code of conduct on plant biotechnology.

The member laboratories of REDBIO have proposed holding a technical meeting every three years as a major event of REDBIO. Argentina has been selected to host the Second Latin American Meeting on Plant Biotechnology (REDBIO 95).

The objectives of the meeting will be:

- Disseminate and discuss progress in the generation of knowledge and biotechnologies for the improvement of agricultural production in Latin America and the Caribbean;
- Present results and promote projects and policies in favour of the development of plant biotechnology;
- Promote the gathering of young researchers and students of institutions of the region with renowned specialists from universities and centres of excellence at the world level;
- Promote interaction between the academic sector and the private sector;
- Discuss the socio-economic and environmental impact of the application of new biotechnologies in the region.

REDBIO will be organized in four subject matter blocks:

I. Agri-biotechnologic Development
II. Socio-economic Development and Environment
III. Academic sector Private sector interactions
IV. Biotechnological Progress by Crops (Workshops).

For more information, contact: Southern Cone Coordinator, Dr. Alejandro Mentaberry, INGEBI-CONICET, Obligado 2490, 1428 Buenos Aires, Argentina; Fax: (54-1) 786 8578).

Biotecnologia Habana '95

The Center of Genetic Engineering and Biotechnology (CIGB) in Havana, Cuba is organizing "Biotecnologia Havana '95: New Opportunities in Plant, Animal and Industrial Biotechnology". Co-sponsored by UNESCO and FAO, the conference will be held 12-17 November 1995, at the CIGB headquarters in Havana, and is dedicated to the application of biotechnology to plant, animal and industrial production.

Three parallel events will take place during the scientific programme:

Biotechnology Applied to Animal Production and Health

- Biotechnology applied to animal improvement;
- Vaccines and drugs for veterinary uses;
- Diagnosis applied to animal production;
- Use of transgenic animals as "biofactories";
- Use of transgenic animals as biomodels;
- Embryology and biology of development;
- Biotechnology applied to aquaculture.

Biotechnology Applied to Plant Production

- Plant tissue culture applied to agriculture and to the production of useful substances in plant cells;
- Biofertilizers and biopesticides;
- Diagnosis of diseases in plants;
- Molecular markers and their application to agriculture;
- Genetic engineering applied to agriculture: genetic transformation; resistance to plagues and diseases; quality improvement of agricultural products.

Biotechnology Applied to Industry

- Fermentation, scaling, recovering and purification of proteins from genetically modified organisms;
- Bioreactors: kinetics of transformation and calculation of industrial bioreactors;
- Gene expression in industrial micro-organisms;
- Bioconversion and biodegradation;
- Immobilization of cells and enzymes;
- Production of industrial enzymes.

In each event there will be poster sessions, short oral communications, symposiums and round-tables with the participation of invited lecturers. The round-table discussions will cover the following subjects:

- Patents and regulations for the application of biotechnology to agricultural production;

- The commerce of biotechnologic products;
- Opportunities of biotechnology as a source of economic and social development.

Inscription fees:

Delegates:	325.00 USD (private sector)
	250.00 USD (academic and government sectors)
	150.00 USD (students)
Non-delegates:	75.00 USD

Commercial Exposition

Parallel to the scientific sessions, there will be a commercial exhibit of reagents and equipment related to these subjects.

For more information, contact: Organization Committee, Biotechnology Havana '95, P.O. Box 6162, Havana 10600 Cuba; Telex: 51-2330 CUBABIOT and 51-1072 CUBACIB, Tel.: 53-7-218008, 216444, 218164, 216832, Fax: 53-7-218070, 336008, E-mail: biot95@ingen.cigb.edu.cu.

Biotechnology Advisory Commission

The recently formed Biotechnology Advisory Commission (BAC) was set up as a result of a biosafety workshop held in December 1990 at Sigtuna, Sweden. At this workshop, the participants considered a proposal for an independent international biosafety panel. This panel would provide advice on request with respect to the release of genetically modified organisms into the environment. It was agreed that the idea had merit and that an advisory panel on agricultural biotechnology should be created. It is important to note that developing nation participants argued strongly that they needed impartial advice on the scientific appropriateness of proposed biotechnology approaches to their particular national goals and the steps that should be taken when evaluating these proposals.

The Stockholm Environment Institute agreed to provide a base for the formation of such a commission. In the ensuing three years, financial support was found through grants from Swedish donor agencies, from the Rockefeller Foundation and from internal Institute resources. Fifteen internationally recognized scientists and legal experts volunteered to constitute the advisory body. These members have a wide range of experience in scientific and other disciplines including applied ecology; ecological genetics; microbiology; molecular biology of plants and micro-organisms; entomology; genetics; marine biotechnology; and plant pathology, as well as international environmental and regulatory law and economics. Equally important is the fact that all of these members have considerable experience in the development and implementation of biosafety guidelines and regulations.

The Commission has been working out of its office at the Stockholm Environment Institute. A secretariat has been formed and a full-time executive secretary is in place. The Commission has established procedures that it will use to provide assistance. In response to specific requests, for example how to assess the biosafety of a proposed field test using a genetically modified organism, the BAC will evaluate the proposal and provide the results of that evaluation in a report. Any advice offered, of course, will be based on background data that is provided from the applicant; information obtained through special sources, for example, ad hoc task forces sponsored by the Commission, and the collective knowledge and experience of the members.

It is intended that any advice given will be in a form that is useful to regulatory authorities in their decision-making process. It should be made clear that the advice itself is not intended to be a regulatory decision. In fact, the BAC is not in a position to make those kinds of determinations. The Commission will, however, try to formulate the advice in such a way that it will be useful to those who are making these decisions. Since the BAC is being supported by the Stockholm Environment Institute and outside funding agencies, it will be possible to maintain a completely impartial view in these evaluations.

Finally, some supplementary activities anticipated being available through the Commission in the near future may be the construction of a variety of information databases and electronic data resources, for example, by UNIDO, OECD, USDA and CABI. Access to these through electronic connection is quite easy in the industrialized countries, but there are perhaps difficulties in using such systems efficiently elsewhere. It is anticipated that the BAC could, in fact, be a centralized resource as an intermediary to providing such information. Upon request, the BAC could formulate search activities on behalf of a requester. Additionally, should it be desired, a preliminary evaluation of that information could be done.

Additional information or application forms and instructions may be obtained from: Dr. Robert Frederick, Executive Secretary, Biotechnology Advisory Commission, Stockholm Environment Institute, P.O. Box 2142, S-103 14 Stockholm, Sweden; Tel.: +46 8 723 02 60, Fax: +46 8 723 03 48, E-mail: seibac *a* nordnet.se.

National differences in biotechnology perception

USA: Only a minority of US citizens is sufficiently well informed, while the majority fears health hazards from biotechnology, despite not being able to assess risk reasonably. They tend to consider genetically modified microbes more harmful to humans than transgenic plants and animals. Despite the high-risk perception and a majority opinion that life in general is changing too fast, acceptance of biotechnology in the USA is rather good. Opposition to biotechnology is quite low; people seem instead to discriminate between various applications. The division seen in 1987 into five groups is still characteristic: 19 per cent considered biotechnology safe and beneficial, 24 per cent risky but beneficial, 6 per cent safe but not beneficial, and 15 per cent risky and not beneficial, while 36 per cent were undecided (Novo, 1987).

Northern (Germanic) Europe. The north-western European countries (except Ireland) share many attitudes in regard to biotechnology: a relatively well-informed public with a high-risk perception and considerable ethical objections accepts this technology hesitatingly. The British have an average level of risk perception and an average acceptance rate (but acceptance is lower for food application (MORI 1985) and non-life-saving human applications (RSGB 1988)). Uniquely in the UK, "biotechnology" is much less well-recognized than "genetic engineering" (52 versus 32 per cent, MORI 1985). Belgians hold "average" opinions. In Luxembourg, risk perception is about average, but acceptance of biotechnology is below average. The Dutch perceive higher risks and their acceptance rate is average (except for transgenic animals, which are rejected). The low Dutch acceptance for novel

foods (SWOKA 1990) was not confirmed by Europe 1993. Denmark has the highest rate of risk perception and, perhaps surprisingly, an above average rate of acceptance, too. This constitutes a considerable change in opinion: in 1986, about 75 per cent of the Danish thought it was morally wrong to interfere with nature, although only around 30 per cent favoured an international ban on genetic engineering (Denmark 1987-1989). The Danish disliked manipulated food and animals (Europe 1991). Denmark, unlike other Germanic countries, did not find biotechnology less acceptable in 1993 than in 1991 (Europe 1993).

Germany is a special case. The western part, though the best informed in Europe, is notorious for high-risk perception (second only to Denmark) and a low acceptance except, surprisingly, for human gene therapy. The former East Germany is well-informed but has a more positive attitude to genetic engineering (apart from gene therapy) (Europe 1991). By the time of the 1993 survey, however, there was a considerable decrease in the acceptability of biotechnology (although it was still higher than in the western part) (Europe 1993).

Southern (Romanic) Europe: The Romanic countries share patterns of opinions on biotechnology with Ireland and Greece: relatively poor knowledge engenders a low perception of risk and an optimistic outlook on new technologies. The French perceived surprisingly high levels of risk, but had average acceptance of biotechnology. Spaniards had a low-risk perception (confirmed by Spain 1990), but found biotechnology more acceptable than the European average (Spain 1990 indicated a broader acceptance: 73.3 per cent). Portugal combined very low-risk perception with high acceptance. Although the Greeks shared the Southern trend of low-risk perception, they balked at genetic manipulation of plants and humans, while welcoming biotechnology for animals and new drugs. Italians could not see much risk, but disliked plant and human manipulations. Irish risk perception was below average and their acceptance rate of plant and microbial engineering was high (Europe 1991, 1993; Ireland 1990). The typical North-South split in Europe is reflected in Switzerland, which straddles cultural borderlines: the acceptability of biotechnology to Alemanic (48 per cent) and Romanic (69 per cent) populations differs considerably (Swiss 1991).

Japan: People of all educational levels seem to know as much about biotechnology as European and US citizens. The Japanese perceive high levels of risk in food biotechnology, human gene therapy and field release. Consequently, while they welcome rDNA for drugs, they tend to reject gene therapy and food. The parallel to Germany is striking. (Extracted from *Bio Technology*, Vol. 12, September 1994)

An international knowledge powerhouse

Ever wish there was some way to cull out the relevant articles from the thousands of journals available worldwide? The Centre for Agriculture and Bioscience International (CABI) has embraced this task as their own and in the process has put together the most comprehensive agricultural database in the world. Mr. James Gilmore, Director General of CABI, explains its organization's mission and possibilities for collaboration.

CABI was formed in 1928, dedicated to "improving human welfare worldwide through the dissemination, application and generation of scientific knowledge in support of sustainable development ... with particular attention to the needs of developing countries." Thirty-six countries, including Canada, are members. A non-profit organization, it gets about 10 per cent of its annual budget from member country's fees and various scientific services it offers. However, fully 90 per cent of CABI funding comes from information publishing in printed and electronic form.

Foremost among these is CAB Abstracts, a database with three million entries available on-line or in various electronic media. Another three million abstracts for earlier years exist in book form. A team of editors peruse 12,000 international journals and 5,000 papers in every language to add 150,000 new entries a year. In general, about 20 years of abstracts fit on one CD-ROM. Ten subject-specific titles include AgEconCD, PlantGeneCD, CropCD and TreeCD, among others.

CABI also runs four research centres in the UK dealing with entomology, parasitology, mycology and biological control. These are augmented by five research stations in five other countries; CABI projects are being carried out in 50 countries world-wide.

The organization also produces numerous periodicals, some specifically targeted. Among these is *Agbiotech News and Information*, *Dairy Science Abstracts*, *Plant Breeding Abstracts* and *Plant Growth Regulator Abstracts*, to name a very few. A wide range of texts are also available.

Contact: CAB International, Wallingford, Oxon OX10 8DE, UK. Tel.: (01491) 832111 or Fax: (01491) 833508. (Source: *The Agbiotech Bulletin*, Vol. 2, Issue 6, October 1994)

Human frontiers

Scientists who are short of funds for basic bio-research could benefit from the Human Frontier Science Programme, an international organization with a secretariat in Strasbourg.

A number of countries, including Canada, France, Germany, Italy, Japan and Switzerland contribute to HFSP, supporting the organization's aim of promoting basic research in brain functions and molecular biology.

Selection of projects is by peer review, and the organization prides itself on being free from political considerations.

Since funding began in March 1990, 640 researchers have been awarded grants averaging $240,000 a year for three years.

Japan, the country initiating the organization, still provides 80 per cent of the $37 million annual budget, but North America and Europe each give 10 per cent. The Japanese, rather than diminishing their contribution, hope the other countries will increase their share.

HFSP is supporting projects around the world, and Ireland is among the eligible countries.

Scientists, such as Walter Gehring, whose group first described homeobox genes a few years ago, are among those to benefit from HFSP funding. Gehring's team in Switzerland is collaborating with scientists in Japan, the UK and the USA on the homeobox genes which control assembly of proteins into entire structures, such as a leg, head or tail. Homeobox genes for the same structures in different species are remarkably similar, and already the researchers have found that homeobox sequences functioned perfectly when transferred from chickens to mice.

Young scientists, who have obtained their doctorates less than five years ago, are encouraged to go international on HFSP fellowships, which provide $44,000 per annum for two years. With such fellowships, scientists, such as 30-year old Dr. Marina Picciotto from New York, can work in centres such as the Pasteur Institute.

The HFSP organization can be contacted at: Tour Europe, 20 place des Halles, 67080 Strasbourg, Cedex, France. (Source: *Lab-Tech*, April 1994)

Streamlining technology transfer

The factors that influence a technology's transferability include the way the technology is transferred, the technology's specific attributes, and the technology's readiness for transfer. Of these, the form of the transfer remains the key element in ensuring its success.

Basically there are three ways to transfer technology. The first is to transfer documentation that describes the process. This is the original philosophy behind published patents: it brings to the attention of outside researchers new ideas described by drawings and text. This is also the basis for "over-the-wall transfers" - transfers in which information is passed from one group to another without the benefit of direct involvement.

The transfer of technology through written sources is a large part of competitive information collecting - including industrial espionage. The transfer of ideas through the written word alone limits the ability of the receiving group to ask questions or gain immediate feedback on their level of understanding. It also limits the transferring group from helping to adjust the technology to the new environment.

The second method of technology transfer involves the cross training of personnel. For example, a member of the development group may spend time with factory workers in order to train them on a new piece of equipment. This type of interactive participation is usually more effective in terms of the rate of information and transfer. Because it provides direct interaction between the transferring group and the receiving group, misunderstandings on both sides about the use and application of the technology are quickly discovered and resolved.

The third method of technology transfer is to actually move personnel, which is believed by most students of technology transfer to be the most powerful form. For biotechnology this could mean the transfer of a manufacturing worker into development during the course of new process design or the transfer of researchers into manufacturing during the installation and start-up phases of a new process. The payoff in terms of building a learning organization can be tremendous.

Some consumer electronics manufacturers have already implemented this transfer method with outstanding results. A development engineer is sent into manufacturing at the time of process transfer. The engineer's mission is, in part, to relieve the manufacturing group of blame for failure. Problems that arise during the transfer of the process from development to manufacturing are development's responsibility - the development engineer present in the manufacturing shop accepts the blame. As a result, manufacturing is more willing to accept new technology - difficulties encountered during the transfer are worked out through on-site information exchange. (Extracted from *Bio Technology*, Vol. 12, September 1994)

Breaking away from the trend

Raising capital for biotechnology companies can be a problem. Many are forced to resort to equity finance because of the long-term nature of their work.

For any company starting out, regardless of which branch of industry it specializes in, raising capital can pose serious problems. For biotechnology companies in particular, the task becomes even greater due to their very nature as a "long-term investment". This means they are forced to rely almost exclusively on equity finance.

According to analysts, stock market interest in biotechnology company flotations has waned at the moment because, as one analyst put it, "institutional investors are disillusioned with them and the public are not well enough informed about them to want to invest".

In the USA, investors are better informed about biotechnology and therefore less conservative when it comes to investing in the sector, helped no doubt by the fact that some biotechnology firms have already started to "deliver". In the UK, to date, nobody has delivered but a lot of companies have products "in the pipeline and many are on track to deliver".

Getting to the flotation stage is also an uphill battle for biotechnology companies. How do they find financial backers when the rewards, when and if they do come, are long term? This means bank financing is out of the question so it is a question of "striking it lucky" with a very small number of sophisticated venture capital houses who back start-ups. However, a biotechnology company can increase its appeal to investors by having a well-developed science and a clearly defined market.

Partnerships with larger pharmaceutical companies are another possible means of raising capital but this can often spell the end for biotechnology companies as the bigger firms tend to take over in the long term. There is also a growing trend among pharmaceutical companies to seek partnerships with biotechnology companies in a bid to keep R&D costs down. (Extracted from *European Chemical News*, 27 June 1994)

Scientific visualization for biotechnology

Researchers and managers in biotechnology need more effective methods for manipulating, analysing and organizing the increasingly complex data generated by research, product development, clinical testing and other areas. Management of that data is becoming more difficult because of both the sheer volume and, more importantly, the new forms of integration needed to construct a meaningful picture of the work.

The ability to depict graphically a theoretical model or the results of an experiment on a computer is termed scientific visualization, which is sometimes called the "third way" in science, after theory and experiment. The gains in computing power and data manipulation during the 1980s and 1990s have given rise to the growing realization that scientific visualization may be yet another way to make discoveries in biotechnology.

To that end, many biotechnology researchers have exploited these capabilities in such areas as rational drug design, protein folding, genetic sequence analysis, molecular modelling and computational chemistry. However, the need for more fundamental data in biology and the even greater complexity of biological phenomena limit the scope of what can be done computationally.

Some progress has been made, but the answers remain unknown. However, the potential has been promising enough to have inspired at least two decades of research into different facets of scientific visualization.

The main advantage to using scientific visualization is the reduction of overwhelming volumes of biological data to sensible images. But the increasingly sophisticated modelling of living systems raises questions about which images to use and how to work with them. As computer-based research into biological structure-function relationships progresses and the volume of data grows, it is becoming clear to software developers that biotechnology is imposing its own set of demands on scientific visualization capabilities.

Effective modelling of living systems requires not only handling structure and dynamics but also adaptive phenomena. Thus there is a need to rethink how scientific visualization will be used for future research in biotechnology.

A group of software-based methods, termed advanced computing techniques (ACT), is the key to rethinking scientific visualization for biotechnology.

For example, the ability of a neural network to extract an ordered string of data embedded in a random string of data implies a capacity for extremely subtle discrimination. This capacity could be of great use in such biotechnology areas as nucleotide sequence analysis and protein folding.

Another example involves neural network models, used to assess heart attack victims, that have been shown to outperform physicians, especially when the clinical data for symptoms is incomplete.

ACT will help develop a way of thinking about complex biological problems that will provide the best tools for making R&D advances. When combined with scientific visualization, users will have an effective collection of tools.

Problems of greater complexity suggest greater ambiguity, and ACT appears to offer solutions, such as the ability of fuzzy logic to handle problems with overlapping categories and otherwise imprecise boundaries.

There are six major classes of functions associated with scientific visualization: arithmetic and geometry, statistics, transforms, image editing, graphs and data organization. While they started as separate areas of software development, in the last few years researchers' needs have brought them much closer together. Software suppliers are finding it increasingly necessary to combine different functions in one package, reflecting the importance of integration.

For a particular research problem, finding the optimal combination of ACT and visualization methods is important.

Many different standard methods of calculation besides ACT, such as statistical analysis, are used in biotechnology. They are not mutually exclusive. Rather, the research objective is to see if there are effective combinations that solve tough R&D problems more quickly.

There are many questions to answer about how to combine these two areas. A number of neural network models draw on statistical techniques and transforms. However, how that might be combined with contrast enhancements or subset images is an open issue.

In summary, scientific visualization is, conceptually, a work-space into which users introduce various tools. How well that work-space is used depends both on the skill of the users and the quality of the tools. The effectiveness of a tool can be considered in terms of how well it fits the problems, much as a wrench would fit a nut. The tools for this work-space, such as neural networks and fuzzy logic, are new and need to be tested and adapted for biotechnology problems. (Extracted from *Genetic Engineering News*, 15 June 1994)

World Bank bows to NGO pressure on control over genebanks

At a heated closing of the Second Session of the Intergovernmental Committee on the Convention on Biological Diversity, held at Nairobi in June 1994, 112 Governments unanimously called for the establishment of intergovernmental control over the genetic resources held in the genebanks of the International Agricultural Research Centres (IARCs). The germplasm collections, comprising almost half a million samples of crop biodiversity, were donated by farmers in developing countries and account for 40 per cent of the total world-wide unique collections of agricultural genetic materials. The legal status of these and all other existing *ex situ* collections were not included in the Convention on Biological Diversity, which sets new rules of equity in access to the world's genetic resources.

The International Agricultural Research Centres, which gathered the germplasm collections, are sponsored by the Consultative Group on International Agricultural Research (CGIAR), which is co-sponsored jointly by United Nations Food and Agriculture Organization (FAO), United Nations Development Programme and the World Bank.

Early in 1994, an agreement to establish intergovernmental authority over these collections was negotiated between the Consultative Groups and FAO, and was to have been endorsed at a meeting of the CGIAR in New Delhi, India, in late May. However, the World Bank blocked ratification of the agreement between CGIAR and the FAO, and announced that the Bank itself would provide leadership in this matter. Subsequently, Bank officials stated that they were holding separate discussions with the recently established World Trade Organization about the disposition of the group's germplasm and the intellectual property provisions in the General Agreement on Tariffs and Trade.

The Bank's move was brought to the attention of the Governments in Nairobi by some 40 major environment and development NGOs who wanted the Committee to ensure that control over these germplasm collections would be given to an intergovernmental body that is based on a one nation one vote system. At the end of the Nairobi meeting, over 50 countries took the floor to express their concern on this matter, which had come to dominate the two-week session. The Committee called specifically upon the United Nations Food and Agriculture Organization (FAO) to finalize an agreement with the CG Centres to grant the IARCs trusteeship over the germplasm "as soon as possible". (Source: *PANUPS*, 21 June and 8 July 1994)

Lost crops of the Americas

A portion from the sales of foods produced by Frieda's will be donated to support the development and awareness of indigenous crops of the Americas. Frieda's, a small California-based company that helps to conserve germplasm of native American crops by attempting to popularize them, is making an important niche for Latin American and Mediterranean foods in US supermarkets. The line called "Lost Crops of the Americas" features coquito nuts, black

and white quinoa, yuca root, blue and white posole, oca, jicama, blue and red cornmeal, cactus leaves, rattlesnake beans, white sapotes, pepinos, feijoas, cape gooseberries, and others. For additional information, contact: Ms. Bess Petlack, Communications, Frieda's Inc., 4465 Corporate Center Drive, Los Alamitos, CA 90720-2561 USA. Tel.: 1-714-826-6100, Fax: 1-714-816-0277. (Source: *Diversity*, Vol. 10, No. 4, 1994)

What role for RTOs?

Research and Technology Organizations (RTOs) are gaining a new focus as the European Union places an increasing emphasis on the exploitation and dissemination of EC-funded research. Transferring technology into the market has always been one of the core missions of these organizations, whose projects range over the development of technology to solve a problem for a single client (though it could equally be a multi-client group); adapting existing technology and transferring it from one industrial sector to another; consultancy on technological issues; and project coordination on an industrial, national or international scale.

RTOs also join with partners for cooperative work on a particular development project, often bridging universities, industries and public bodies. They run information services and seminars and some are concerned with training, instrumentation testing and certification.

RTOs have become an indispensable part of the knowledge-based industrial and commercial world that is taking shape on the threshold of the 21st century.

Many RTOs owe their origins to the research associations which were set up within specific industrial sectors, funded partly by member companies and partly by the Government. (Extracted from *BMT News*, November 1994)

C. COUNTRY NEWS

Albania

Dire conditions threaten rich genetic resources

Researchers returning from explorations into the previously forbidden Albania are expressing great concern about valuable germplasm collections that are in danger of eroding due to sparsely equipped facilities, poor seed storage conditions, and the lack of a cohesive national plant genetic resources programme.

Largely agricultural, Albania is one of the poorest countries in Europe. Among the crops Albania produces are wheat, maize and barley. Albania is reportedly rich in various old cultivars and landraces of vegetables, but sparse information makes the value of any holdings difficult to assess. It is a mountainous country with a relatively isolated population. The country is largely unexplored even by Albanian researchers, and explorers have only begun to delve into the nation's genetic resources. It is these decades of seclusion that now make Albania tantalizing to international researchers who simply do not know what they will now discover.

Observers believe the causes of genetic erosion in Albania give an immediacy to the need for foreign aid intervention. In addition to the inadequate storage facilities and what one observer called "the appalling conditions" of the collections, the newly found freedom of the citizens is also contributing to genetic erosion as areas are being abandoned as people move towards the city, leading to a rapid genetic erosion.

In 1993 the International Plant Genetic Resources Institute (IPGRI), in cooperation with the Central Institute for Genetic and Cultivated Plant Research in Gatersleben, Germany, the Germplasm Institute of Bari, Italy, and the Agricultural University in Tirana, the country's capital, organized and began a three-year project to collect germplasm and provide supplies.

In 1994 the United States Department of Agriculture (USDA) began enacting its first Memorandum of Understanding (MOU) with the plant genetics department of Albania's Agricultural University. The MOU states that the United States will store approximately 350 accessions of Albania's maize collection at the US National Seed Storage Laboratory (NSSL) in Fort Collins, Colorado. The accessions will consist of populations, inbreds and synthetic lines.

The USDA has also recently received the first seed index from an Albanian botanical garden.

In 1994, researchers in the IPGRI project conducted a two-part expedition with emphasis on vegetable, pulse and cereal crops. The scientists collected roughly 220 accessions of 67 different species from 36 sites. Among the samples collected was the ancient einkorn (*Triticum monococcum*), a hard wheat that is extremely rare. The next expedition focused on vegetables, according to Pietro Perrino, director of the Germplasm Institute at Bari and one of the participants in the explorations. There are more chances of finding genetic diversity among vegetables, Perrino says, as there are more family vegetable gardens.

During a two-week tour in Albania, an expert from USDA's Agricultural Research Service found the facilities dark, cold and badly in need of equipment. Researchers are lacking even basic information, such as books and scientific journals. Previous collections are limited with no updated and organized method to account for inventories. As part of the current project, IPGRI has furnished the Albanian facilities with some equipment, such as a computer, software and materials to dry and store seeds. There is also an urgent need for a national seedbank. The Italian Government has provided funds for conservation equipment that will improve storage conditions. The introduction of superior foreign cultivars will contribute to genetic erosion through the rapid replacement of currently cultivated materials, which could be lessened significantly through immediate construction and operation of a national seedbank.

From most reports, Albania's genetic resource problems go far deeper than scarce resources and collections. The country needs to look at the development of a comprehensive national programme. A national seedbank would emerge from a strong national programme on plant genetic resources.

For additional information on Albania, contact: Dr. George A. White, USDA ARS, Bldg. 003, Room 409, BARC-West, 10300 Baltimore Avenue, Beltsville, MD 20705-2350, USA. Tel.: 1-301-504-5328. Fax: 1-301-504-6305. (Extracted from *Diversity*, Vol. 10, No. 4, 1994)

Australia

Biodiversity plan

The Marion, Australia "Biodiversity Plan" is a conservation and ecological restoration programme aimed at preserving native habitat and rehabilitating all urban natural open spaces. Specific goals are to retain all existing natural communities and remnant native vegetation, to restore degraded natural communities, and to rehabilitate cleared areas. There is a series of ecological restoration and biodiversity preservation activities planned which includes conditions on development and coordinated action with adjoining jurisdictions. In addition, there are plans to educate residents about ecological restoration and biodiversity and to integrate natural habitats more intimately into community life.

Contact: Richard W. Atkin, Manager, Public Infrastructure & The Environment, City of Marion, P.O. Box 21, Oaklands Park, South Australia 5046. Tel.: +61-8 375 66 00. Fax: +61-8 375-66 99. (Source: *Initiatives*, 1994)

Wild pigeonpea germplasm

After the Indian subcontinent, the largest number of wild pigeonpeas are found in the northern parts of Australia. Some of these are endemic to Australia and are not found anywhere else.

Over the years, the Australian Tropical Forages Genetic Resources, an agency of the Commonwealth Scientific and Industrial Research Organisation (CSIRO), has assembled, evaluated and documented a world collection of *Rhynchosia*, a wild relative of pigeonpea, for utilization and conservation. This includes samples collected from Africa, South America and India.

In February 1994 a duplicate set of this entire world collection of *Rhynchosia* was transferred from Australia to ICRISAT Asia Centre. The 263 accessions arrived complete with passport and evaluation data. These wild relatives of the pigeonpea are an important source of such valuable traits as high seed protein and insect resistance. (Source: *SAT News No. 16*, 1994)

Canada

Biodiversity strategy nearing completion

Canada will soon have a strategy to protect its rich biological heritage, fulfilling part of a commitment made at the 1992 United Nations Earth Summit in Brazil.

The national Biodiversity Strategy was in part prompted by obligations in the UN Convention on Biological Diversity. The Canadian plan will set out the guidelines for using natural resources while maintaining biological diversity for the future. Federal, provincial and territorial governments will be responsible for implementing the strategy within the context of their local priorities and resources.

In a draft of the strategy prepared for public discussion in June 1994, several guiding principles were set out. Among them was that all life forms have intrinsic value and the best place to preserve them is in the wild. Canadians, being dependent on this biodiversity, have a responsibility to protect it. To do this, they should have a chance to understand and appreciate biodiversity and participate in the decisions that affect it. As well, development must be both economically and ecologically sustainable. Indigenous knowledge and methods should also be respected and maintained. Finally, conservation of biodiversity should be an international effort, with global cooperation.

The draft strategy itself lays out specific goals such as enhancing biodiversity preservation in resource-based industries such as agriculture, forestry and fisheries. Appropriate legislation and incentives to encourage behaviour that protects biodiversity is suggested, as is public education. Gathering and disseminating ecological knowledge, including that of indigenous peoples, is called for.

A wide range of people, from industry to government to academics and indigenous organizations have had input to the strategy. The draft version was intended as a chance for all Canadians to have a say. The final document was expected to be presented to the national, provincial and territorial ministers of the environment in late 1994.

Contact: Biodiversity Convention Office, 351 St. Joseph Blvd., 5th Floor, Hull, Quebec, K1A 0H3. Tel.: (819) 953-4374 or Fax: 953-1765. (Source: *The AGBiotech Bulletin*, Vol. 2, Issue 6, October 1994)

Canadian Government and industry agree to delay BST

Following an agreement between industry and Government, the sale or use of bovine somatropin (BST) in Canada will be delayed until 1 July 1995. According to a report released by the Minister of Agriculture in August 1994, a task force made up of members from industry, consumers and Government will use the time to assess recombinant BST's likely impact on the dairy industry, animal health and genetics, and human health. (Source: *Biotechnology Bulletin*, October 1994)

Reaching out to farmers in developing countries

Getting information on agricultural innovation to developing countries is a daunting task. Languages differ. Governments differ and communications services are often minimal. The Developing Countries Farm Radio Network overcomes these hurdles by enlisting the help of the people themselves. The network provides quarterly radio scripts to about 1,200 organizations in over 110 different countries. Rural communicators then add local content and translate them into one of over 200 different languages. At least 150 million people are reached each month.

According to Ms. Elizabeth Wilson, executive director for the non-profit network, suggestions in the scripts have proved useful in the developing world. Covering everything that affects farm families, from cooking and nutrition tips to crop protection, their aim is to promote sustainable development. Ms. Wilson says the challenges faced by farmers around the world demand a wide range of solutions. These may include something as simple as providing information on how to make compost, or more complex, like integrated pest management or how to use animal feeds for maximum milk and meat production. She says the agbiotech industry has a role to play as well. She welcomes information and suggestions.

Contact: Ms. Elizabeth Wilson, Developing Countries Farm Radio Network, Box 12, 40 Dundas Street, Toronto, Ontario, M5G 2C2. Tel. or fax: (416) 593-3752. (Source: *The AGBiotech Bulletin*, Vol. 2, Issue 6, October 1994)

China

"Biodiversity action plan" issued

China has unveiled a biodiversity action plan, to implement the 1992 Rio de Janeiro Biological Diversity Convention, of which China was a signatory.

The plan was drawn up by the State Environment Protection Agency (EPA), the State Planning Commission, the Ministry of Agriculture, the Ministry of Forestry, other ministries and the Chinese Academy of Sciences, and is the first national biodiversity protection plan aided by the Global Environment Fund.

Xie Zhenhua, director-general of EPA, said that sustainable development is at the core of China's strategy to conserve biodiversity. The strategy – a sustainable use of living things and a guarantee of a healthy cycle for the ecosystem – is expected to help create sound material and environmental conditions for a sustainable development of the national economy and society as a whole. He said that China would soon take some specific measures to ensure the fulfilment of the overall biodiversity protection plan.

China would first decide which places and species need the most urgent protection, set up a monitoring system and information centres on biodiversity, launch experimental projects to return artificially-bred species to nature, introduce a biodiversity appraisal system, establish special funds for biodiversity protection and expand international cooperation in this sphere.

Song Jian, state councillor and minister of the State Science and Technology Commission, noted that currently biodiversity is seriously endangered by the felling and burning of trees on a large scale, improperly reclaiming grasslands and wetlands, over-hunting of wild animals and over-gathering of wild plants, inappropriate use of pesti-

cides, destructive fishing and environmental pollution. He said China is one of the dozen "mega-diversity" countries in the world. It has some 2,340 kinds of land vertebrates, or 10 per cent of the world's total, and more than 300,000 species of flora, which ranks it third in the world. "In view of these facts, biodiversity conservation in China is of great international significance", Song stressed.

The Chinese Government has been consistent in its efforts to protect the eco-environment while developing its economy and eliminating poverty, he said. The newly-launched action plan, a set of guidelines for biodiversity conservation throughout China, will prove to be of great value in getting the whole of society to conserve the unique, rich and varied biodiversity of China. (Source: *Xinhua*, 13 June 1994)

Shandong plans biotechnological development zone

Weifang city, known as "the capital of kites", in east China's Shandong Province, has agreed to jointly establish a biotechnological development zone together with Beijing University.

The development zone will be China's first of its kind and will cover 5.1 sq km. The first phase of the development zone will cover 1.8 sq km.

According to local officials, priority in the development zone will go towards production of biological products, research in marine breeding technology, and development of bio-environmental protection technology. Some 50 biological high-tech enterprises will be established in the zone to produce biological products.

Wang Yiqiu, deputy president of Beijing University, said in Jinan, provincial capital of Shandong, that his university will build the biotechnological development zone into an experimental base for its personnel and technological achievements of his university, as well as a "window" for combining theory with practice.

According to him, his university will send 40 professors to help construct the Weifang Biotechnological Development Zone, in cooperation with 10 domestic biological research institutes across the country.

The university will also help establish Weifang School of the university's Biological Engineering College and a biological research institute and help train postgraduates and doctors of biology in the zone.

He added that the university will also be responsible for designing and introducing new technology, giving guidance in scientific research, reviewing of projects, developing products and training personnel of the zone. (Source: *Xinhua*, 12 August 1994)

Beijing to build international biotechnology centre

China plans to build an international biotechnology development centre in Zhejiang Province, East China, to boost the industrialization and scale of China's biotechnological development.

Situated between the banks of Xihu, or West Lake, in Hangzhou Bay, and Qiantang River, the centre will be constructed by Beijing Globe Biotechnology Development Centre affiliated with the Chinese Academy of Sciences. The new centre will dedicate itself to the development of new biotechnology products by closely watching the world's latest developments in research. (Source: *Xinhua*, 21 May 1994)

Chinese connection boosts canola yield

A new variety of Argentine canola that promises to increase yields by about 15 per cent will be used in Canadian fields in the spring of 1995, thanks to a joint Canadian-Chinese effort.

Scientists from the Agriculture Canada Research Station in Saskatoon, the Agriculture Commission of Shanghai and the International Development Research Centre announced the new hybrid, AC-H102, in July.

Researchers used genes from Swedish and Canadian plants and a Chinese pollen control system called Polima to develop the better-yielding variety, which also boasts increased blackleg resistance. (Source: *The IDRC Biotech Bulletin*, Vol. 2, No. 5, September 1994)

Tips for joint ventures in China

Nellie Cheng, B.C. Trade Manager for China, Hong Kong and Taiwan, writes in *The B.C. Exporter* that setting up shop in China usually means a joint venture. This is something that can take time and patience to set up. Prepare a list of questions and get them answered from as many different angles as possible. The first question to answer is what your Chinese partner understands "joint venture" to mean.

Expect land, buildings, labour and some cash flow. The western partner is expected to bring equipment, technological expertise and some start-up funds.

Next, make sure a joint venture is worth your while. Tax incentives, low labour rates and a massive market – about a quarter of the world's population – are enticing. However, labour costs in relation to productivity and the hidden costs of social benefits (e.g. housing and schools) must be factored in. Also, to put things in perspective, ask your potential partner what incentives he is being offered.

Select your Chinese partner carefully. It takes time to apply for and receive permission for a joint venture, as well as knowledge about how the system works. A good local partner will be knowledgeable in this respect, as well as being a good manager and aggressive marketer when the venture is up and running. Because you will have to rely on the partner to look after your interests, be sure to sign up with someone you can trust. (Source: *The IDRC Biotech Bulletin*, Vol. 2, Issue 5, September 1994)

Denmark

Denmark opposes genetic crops

Denmark has raised objections to the marketing of herbicide-tolerant genetically modified rapeseed in Europe. The country is requesting that EU-wide marketing approval be denied until a full assessment of the long-term environmental impact of releasing genetically modified rapeseed crops has been carried out – which could take many years.

The Belgian company Plant Genetic Systems (PGS) won marketing approval from the UK authorities for a genetically modified rapeseed tolerant to the Hoechst herbicide *Basta* earlier in 1994. Application is now required to be submitted to other member States for comment before the rapeseed can be marketed across the EU.

Denmark's concern stems from the fact that rapeseed becomes a weed if in subsequent years a field is planted with a different crop and farmers may then resort to more even stronger or multiple herbicides.

The issue is to be referred to a committee of experts from the member States, which will make its decision by quality majority. (Extracted from *European Chemical News*, 24 October 1994)

Egypt

Progress towards biosafety regulation in Egypt

One approach to developing a biosafety system can be illustrated by the activities currently under way in Egypt. The population of Egypt is expected to grow to about 70 million by the year 2000, and swell to 110 million by the year 2025. The Egyptian Government is faced with the task of bridging the food gap and fulfilling the goal of self-reliance. Simply placing more land under cultivation will not solve this problem. Increasing the agricultural land base from the present 7.4 million to 14 million feddans would satisfy only half the land requirement for the current population of 60 million. Modern biotechnology research methods offer new approaches to agricultural sustainability that will meet human requirements and enhance the environment.

The Agricultural Genetic Engineering Research Institute (AGERI), within the Agricultural Research Centre (ARC) of the Ministry of Agriculture, is the primary institute that deals with biotechnology in Egypt. AGERI's research projects have now reached the stage of evaluating genetically modified organisms in a containment greenhouse that began construction in 1994 as part of an AGERI ABSP agreement with the University of Arizona. Existing regulations in Egypt do not include guidelines for handling transgenic materials under contained conditions nor do they cover the release of GMOs into the environment. Thus, there is a critical need to build a national biosafety policy that could regulate such articles.

Recently a National Biosafety Committee (NBC) was formed, consisting of representatives from the Ministries of Agriculture, Health, Industry, Education, Sectors of Environmental Affairs and Scientific Research. The NBC also includes members from the private sector, non-technical members that represent community interests, and policy makers. To formulate a biosafety system for Egypt, the first step is gathering information from different nations on their regulations, guidelines and system designs. A draft document, entitled "The Establishment of a National Biosafety System in Egypt: Regulations and Guidelines", will be submitted to the NBC in the near future. The draft incorporates information on the structure, composition and activities of both national and institutional biosafety committees.

In Egypt, as in other developing nations, a national biosafety system will ensure the safe development of biotechnology products and facilitate collaborative research activities with other countries. (Source: *Bio Link*, Vol. 2, No. 2, 1994)

European Union

Call for eased biotechnology rules

The EU Industry Council, under the presidency of German economics minister Gunther Rexrodt, has called for an improvement in the business environment and competitiveness for biotechnology in Europe.

Specifically, the Council is seeking a reduction in administrative procedures, a review of the legal framework and greater public debate on the ethics of biotechnology.

Given the technical and scientific progress made in recent years, Rexrodt reported that the majority of States have agreed to ask the Commission to re-examine the existing regulations with a view to possibly easing restrictions and administrative constraints placed on the industry and users of biotechnology. But he stressed that any simplification must not lower safety levels.

EU policy should also provide greater encouragement for the development of small and medium-sized biotechnology businesses, he said, and compilation of biotechnology statistics should be facilitated. (Source: *European Chemical News*, 10 October 1994)

EU plans to streamline GMO regulations

The European Union's (EU, Brussels) European Commission (EC)—the EU's regulation-drafting body—is preparing to streamline the regulations governing the contained use of genetically modified organisms (GMOs) and the deliberate release into the environment of GMOs.

The EC plans to implement a two-track approach to ease current GMO regulations. Overall, the approach should allow some parts of the current regulations to be changed with a minimum of fuss on the basis of a substantially increased understanding of the risks associated with the use of GMOs. The EC states that, through one track, it will exploit "existing possibilities for revising measures procedures degree of oversight requirements through the use of the light procedure of adaptation to technical progress" and that, through a second track, it will bring "forward amendments to existing legislation in order to incorporate changes which cannot be achieved by technical adaptation, while leaving the basic structure of the framework intact".

Concerning the contained use of GMOs, the EC wants to ease the administrative notification consent requirements, where such easing does not compromise safety. It also wants to redefine the risk categories of GMOs and revise the guidelines for classifying GMOs. Furthermore, the EC believes that there may be scope for lightening consent requirements when GMO experiments involve activities now known to present low risks to human health and the environment. "This would allow a greater focusing of attention on higher-risk possibilities", notes the EC. It plans to add a number of specific amendments to the contained-use directive, including:

- For certain low-risk activities, replacing consent requirements by record-keeping or notification for information purposes;
- For certain higher-risk activities, replacing explicit consent requirements by implicit consent;
- Reducing the time periods involved in such consent procedures;
- Removing the differentiation between activities in research laboratories and those in production plants.

Changes are already under way to the directive on the deliberate release of GMOs into the environment. However, the EC recognizes that further streamlining of the directive might be needed, and it has pledged to conduct a further review of the directive during the first half of 1995. (Extracted from *Bio Technology*, Vol. 12, September 1994)

Germany

Biotechnology in Bavaria

As part of a scheme to promote innovation, Germany's southernmost federal state, Bavaria, has announced plans to establish a centre for biotechnology at Martinsried, near Munich. Dubbed "Offensive Future of Bavaria", the scheme will also aid the set-up of new high technology businesses.

Funding for the biotechnology project, which is to be "unique in Germany", will be raised by the sale of government-held shares in companies.

The centre, to be built on the grounds of the Max Planck Institute for Biochemistry, will provide facilities for 30-40 biotechnology firms. The centre's link to the Max Planck Institute, an established biotechnology think-tank, "could attract research-oriented companies" to southern Germany. It would therefore provide "a catalyst for innovation" to smaller firms, who would otherwise not have any access to the required specialized skills and information.

Bavaria's biotechnology "offensive" also plans to provide DM 150 million to create a German venture capital firm to fund biotechnology companies and "other key technologies". (Source: *Chemistry & Industry*, 3 October 1994)

Biotechnology in Germany—another view

Industrial biotechnology in Germany has been badly mauled by a tight regulatory regime. German companies are searching for a friendly biotechnology environment and are investing heavily in the United States.

Germany has always been a front runner in the chemical and pharmaceutical industries, but it has effectively shut the door on biotechnology by developing some of the world's strictest regulations covering genetic engineering. Some industrialists regard this as an overreaction that has its roots in the history of the Nazi eugenics and genocide programme. Tough regulation has diverted German investment dollars to the United States on a large scale.

German firms now trail their US rivals and are walking away from a lucrative market. By 1995 the whole range of biotechnology drugs, including those produced via genetic engineering, will reach $19 billion in sales. The world market for genetically engineered pharmaceuticals is expected to reach almost $100 billion by the year 2000. Even recent improvements to Germany's gene law will not bring back production and research that has already moved abroad. (Extracted from *Genetic Engineering News*, 15 September 1994)

Hungary

More western investment for Hungarian biotechnology

A significant number of western companies are targeting the Hungarian bioindustry for investment and collaborative ventures. The latest pharmaceutical manufacturer to join their ranks is the Canadian company Novopharm who, under the Hungarian Government's privatization programme, has just purchased a 15 per cent share of the Godollo-based Human Serum and Pharmaceutical Company. The Hungarian Government is to remain the majority shareholder.

The Human Serum Company, with 950 employees, is Hungary's largest producer of vaccines and also specializes in insulin, injectables, blood and sterile products and infusions. Novopharm had already formed a joint venture Humanpharma with the Hungarian company in 1992 to manufacture pharmaceuticals for domestic use and export.

One of the main reasons for the continuing interest of western companies in acquiring such production facilities is the success of the Hungarian bioindustry, relative to the rest of eastern Europe, in achieving good manufacturing practice. The other prime consideration is Hungary's access to the markets of the former Soviet Union where doctors and patients remain familiar with products supplied by the Hungarian pharmaceutical industry. (Source: *Microbiology Europe*, Vol. 2, No. 4, July August 1994)

India

DNA fingerprinting in India

The field of DNA fingerprinting is vibrant in India. Pioneering work in the area has come from the Centre for Cellular and Molecular Biology (CCMB), located in Hyderabad in the state of Andhra Pradesh. CCMB is a constituent laboratory of the Council of Scientific & Industrial Research, New Delhi. Dr. Lalji Singh of CCMB had earlier identified and developed a particularly ubiquitous repeat sequence in the form of a minor satellite DNA. Originally isolated from the Branded Krait snake, this is referred to as the Bkm sequence or the Bkm probe. Shortly after its identification, Singh and co-workers were able to confirm its presence in a very large number of species and organisms, both from the plant and animal kingdoms. Soon after its identification, CCMB scientists were able to apply it as an excellent probe for DNA fingerprinting. The very first was in a case that involved disputed parentage of a child and the state court decided on genetic identification. It is to be said to the credit of the Indian judiciary that a series of lectures and promotional articles written by CCMB people persuaded several judges to allow DNA fingerprinting as a corroborative evidence. To date the CCMB scientists have helped in close to 150 court cases through their DNA typing as evidence.

More recently, DNA fingerprinting has also been taken up as a method by the Central Silk Board of India who wishes to type and pedigree silkworm races through a collaboration with CCMB, and the Zoo Authority of India has entered into a similar agreement for the use of DNA fingerprinting for wild life management and for determining the pedigree and parentage of many an endangered species including the royal Bengal tiger and the Indian lion. A few months from now the Department of Biotechnology, Government of India, is setting up a Centre for DNA Fingerprinting and Diagnostics (CDFD) at Hyderabad. CDFD will have close collaborative and organic links with CCMB and will operate in the first year at the premises of CCMB, subsequent to which it will be housed in its own campus, five minutes away. CDFD will be involved in providing fingerprinting services to the judiciary, the medical community and other professional bodies and will also be involved in R&D efforts associated with its charter. (Source: *Biotechnology Newsletter*, Vol. 4, No. 5, October 1994)

Indonesia

Indonesian agricultural biotechnology

Indonesia's approach to biotechnology has been to split it into three streams handled out of separate inter-university centres: University of Gajah Mada (medical biotechnology), Badung Institute of Technology (industrial biotechnology) and Bogor Agricultural University (agrobiotechnology). Starting in 1986 from zero - no staff, no facilities, no reference materials - the centres grew into functioning entities.

The Bogor group is working on plant tissue cultures, particularly for micropropagation. It is also investigating ways of enlarging and improving the local pool of soybean varieties. Investigations of *bacillus thuringiensis* (bT) for use as a bioinsecticide on local pests are under way, and research on *mycorrhiza* has been carried out. Embryo transfer in cattle is being developed, as well as work in fermentation technology.

On another tack, the Agency for the Assessment and Application of Technology established three centres for advanced biotechnology, again along medical, industrial and agricultural lines. The Centre on Agricultural Biotechnology is located in the Research and Development Centre of Food Crops of the Ministry of Agriculture. The Indonesian Companies for Estate Crops has also established its own research centre. The two facilities are focusing on improving food crop varieties and estate crops, respectively. (Extracted from *The AGBiotech Bulletin*, Vol. 2, Issue 5, September 1994)

Japan

Agriculture Ministry to develop clinical kits

Starting in fiscal year 1995, the Ministry of Agriculture, Forestry and Fisheries will launch a research project to develop rapid inspection methods for analysing the genes that encode plant and animal pathogens and possibly develop vaccines against them.

The project will develop "clinical kits" for plants and animals that screen out genes for diseases and toxins which will be used by quarantine stations, seedling producers and livestock farmers. Current inspection methods often require considerable time in laboratories to confirm the presence of, for example, mosaic virus in cucumbers or salmonella in meat products. Imported agricultural products can spend from 10 days to two weeks passing through quarantine inspections. Research will focus on toxic genes that induce pathogenesis and characterizing genes that stimulate infection, invasion or proliferation and other genes responsible for infecting specific hosts. (Source: *McGraw Hill's Biotechnology Newswatch*, 19 September 1994)

Revised DNA experimental procedures

The Science and Technology Agency announced a revision in the application of recombinant DNA experimental procedures, which for the first time will permit environmental release of recombinant animal species.

Six other countries including the United States, Belgium, France and Argentina now permit raising 15 categories of recombinant species, excluding rats and mice, out of doors. For the most part the experiments involve live vaccines in domestic farm animals, but two protocols cover higher orders of animals.

The new Japanese standards specify that the number of animal species involved in outdoor experiments must be limited to the minimum necessary, provisions must be made to prevent escape from rearing areas, excreta from the experimental animals must be detoxified and burned, and similar restrictions.

Before outdoor experiments can proceed, such safety measures must be inspected for approval. The provisions are viewed as a preliminary to conducting totally open system experiments with recombinant animal species in Japan. The Agency took similar measures for recombinant plant species in 1988. (Source: *McGraw Hill's Biotechnology Newswatch*, 5 September 1994)

Report calls for more brain R&D

The Japanese Council for Aeronautics, Electronics and other Advanced Technology submitted a report to the Science and Technology Agency on policies needed to promote the comprehensive research and development that will form the basis of furthering understanding of brain and neurological functions. About 9 per cent of Japan's population suffers from cranial nerve and psychiatric disorders and the nation spends over US$ 40 billion annually to treat the conditions. Further, statistics indicate that the situation will continue to worsen.

The Council indicated that the most important areas for research include:

- Searches for neurotransmitters and gene-level analysis;
- Discovery of factors mediating differentiation and genesis of nerve cells;
- Anatomical designation of functional positions;
- Elucidation of repair mechanisms for impairment of cerebral and neurological systems; and
- Development of new laboratory models such as animals with specific genetic defects.

The report indicated that funding of research to elucidate brain functions by Japanese research institutions is only 5 per cent of the amount spent in the United States. The Council stressed that research methodologies and researchers must move freely among industry, academic and government institutions and participate more actively in cooperative international research efforts.

In other areas, the advisory body called for rapid expansion of such databases as the human genome data network and improvements in peripheral support technologies such as medical equipment and instrumentation. (Source: *McGraw Hill's Biotechnology Newswatch*, 18 July 1994)

Malaysia

Malaysia recognizes role for biotechnology

In its drive to reach developed nation status by the year 2020, Malaysia has recognized the potential of biotechnology for economic development.

The Malaysian National Council for Scientific Research and Development has taken steps to stimulate the industry, largely through R&D funding efforts. Through the Intensification of Research in Priority Areas (IRPA) programme, biotechnology has been getting a healthy slice of the pie - 30 to 40 per cent from 1991-1995.

Of total R&D funds, agriculture received 46 per cent (reflecting Malaysia's agriculture-based economy). Of the remainder, industry received 28 per cent, 13 per cent went

to strategic, 10 per cent to medical and 3 per cent to social science research.

The Government has also set up the Malaysian Technology Development Corporation, a joint venture with industry aimed at commercializing technologies developed domestically or imported from abroad. Several national working groups have also been set up to explore emerging technologies in the areas of biotechnology, advanced materials, advanced manufacturing and energy and microelectronics and information technology.

The biotechnology group has been active since 1987, involved in funding research, organizing national seminars and training courses and arranging the publication of the journal, the *Asia-Pacific Journal of Molecular Biology and Biotechnology*. (Source: *The AGBiotech Bulletin*, Vol. 2, Issue 5, September 1994)

Mexico

Conservation monitoring centre studies genetic resources

The World Conservation Monitoring Centre is undertaking a study of *in situ* conservation of plant genetic resources of Mexico and Central America. The project, a collaboration with the Mesoamerican Plant Genetic Resources Network (REMERFI) and the Smithsonian Institution, aims to coordinate information and expertise from inside and outside the region, linking the plant genetic resource sector with other agencies of biodiversity conservation. For additional information, contact: Harriet Gillett, World Conservation Monitoring Centre, 219 Huntingdon Road, Cambridge CB3 9JG, England. Tel.: 44-223-277314; Fax: 44-223-277136; E-mail: plants *a* wcmc.org.uk. (Source: *Diversity*, Vol. 10, No. 3, 1994)

New breed of tropical maize

The International Maize and Wheat Improvement Center (CIMMYT) in Mexico has developed new breeds of tropical corn that can produce a 40 per cent larger harvest in hostile environments. The new varieties of maize were created to solve two problems maize-growers have continually encountered in tropical regions around the world periodic droughts and highly acidic soils. CIMMYT believes that, if used properly, the new strains of maize could feed an additional 50 million people per year in developing countries. The strains will help to preserve the environment since farmers will be able to use their formerly unproductive lands instead of having to clear away rain forests and other delicate tropical lands. For more information, contact: Mr. Heinrich von Loesch, CGIAR, World Bank, 1717 H Street, NW, Room J, Washington, DC, 20006, USA. Tel.: 1-202-473-8913, Fax: 1-202-334-8750. E-mail: hvonloesch *a* worldbank org. (Source: *Diversity*, Vol. 10, No. 2, 1994)

Nepal

The Biodiversity Unit

The Asia Network for Small-Scale Agricultural Biotechnologies (ANSAB), an international non-governmental organization headquartered in Kathmandu, Nepal, with the support of the Ford Foundation, IDRC and ATI, has recently initiated the operation of a special group within the Asia Network. The Biodiversity Unit. The Biodiversity Unit will focus on assisting communities and development practitioners to sustainably utilize non-timber forest products (NTFPs) while conserving their ecosystems in Nepal and other countries of the Himalayas. Through the integration of the socio-economic, biological and commercial aspects of natural resource control, extraction and sale, the Unit will promote a holistic approach to the development of rural incomes and communities while protecting the environment.

The Biodiversity Unit has the capacity to implement its own research and development activities, as well as work with individuals, government, NGOs, academic and foreign donor agencies to coordinate and promote applied field research and development of non-timber forest products, biodiversity conservation and resource management. Currently, the Biodiversity Unit is collaborating on a pilot project to strengthen the institutional capacity of communities and resource user groups to control and enhance the commercial utilization of their natural resources as a strategy to promote economic development while conserving the existing biological diversity in Humla district, Nepal. The Unit will also make funds available to researchers and project implementors to financially support timely applied research on issues related to the conservation and sustainable utilization of biological resources.

The objective of the Biodiversity Unit-funded research will be to clarify issues and obtain information that is needed in order to increase the understanding of biological diversity in Nepal. The Biodiversity Unit will give priority to research that is applied, involves field work and employs the underlying premise of the programme, e.g., the sustainable harvesting and local commercial processing of NTFPs as a strategy for promoting the conservation of the environment. This will ensure that essential research is conducted to bridge gaps in the overall body of knowledge of Nepal's biological resource base. Work completed under the auspices of the fund will have direct relevance and application to the communities of the study areas and be disseminated on the national level for use by policy makers and practitioners.

Suggested focus areas for support by the research fund could include:

- Indigenous systems and practices for resource utilization and management;
- Forest and pasture management system across a variety of biomes in Nepal;
- Community control structures for NTFP resources;
- Institutional issues surrounding the development, use and management of natural resources;
- Trade patterns, market channels and the interaction of the participants in these activities;
- Volume of trade and the distribution of benefits;
- The relationship between economic and environmental sustainability;
- Methods of adding value to NTFPs; and
- Increasing and or augmenting productivity through managed propagation and other technological interventions

In addition, the Nepal NTFP Network (NNN) will strive to promote the sustainable development, use and management of non-timber forest products as a strategy for promoting biodiversity conservation. It is a forum for individuals and institutions to obtain, study and compare research findings, as well as disseminate information for the advancement of national and international understanding of the importance of biological diversity and the ass-

tainable utilization of the benefits that result from wild plant resources.

The Nepal NTFP Network will be assisted by the Biodiversity Unit to identify areas in need of investigation, review grant requests and critique and disseminate reports resulting from research activities. The Biodiversity Unit will also assist Network member applicants in acquiring other research support and in the preparation of grant applications, in getting their work published in relevant journals, disseminating Network-generated information through a newsletter, and publishing a collection of the works by Network members.

For additional information about the Biodiversity Unit, the Research Fund and grant application procedures, as well as the Nepal NTFP Network (NNN), please contact: Dr. Nirmal Kumar Bhattarai, Research Director, Biodiversity Unit, ANSAB, P.O. Box 16, Lazimpat, Kathmandu, Nepal. Tel.: 977-1-411964; Fax: 977-1-411859. (Source: *ANSAB Newsletter*, 1994)

Philippines

Ciba to supply free technology to Philippines

In an example of technology transfer, Ciba-Geigy is providing proprietary technology free of charge to an agricultural project based in the Philippines.

Ciba Seeds has signed an agreement with the International Rice Research Institute in Manila offering its gene constructs *Bacillus thuringiensis* for use in rice and free distribution of the resulting rice varieties in developing countries.

The Bt-gene constructs code for a protection protein that, when present in plants, protects it against certain insect pests.

The agreement enables the Institute to use the gene in its own research and the development of rice varieties with improved resistance to pests such as the yellow stem borer. (Source: *European Chemical News*, 31 October 1994)

Russian Federation

Russia enters world biotechnology market

The Russian Ministry of Science has named three institutes as centres of excellence in an attempt to enter the world market in biotechnology. These are the State Scientific Centre for Virology at Novosibirsk, and for Applied Microbiology at Oblensk (both were off-limits to outsiders until recently), and the Debabov Institute in Moscow. The Government is to increase the budgets of these centres.

Despite the optimism surrounding Russia's big push in biotechnology, there are huge obstacles to overcome. Most of Russia's 200 or so research institutes and factories dedicated to biotechnology are desperately short of money and equipment and, as in other areas of science, talented researchers are leaving to join western biotechnology companies, or moving to more lucrative jobs outside science.

Another problem is that Russian plants making antibiotics and vaccines do not meet western standards of hygiene. As a result, manufacturers can only sell their products in developing countries, or for use by vets.

The biggest problem is probably the public opposition to biotechnology. The Russian public tends to associate biotechnology with the huge factories that turn out animal feeds made up of protein-rich micro-organisms such as yeasts. In 1988, news emerged that people living in towns around the dozen or so factories had complained that inhaling the tiny particles of yeast released from the plants was making them ill. In the town of Kirishi, 200 kilometres from St. Petersburg, these emissions were blamed for the deaths of 12 children and a local incidence of asthma running at 10 times the Russian average.

The Institute of Applied Microbiology. Formerly known as Biosintez, the Institute of Applied Microbiology (IAM, Oblensk, Russia) has been described as the engine-room of Russian fermentation. It has a high containment facility, and many of its 1,000 scientific staff are focusing on improvements to gamma interferon production.

IAM intends to produce recombinant insulin in collaboration with a plant in Stepnagorsk. It has constructed a biofilm reactor on a 2,500 cubic metres day scale to treat liquid wastes containing nitrophenol, methanol, organic chlorides and acetone. It also produces some 100 tons year of dry nutrient media which is supplied throughout Russia.

IAM is no stranger to foreign industrial partners. It has previously worked with Merck Sharp & Dohme, Lederle, Hoechst and a number of South-East Asian companies. IAM is currently working with a Vietnamese organization to construct a factory to produce plant protection agents, while collaboration on transgenic animals and plants has been established with an unnamed German company. A toxicology centre is being established, and part of the Institute is being privatized.

The Debabov Institute. Formerly known as Nil Genetika, the Debabov Institute was founded to supply producing strains to industry; now, it is becoming a federal centre for applied science. It receives 40-50 per cent direct State funding with the remainder coming from industry and grants.

It has a pilot plant of 500-litre capacity, which is principally used to investigate the production of low volume high value products. It has established a small internal enterprise, called Teknobik, to use the pilot plant on a commercial basis. Main areas of work and research at the Debabov include amino acids, vitamins, enzymes, pharmaceutical proteins, bioremediation and plant protection.

The Institute has a good collection of yeast strains for the production of leucine, valine, isoleucine and other amino acids; it produces riboflavin and some other commercialized nucleotides, while strain selection procedures have been used in connection with the production of proteases, metalloproteases, thermostable alpha-amylases and beta-galactosidases.

For example, a genetically modified *Bacillus amyloliquefaciens* has been used to make thermostable alpha amylases for the food and textile industries. Using a strain of *Rhodococcus* with high hydratase activity, a process for the bioconversion of nitriles has been developed, involving the production of acrylamide by enzymatic hydration of acrylonitrile.

GMOs are being used to make interferons and interleukins and it has a small group working on monoclonal antibodies. Processes have been developed by the Institute for the treatment of detergents, phenol and oil. *Bacillus thuringiensis* is currently being fermented on a large scale and used successfully in field trials against colorado beetle. (Extracted from *New Scientist*, 28 May 1994 and *Outlook on Science Policy*, June 1994)

Russia set to launch State biotechnology programme

At the request of the Government, a group of Russia's leading biotechnologists, drawn from the academic and industrial sectors, has been engaged for the past 12 months in drawing up a new *State Programme for the Development of Biotechnology During the Period 1994 to 2000*. This focuses on several main areas of the Russian bioindustry that should receive State support, including the development of microbial biomass production (based on methanol and ethanol) for human consumption. The eventual aim is to produce 2 million tons per annum of such high-protein biomass that could then be incorporated into traditional human foodstuffs. Other parts of the programme are devoted to the application of biotechnology in the pharmaceutical industry and agriculture.

To implement this programme, the Committee of the Russian Federation on the Chemical and Petrochemical Industry's Main Administration for Biotechnology, headed by Dr. Villen Matveev, has drafted a decree for the Russian Government, *Concerning the Priority Development of the Biotechnology Industry*. This seeks major State backing for industrial biotechnology in Russia and the implementation of a range of privileges, including a favourable tax regime, relaxation of customs duties, and allocation of regional budgetary resources to local bioindustries. Moreover, the decree also envisages tax breaks for domestic and foreign banks and companies investing in the Russian biotechnology industry. If, as expected, the Government adopts the new programme and its attendant incentives, biotechnology could soon become one of the most rapidly expanding sectors of the Russian economy.

Further details from Dr. Anthony Rimmington, Centre for Russian and East European Studies, School of Social Sciences, The University of Birmingham, Edgbaston, Birmingham B15 2TT, UK. (Source: *Microbiology Europe*, Vol. 2, No. 5, September October 1994)

Taiwan Province of China

Taiwan pushes into Viet Nam

Taiwan Province of China is beginning to develop trade into the formerly closed markets of Viet Nam and Russia, according to a report in the journal *Foreign Trade*.

With $1 billion in the market so far, the island is the largest foreign investor in Viet Nam. However, being first has its headaches, such as the inability to own 100 per cent of any business. Bureaucratic hurdles have also been a problem: only one Taiwanese financial institution has managed to set up a branch office so far. The Vietnamese Government has since moved somewhat, giving priority status to future branch office applications and giving Taiwan the go-ahead to set up Chinese language schools.

Taiwan has also developed a flourishing trade with Russia, selling $71 million into the country while buying $638 million, mostly in raw materials such as gold, aluminium and steel.

Half of Taiwan's foreign trade is with the United States, Japan and western Europe, however a full 8 per cent is with China (through Hong Kong, direct shipments are forbidden).

At home, Taiwan enjoys a thriving export market (up by 4.3 per cent in 1993) and an expanding economy (10 per cent annually from 1981-1991). (Source: *Asia Biotech Bulletin*, Vol. 2, No. 5, September 1994)

United Kingdom

Britain's culture collections

Culture collections store living samples of microbes in "suspended animation", both to conserve biodiversity and as a resource for research and industry. However, Britain's collection – scatteredover 11 sites and funded by a complicated tangle of industry, government departments and research councils – needs urgent coordination if it is to survive, says the independent working group commissioned by the Office of Science and Technology.

The collections contain around 42,500 samples, making them among the most comprehensive in the world. The working group recommends bringing all 11 collections under the aegis of the Biotechnology and Biological Sciences Research Council (BBSRC), whose budget would be expanded.

Presently, industry supplies between a third and half of each collection's funds, buying samples and services; public funds make up the rest. Any – or all – of the five government department sponsors could cut their funding under the current shake-up of public sector research in the United Kingdom.

The collections should also be concentrated on fewer sites, the report says. They should share a common catalogue, database and marketing strategy, improving their links with each other and helping industry to find the information it needs.

There are three main culture collections in the United Kingdom: the International Mycological Institute (IMI) in Surrey, which holds fungi, yeasts and plant bacteria; the European Collection of Animal Cell Cultures (ECACC) at Porton Down, which includes cell lines from people with inherited diseases; and the National Collection of Industrial and Marine Bacteria (NCIMA) in Aberdeen. Eight smaller centres specialize in microbes such as pathogenic bacteria, brewing yeasts and wood-rotting fungi. (Source: *Chemistry & Industry*, 21 November 1994)

Coventry University expands into biomedical technology transfer

Coventry University's School of Natural and Environmental Sciences has set up a biomedical and technology transfer and business information service called Biophoenix intended for clients, including medical diagnostics companies, exploring the potential of technologies such as gene probes, pharmaceutical executives needing to keep abreast of market developments in their field, and companies wishing to offer customized market research in these areas.

Scientists at Biophoenix have carried out analyses of the markets for gene probe diagnostics, immunoassays, *in vitro* cancer-related tests, hormone-related tests, biotechnology pharmaceuticals, allergy tests and the treatment of obesity. (Source: *Genetic Engineering News*, 15 June 1994)

United States of America

Report cites Federal laboratories as leaders in biotechnology transfer

US Government laboratories take first place in technology transfer in the biomedical, biotechnology and pharmaceutical areas, reports a new study. Federal laboratories, including the Public Health Service (PHS) and its main

component, the National Institutes of Health (NIH), are number one in inventions available for licensing, patents received and patent applications pending, inventions that have been licensed out and therapeutics in active development (both in terms of those licensed out and those being developed internally).

According to the *Federal Bio-Technology Transfer Directory*, published by the Biotechnology Information Institute (BII, Rockville, MD), PHS and NIH are: (1) the US biotechnology and pharmaceutical industries' leading source for new technologies, introducing new products and broadly enabling technologies; (2) the leaders in collaborative research and development with the biotechnology and pharmaceutical industries, including therapeutics in development and clinical trials; and (3) the source for many products and technologies in the market-place.

Federal agencies and laboratories have received patents for 2,100 biomedical, biotechnology and pharmaceutical inventions from 1980-1993. PHS (with 60 per cent) and NIH (with 49 per cent) are the leaders among federal agencies.

Biotechnology is involved in the majority of federal technology transfer. This includes over 50 per cent of inventions; about 70 per cent or more of patent licences granted; and 60 per cent of collaborative research and development arrangements (CRADAs). (Extracted from *Genetic Engineering News*, 15 September 1994)

Technology transfer by technologies/uses[1]

Technologies/uses	Patents	Applications	Licences[2]	CRADAs
Drugs Chemical	661	359	312 (137)	227
Biologics Biotechnology	480	606	734 (138)	300
Apparatus Devices	386	118	121 (45)	114
Recomb. DNA Gen. Eng.	126	353	308 (67)	127
Genes-Cloned Seq.	101	331	267 (63)	82
Antibodies	148	176	325 (46)	58
Therapeutics	679	600	669 (200)	332
Diagnostics	534	413	564 (88)	172
Cancer	186	162	240 (67)	61
Therapeutics	151	126	213 (55)	46
Diagnostics	70	81	137 (26)	13
Infectious diseases	279	349	423 (82)	179
Viral Antiviral	136	240	329 (63)	110
HIV-infection	56	122	178 (34)	46
Therapeutics	50	106	166 (33)	45
Diagnostics	26	42	23	3
Radiopharmacy	119	37	92 (23)	32
Screening (drugs)	63	129	164 (33)	29
Clinical trials stage	68	46	141 (75)	153

Source: *Federal Bio-Technology Transfer Directory*

[1] Inventions and CRADAs are indexed with as many technologies uses as are relevant.

[2] Total number of invention licences followed by number of exclusive licences in parentheses.

Bio Science builds biotechnology centre in Baltimore

Bio Science Contract Production Corporation has broken ground for a new biotechnology centre in Baltimore, Maryland. The company, which designs and builds good-manufacturing-practices facilities for the biotechnology industry, says the new centre is designed to be a multi-user, GMP biopharmaceutical production facility, offering biotechnology companies production capacity for clinical trials and eventual product marketing. Operation of the facility is expected to begin in 1996.

Bio Science was selected by the Maryland Processing Center to build and operate the biocentre.

Maryland Processing Center is a private, non-profit corporation whose 12-member board includes representatives from Johns Hopkins University, the University of Maryland System, regional biotechnology companies and the venture capital community. (Extracted from *Chemical Marketing Reporter*, 24 October 1994)

EPA finally issues TSCA and FIFRA rules

After years of drafting, revising and behind-the-scenes negotiating, officials of the Environmental Protection Agency (EPA, Washington, DC) recently issued two sets of revised proposals for regulating biotechnology.

One set of EPA proposals delineates the Agency's approach to evaluating modified micro-organisms under the Toxic Substances Control Act (TSCA), while the second set of proposals explains how the Agency will oversee small-scale field tests of certain pesticides under the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA). In both cases, EPA officials laboured to adapt their rules to federal statutes that were designed to deal with chemical products. In cases where TSCA is the signal statute, EPA officials plan to regulate many intergeneric micro-organisms — micro-organisms engineered to contain genetic material from organisms in different genera — as "new chemical substances". When a biotechnology company, or some other concern, plans to manufacture, import or otherwise use such micro-organisms for commercial purposes, a "microbial commercial activity notice" needs to be submitted to the EPA 90 days in advance, so the Agency can determine whether the micro-organism presents "an unreasonable risk to human health or the environment". Moreover, EPA officials reserve the right to review plans for field trials of intergeneric micro-organisms.

Although the scope of these TSCA rules is potentially universal, EPA officials are proposing several broad exemptions.

EPA's new proposals under FIFRA pertain to the small-scale testing and planned commercial use of microbial pesticides and plants engineered to produce pesticides. Although earlier proposals called for notifying EPA of all contemplated small-scale field testing of all such pesticides, the newer proposals somewhat narrow that scope, exempting genetic changes made within a particular micro-organism or those that mimic changes that occur in nature.

EPA officials project that the initial costs to industry of complying with the proposed TSCA rule will be as high as $2.2 million a year but will drop to $56,000-$460,000 a year within five years, as industry becomes more familiar with TSCA's provisions. (Source *Bio Technology*, Vol 12, October 1994)

US biotechnology—vigorous and creative

According to the annual survey of biotechnology companies by consultants Ernst & Young, the US biotechnology industry is responding vigorously and creatively to the changes in the health-care market-place by seeking alignments with other companies and shifting production methods.

Smaller biotechnology companies face the risk of being blocked from the US health-care market-place because of the recent restructuring and consolidation in the drugs industry, says the report. However, the new system will also offer opportunities for biotechnology, as the new "health-care providers" will look for partners to develop new products.

Biotechnology companies are increasingly forming alliances with each other and with big pharmaceutical companies, the report found. Their goal is to raise capital and to find help for product development and marketing. Both the biotechnology and pharmaceutical sectors are increasingly turning to contract research organizations, Ernst & Young found, saving money and gaining flexibility in starting up or abandoning development of new products.

Public biotechnology companies' sales grew in 1993 by 20 per cent. This may soon increase as products currently in the pipeline reach the market. Research spending increased by 23 per cent to $7 billion. The report calls this both "a blessing and a curse. technology embodies the future value of the industry but consumes much capital".

Despite the unfavourable figures, biotechnology remains popular among venture capitalists. On average, each venture capital firm made six investments in biotechnology companies during the first six months of 1994, with an average investment of $1.7 million per deal. (Extracted from *Chemistry & Industry*, 3 October 1994)

EPA to streamline rules on release of modified organisms

Environmental biotechnology, the use of biological systems and products to clean up and manage the environment, should be a boom industry — but has faced severe hurdles in the form of rules and regulations introduced over the years by the US Environmental Protection Agency (EPA). Under the new rules now proposed, researchers would have to notify the EPA 90 days prior to releasing genetically modified organisms — and could proceed if the Agency did not say no. In addition, it seems likely that EPA will look favourably on products likely to substitute for traditional chemicals that cause greater environmental problems. Once issued, the EPA rule will be available on the Internet, via EPA's gopher server, whose address is: gopher.epa.gov. (Source *Biotechnology Bulletin*, September 1994)

US demand for biotechnology therapies projected to double by 1998

US demand for biotechnology therapies quadrupled from $808 million in 1988 to $3.35 billion in 1993, and will double again to $6.8 billion over the succeeding five-year period, according to a new study from The Freedonia Group.

Looking at specific biotechnology products, the Cleveland-based research and consulting firm sees three classes of bioengineered medicines — erythropoietins,

colony stimulating factors and vaccines generating demand of more than $1 billion in 1998. In the same year, five additional classes – interferons, human insulin, human growth hormone, enzymes and interleukins – will account for demand ranging from $430 million to $575 million.

In addition, "the 1998 US bioengineered pharmaceutical market will include three $100 million to $400 million product groups: tissue plasminogen activator, anti-haemophilic blood factors and therapeutic monoclonal antibodies", the report predicts.

However, Freedonia cautions that, while "product demand will grow rapidly over the next decade, nearly 60 per cent of available opportunities" for biotech drugs "will remain untapped. Even with the anticipated introduction of gene-based therapies, nerve and insulin-like growth factors, anti-tumour monoclonal antibodies and AIDS vaccines during the 1998-2003 period, the industry will fall short of reaching its full potential", the study maintains.

"New discoveries and continuous advances in life science technologies will keep bioengineered pharmaceuticals in an embryonic stage of development until well into the next century", Freedonia states.

Cancer therapies will be the leader among bioengineered pharmaceuticals by 1998, according to the study. Among other diseases that should provide "favourable growth opportunities", according to Freedonia, "are AIDS, anaemia, cystic fibrosis, diabetes mellitus, dwarfism, haemophilia, hepatitis, herpes, multiple sclerosis, transplant organ rejection and several less prevalent genetic and infectious disorders". (Extracted from *McGraw Hill's Biotechnology Newswatch*, 19 September 1994)

New organization formed to promote bio-business collaborations with Israel

With more physicians and scientists per capita than any other country, Israel is being increasingly recognized as a global leader in biotechnology R&D, with high-quality, proprietary technology with strong commercial potential.

During the past three years the number of Israeli biotechnology companies has doubled to 60. Moreover, the ongoing peace process is increasing the interest and confidence of overseas partners and investors.

Despite the rapid growth of Israel as an innovative biotechnology centre, a recent report to the Israel Export Institute suggested that the following are needed for Israel's bioindustry to flourish: (1) skilled managers, (2) professionals experienced in post-R&D manufacturing and quality control, regulatory and clinical affairs and marketing, and (3) strategic alliances with overseas companies to compensate for the above needs. According to the report's author, "The time is right now for multinational companies in general and drug companies in particular to become important players in the Israeli biotechnology industry for the benefit of all parties involved. The multinationals could benefit from the abundance of new proprietary technologies. The Israeli companies can benefit considerably from the management capabilities and the post-R&D expertise of the multinationals in bringing products to market."

To help foster more alliances between the American and Israeli biotechnology industries, a new association – the US Israel Biotechnology Council – has been formed. A study by KPMG Peat Marwick indicates that the majority of foreign investment in Israel is from the United States. Sixty-one per cent of Israeli firms surveyed identified their main source of foreign investment as American. Several Israeli biotechnology companies are subsidiaries of American enterprises or have joint projects and/or investment from American sources.

The US Israel Biotechnology Council functions as a catalyst between the growing biotechnology communities of Israel and the United States, helping to facilitate new binational alliances – such as licence and cooperative research and development agreements – through networking, information exchange and public policy initiatives.

In January 1994 the Governments of the United States and Israel established a high-level Science and Technology Commission to promote joint high-technology development and create new jobs. Co-chaired by Commerce Secretary Ron Brown and his Israeli counterpart, the Commission has designated biotechnology as one of its priorities.

The Biotechnology Council has been helping the US-Israel Science and Technology Commission identify funding and other initiatives that promote binational alliances in the private sector. For further information, please contact the President, US Israel Biotechnology Council, PO Box 1742, Rockville, MD 20849, USA. Tel.: 301-899-4893. (Extracted from *Genetic Engineering News*, August 1994)

D. RESEARCH

Research on human genes

Study describes actions of cancer-cell movement

Scientists at Penn State's College of Engineering (University Park) have described some of the little-known biochemical and molecular activities in and around a cancer cell that dictate its crawling-like moves through the body to start new tumours. Penn State's Dr. Cheng Dong, along with Drs. Sadie Aznavoorian and Lance Liotta, at the National Institutes of Health, developed a way to view a cancer cell crawling through a micropipette. They found that the cancer cells move by temporarily projecting their protoplasm forward, called pseudopod protrusion.

The researchers watched the leading edge of a migrating melanoma cell thrust forward in two phases as the cell moved in response to a chemical attractant found in the body. In the initial phase, regulated by osmotic pressure, a cancer cell swelled to form a convex, symmetrical, outward-reaching pouch. During the second phase, the cancer cell extended in an irregular shape and proteins in the pseudopod combined to form larger molecules. These lined up into a rigid needle-like structure that aided the cell extension. The researchers found that cell surface texture influenced movement.

"It appears that one way to knock off the entire process of cancer-cell moving is to inhibit the initial protrusion process", according to Dr Dong. He is currently working to see if altering cancer-cell genes affects how and when a cancer cell moves. (Source: *Genetic Engineering News*, August 1994)

Research effort to diagnose foetal disorders from mother's blood

The National Institute of Child Health and Human Development (NICHD; Bethesda, MD) launched a major research effort to determine if it is possible to routinely diagnose chromosomal disorders in unborn babies by analysing foetal cells taken from the mother's blood. The effort could result in a less invasive method for detecting foetal genetic disorders that is safer than current diagnostic techniques and can detect foetal defects much earlier in pregnancy.

Diana Bianchi, M.D., at the New England Medical Center Hospitals (Boston), was one of the early investigators who developed a technique for isolating foetal cells from maternal circulation. She used monoclonal antibodies to the transferrin receptor, which is present on a certain type of foetal blood cell but missing from maternal circulation. The antibodies were chemically bound to a fluorescent molecule, which allowed the cells to which they were bound to be identified by a flow cytometer.

The current research effort seeks to expand on the earlier attempt, to determine whether it is possible to diagnose a wide range of foetal disorders, and to focus on the technical barriers to routine isolation of foetal cells from mother's blood and analysis of the chromosomal material they contain (Source *Genetic Engineering News*, 15 June 1994)

Collaboration on drug screening

Bristol-Myers Squibb has signed a major collaborative research agreement with New York-based Cadus Pharmaceutical, an early-stage biotechnology company which specializes in rapid drug screening techniques. B-MS will fund Cadus' research into novel yeast-based screening technologies.

Cadus' research centres on G protein coupled receptors. These regulate the physiological behaviour of cells by blocking or transmitting signals from outside, through G proteins, to the cells' interior. Over 1,000 types of G protein coupled receptors have been identified, including receptors known or suspected to play a role in diseases such as Alzheimer's, rheumatoid arthritis, hypertension, atherosclerosis and some cancers.

Cadus has developed a method to simplify the testing of compounds against G protein signalling pathways. The method involves transferring the genes for a single human receptor complex into yeast cells. Such yeast cells contain human G protein coupled receptors that act as if they were in human cells. Cadus has constructed a series of such yeast strains which can be used to test thousands of compounds a day. (Source: *European Chemical News*, 8 August 1994)

Brief encounters in the immune system

Researchers at the UK's Medical Research Council's Cellular Immunology Unit in Oxford have shown that the interactions between proteins on the cell surfaces of the immune system are extremely weak. The finding, which is reported in *Trends in Biochemical Sciences* (19, pp. 354-358), could have important implications for the design of new drugs.

There are a host of interactions between cells in the body. Some are relatively stable, such as those that occur as the body's organs develop. Others are more transient, particularly those involving white blood cells that mediate immunity. The researchers had been looking at proteins present on the T lymphocyte, a white blood cell that patrols the bloodstream and scouts for viruses, bacteria and foreign materials, or antigens. The proteins are known as adhesion molecules, many of which are distributed on the T-cell's surface. Their job is to make contact with other cells and gain sufficient information to let the T-cell know how to stick to the antigen, identify it and summon help from the rest of the immune system's army of cells.

There had been speculation that the adhesion molecules might bind very weakly, but the actual speed of their dissociation was still a surprise. The interactions are of very low affinity, so that a large number of adhesion molecules on each cell are required for successful identification.

The researchers speculate that this low affinity is common in the short-lived interactions that are typical of white blood cells. Indeed, the speed is probably vital. Without it, lingering contact with other cells might set up irreversible interactions and prevent the molecules that recognize the specific antigens from doing their job.

An appreciation of the speed of these interactions will be vital in designing the new generation of genetically engineering drugs based on inhibiting adhesion molecules, for example, in diseases such as rheumatoid arthritis, where the immune system wrongly identifies the body's own cells as antigens. Details from: Dr. Neil Barclay, MRC Cellular Immunology Unit, on 0865 275598. (Source: *Biotechnology Bulletin*, September 1994)

Zymogenetics in blood cloning breakthrough

Zymogenetics, the Seattle-based subsidiary of Denmark's Novo Nordisk, and the nearby University of Washington have reported the isolation and successful cloning of thrombopoietin, a critical hormone for blood platelet production. Researchers hope the discovery may lead to a treatment to counter thrombocytopenia, a sometimes fatal drop in blood platelet counts that all-too-often follows chemotherapy.

At present, thrombocytopenia is treatable only with transfusion of platelets, but this suffers the disadvantage that the foreign platelets are often attacked by the body's own immune system. By stimulating production of the body's own platelets, thrombopoietin has the potential to restore platelet counts to near-normal levels.

In initial research, recombinant thrombopoietin was shown to increase platelet levels in laboratory mice by over 400 per cent, Zymogenetics says. The company now plans to conduct extensive studies to evaluate the cytokine's therapeutic potential. (Source: *European Chemical News*, 27 June 1994)

Enzyme sorts stereoisomers

A research group at Tohoku University has successfully separated a nucleic acid compound that has anti-AIDS properties using adenosine-deaminase mediated enzymatic reactions under 5,000 atmospheres of pressure.

Proteins, including enzymes, ordinarily lose their activity at 3,000 atmospheres. However, when high pressure was applied to an adenine anti-AIDS compound developed by the group, it was found that while the enzymatic reaction proceeds to only 2.9 per cent of the compound at normal pressure, enzymatic reactions increased to 39 per cent after 20 minutes under 4,000 atmospheres of pressure. Furthermore, the reaction involved almost all L-isomers which act against the AIDS virus, allowing the group to easily separate products with anti-AIDS properties. (Source: *McGraw Hill's Biotechnology Newswatch*, 18 July 1994)

Scientists identify genes causing dwarfism

Scientists at the University of California, Irvine, have identified the gene and exact mutations that cause the most common genetic form of dwarfism, achondroplasia.

The research team was headed by John J. Wasmuth, Ph.D., professor of biological chemistry at UCI's College of Medicine. This discovery comes after studies reported that the gene for achondroplasia was located near one end of human chromosome number 4.

Achondroplasia, which affects about one in 20,000 people, causes alterations in bone growth and development, resulting in an enlarged head, normal-sized trunk and short limbs. The defective gene identified by the UCI group, called FGFR3, makes a cell surface protein, which binds specific types of growth factors and induces the growth and development of several tissues, including bone and cartilage. Most people with achondroplasia are born to average sized parents, but someone with achondroplasia has a 50-50 chance of having a dwarf child.

The UCI scientists emphasized that the test they developed should be used only for prenatal screening of foetuses at risk for having two copies of the aberrant achondroplasia gene. Even though dwarfs with one abnormal copy of the achondroplasic gene are generally healthy, couples in whom both people have this form of dwarfism have a 25 per cent chance of having a child with two altered copies of the gene, which is invariably fatal shortly after birth. (Source: *Genetic Engineering News*, August 1994)

Team develops SOD gene therapy

A Kobe University medical school research team has developed a way to insert the gene for superoxide dismutase in cells which would prevent damage by active oxygen. Superoxide dismutase gene insertion also proved to suppress formation of lipoperoxides. The technique offers promise as an effective gene therapy for some of the more intractable diseases of aging such as rheumatic arthritis. The researchers plan to conduct animal trials of the technique soon. Clinical trials of injectable superoxide dismutase are currently underway in Japan. Superoxide dismutase gene therapy offers considerable advantages since none of the substances would be metabolized and there would be no problems associated with dosage administration. (Source: *McGraw Hill's Biotechnology Newswatch*, 6 June 1994)

Multiple cancer-causing gene stirs scientists

Researchers claim to have found a "multiple tumour suppressor" (MTS) gene that when disrupted or mutated may cause many common cancers of brain, bladder, breast, lung, skin, bone, ovary, kidney and lymphocyte. And when inherited in a flawed form, it may cause a familial type of melanoma, lethal skin cancer.

It is the first suppressor gene that acts directly on cell division, researchers say, and its discovery further links the search for oncogenes with the much-applauded recent research on cell cycle.

The MTS 1 gene encodes for a protein recently identified as an inhibitor of the cell cycle and called p16. When normal, the MTS 1 gene apparently provides a "molecular brake" or switch governing a crucial early step in cell division. It stops a parent cell from dividing and, keeps it resting. When it is defective, cells multiply endlessly, developing into a tumour.

Researchers can now envisage a safe, targeted anti-tumour strategy by replacing the defective MTS 1 gene or by mimicking the activities of the p16 protein with drugs. Such an approach which is probably a long way down the road could treat almost all types of cancer, whenever the faulty gene is found in a patient's tumour.

At a great rate, other researchers have already identified a dozen tumour suppressor genes that indirectly control different steps in the cell cycle. In a few years, they have found such genetic faults in cells of virtually all types of tumours. They also foresee the identification of at least 50 tumour suppressor genes, genetic analysis of every patient's tumour, and the use of specific drugs to repair the defects.

Scientists have not yet found what damages this key MTS 1 gene: cigarette smoke, radiation, or an error in

reproduction. But many believe that the origin and the "biology" of cancer is at last becoming clearer.

MTS 1's discovery was announced by a team led by molecular geneticists Alexander Kamb of Myriad Genetics, Inc., Salt Lake City (UT), and Mark H. Skolnick of Myriad Genetics and the University of Utah Medical Center.

Independently, in late 1993, the groups of David Beach of Cold Spring Harbor Laboratories, Long Island, and Curtis Harris, Chief, Cancer Gene Research of the US National Institutes of Health (NIH), had reported the discovery and sequence of the p16 protein and its vital role in the suppression of cell division. The p16 protein was found to block the action of an enzyme called cyclin-dependent kinase 4 that initiates cell division. These teams have also been searching for p16 mutations in a wide variety of tumours and expected to report similar findings soon.

Swiftly, several other leading research groups independently sought to confirm the discovery and soon reported that they did not find the p16 gene mutation in very many tumour specimens taken directly from patients. A group at Johns Hopkins found 7 in 75 cancer cases of various types (*Science* 265: 415-417, 1994). A group at the University of Southern California found 7 in 31 bladder tumours (*Nature* 370: 183-184, 1994). More reports from the National Cancer Institute and California would follow. (*Science* 264: 436-439; commentary: 344-345, 1994) (Source: *Health Horizons*, No. 23 Autumn 1994)

IDUN Pharmaceuticals licenses cell death gene

IDUN Pharmaceuticals Inc. has entered into an exclusive licensing agreement with Washington University in St. Louis for the therapeutic rights to the human programmed cell death gene *bax*.

The protein expressed by the *bax* gene is a member of the *bcl*-2 gene family. Members of this family act within cells as master switches to control whether a cell lives or dies. "Because the *bax* gene appears to act as the antithesis to the *bcl*-2 gene, the master endogenous inhibitor of the normal cell death program", explains IDUN Vice President of R&D, Dr. Lawrence C. Fritz, "it is a promising target for anti-cancer, neurodegenerative and anti-inflammatory diseases". Details from: IDUN Pharmaceuticals Inc., 3050 Science Park Road, San Diego, CA 92121, USA or on +1 (619) 623-1330. (Source: *Biotechnology Bi... tin*, August 1994)

Liposomes protect antisense compounds

Researchers at the Fujita Health University School of Medicine have encapsulated antisense DNA into liposome microparticles to protect them from enzymatic degradation. Current stabilization approaches bind antisense DNA to sulphur although such compounds are somewhat toxic and only 1–2 per cent of antisense DNA can be introduced in cells.

In an experiment, an antisense DNA of 15 bases that corresponds to carcinogenic genes was encapsulated in liposome microparticles. When human leukaemia cells were treated with the micro-encapsulated antisense preparation, the antisense DNA remained viable five times longer and successfully suppressed the growth of leukaemia cells. The researchers say that adding antibodies that bind to target receptors on the surface of the microcapsule would facilitate entry of both antibodies and antisense DNAs into cells. (Source: *McGraw Hill's Biotechnology Newswatch*, 15 August 1994)

New approach to treating toxic shock

In a novel approach to treating toxic shock syndrome, researchers in Seattle have developed a chemical that blocks the formation of a protein responsible for the life-threatening consequences of the disease.

The protein, tumour necrosis factor, plays a critical role in the body's normal immune response to tumour cells and infection but can cause severe damage when produced in excess amounts. This is what happens in the case of toxic shock. The protein exists in two forms, a long form that is anchored inside the cell but extends outside its membrane, and a shorter form that is soluble and is released to roam in the blood. Problems occur when too much of the soluble form is released.

Dr. Roy A. Black and a team of researchers at the Immunex Research and Development Corporation have found a way to prevent the release of soluble tumour necrosis factor into the blood by blocking the protease, the enzyme that directs the cell to turn it loose. Their findings are reported in the journal *Nature*.

The tests so far have been on mice, and Immunex officials said more animal testing must be done before the company decides whether to begin the long process of clinical trials needed to obtain US approval of a drug. (Extracted from: *International Herald Tribune*, 28 July 1994)

Gene therapy for de facto bypass

An advisory committee at the US National Institutes of Health has recommended approval of a proposal in which gene therapy is to be used for the first time to treat cardiovascular disease.

The idea is to add genes near a clogged artery in the leg to get new blood vessels to grow around a blockage. One researcher compared the procedure to a bypass without the surgeon.

The study brings the beginning of a new era in the treatment of cardiovascular disease, said Dr. Judith Swain, a professor of medicine and genetics at the University of Pennsylvania and director of cardiovascular medicine there. But gene therapy, she said, offers the hope not only of treatments for blocked arteries that resist available therapies but also of better therapies for conditions that currently lend themselves to treatment.

The idea behind the gene therapy is to mimic what naturally occurs in some people when their arteries are blocked. These people form 10 to 50 extra blood vessels, called collateral vessels, that wind their way past the blockage and provide a new pathway for blood to get through.

Many people, however, do not form collateral vessels, or do not form enough. Molecular biologists have identified the substance that signals collaterals to form. The substance, a protein called vascular endothelial growth factor, or vegf, is secreted by cells lining an artery.

Dr. Isner, a cardiologist at St. Elizabeth's Medical Center in Boston, and his colleagues propose to provide a gene for vegf molecules that will allow formation of collateral vessels in patients who do not make them on their own.

The researchers will coat a tiny angioplasty balloon with a polymer that is impregnated with vegf genes. Then they will inflate the balloon in a region of the artery adjacent to the blockage.

The genes should be taken up by the cells of the artery wall, and those cells should churn out vegf proteins for the next couple of weeks. The hope is that vegf proteins, in turn, will coax new blood vessels to grow around the blockage. (Extracted from *International Herald Tribune*, 15 September 1994)

Research on apoptosis

Cantab Pharmaceuticals plc and the Imperial Cancer Research Fund (ICRF) are collaborating on a research programme to investigate the potential for enhancing the growth of cells used for the manufacture of biopharmaceuticals. The research will focus on enhancing the survival of mammalian cells cultured in the laboratory through recent advances in the understanding of apoptosis, the process that controls cell death. Cells are routinely used in the biopharmaceutical industry for the manufacture of protein and virus based products that are used for the diagnosis, prevention and treatment of human and animal diseases. If the research is successful in prolonging cell life, this may enable the production of new biopharmaceuticals and improve the economics of existing manufacturing processes. According to Dr. Gerard Evan, head of the ICRF team and a leading apoptosis expert, the unregulated growth of cancer cells may reflect their failure to "commit suicide" at the appropriate time. Dr. Evan's studies have led to the identification of particular genes which contribute to this failure. Details from: Cantab Pharmaceuticals plc, 184 Cambridge Science Park, Milton Road, Cambridge CB4 4GN, UK. (Source: *Biotechnology Bulletin*, June 1994)

Gene that triggers breast cancer isolated

Scientists from an urban teaching hospital, the federal government and a contract laboratory report that together they have discovered a gene involved in the initial development of breast cancer. If validated by further research, the discovery suggests that a simple tissue or blood test could be produced to detect breast cancer at its earliest stage – long before a tumour takes shape.

Such an advance would immediately draw the attention of a number of biotechnology companies that are working on oncogene diagnostics. Much of their work currently focuses on identifying patients at risk of a recurrence of breast cancer, so that they can be aggressively treated. A test based on this standard approach, using as a marker the HER-2 neu gene, which is highly expressed in 30–60 per cent of breast cancers where the lymph nodes are already infiltrated by cancer cells, is expected to be marketed by the year 2000.

The new finding was made by researchers from Harper Hospital, a teaching hospital affiliated with Wayne State University (WSU, Detroit, MI), the National Cancer Institute and PRI Dyn Corp., an NCI contract laboratory in Frederick, MD. The principal investigators were Fazlul Sarkar, Ph.D., associate professor of pathology at WSU and director of molecular biology at Harper, and Razuddin, Ph.D., a senior staff scientist from the laboratory of biochemical physiology in NCI's Biological Response Modifiers Program.

The scientists identified and purified a novel DNA-binding protein from malignant human breast tissues that they call HER-2 neu Promoter Binding Factor (HPBF). This gene apparently triggers the mechanism that activates the neu gene to be highly expressed. "But what causes the trigger to go off in the first place is still a mystery", comments Dr. Sarkar. "We are working on that."

He notes that the protein binds to a core element of the neu gene promoter region in a sequence-specific manner. The affinity-purified protein can induce DNA synthesis in quiescent cells, displaying mitogenetic activity, according to Dr. Sarkar. The purified protein induces HER-2 neu expression on the surface of microinjected cells. This DNA-binding protein, a sequence-specific cellular factor associated with high-level expression of the neu gene, appears to play a role in cell transformation, he notes.

For now the work is still preliminary, cautions Dr. Sarkar. "We have yet to clone the HBPF gene".

For further studies they will need to develop an antibody that can detect HPBF. "Since an antibody for the HER-2 neu gene already exists, once we have both antibodies we can see how they correlate with each other in gene expression in the same series of patients, accumulating the data in histochemical staining and statistically", he says.

Their evidence that HPBF is indeed a trigger comes from the pathogenesis of breast cancer. (Source: *Genetic Engineering News*, 15 June 1994)

Research on animal genes

Scientists find protein that stops spread of cancer in mice

Researchers at Stanford University School of Medicine in California have identified a protein on the surface of cells that thwarts tumours in mice from spreading throughout the body. Dr. Irving Weissman, who helped identify the metasis-blocking protein called integrin alpha4-beta1, and colleagues studied the protein's effect on the spread of melanoma.

The scientists became interested in the protein's potential as a metasis blocker when they noticed that it acts as a Velcro-like hook that sticks to certain surfaces. They genetically engineered mouse tumour cells to produce the protein, and then injected these cells under the skin of eight mice. When they examined the animals' lungs 28 days after the injections, they found that only five tumours had arisen, in a group of eight mice injected with tumour cells lacking the protein, 45 tumours had arisen. The researchers repeated the experiment three times, each time obtaining nearly identical results.

Dr. Weissman plans to survey various types of tumours from cancer patients to measure their production of alpha4-beta1. By checking patients' records, he hopes to determine whether production of the protein correlates with metastasis in humans. (Source: *Genetic Engineering News*, 15 June 1994)

Insect genes could hold key to waste clean-up

An entomologist from North Carolina State University (NCSU) has cloned the genes responsible for insect resistance to chemical insecticides. Dr. Michael Roe, an associate professor in the Department of Entomology, sees

potential to use the genes to clean up chemical waste in bioreactors or remediation systems.

Roe was developing a simple immunochemical assay to determine if insects in a farmer's field are resistant to a particular pesticide when the bioremediation idea came to him. The test, a simple colorimetric assay, works by dropping an insect into a vial of solution. If the colour in the vial changes, the insect is resistant. The tests, developed through a grant from the US National Science Foundation-sponsored Center for Integrated Pest Management at NCSU, have been submitted to the NCSU intellectual property committee. The bioremediation idea is relatively simple: take genes from resistant organisms engineer them into fermentation organisms and place with toxins in a bioreactor. One application, for which the NCSU team has a patent application, is to infuse steam in contaminated soil. The steam would liberate the toxic chemicals, which would be sent to a bioreactor for decontamination. The applications are not limited to insecticides, according to Roe. One of the enzymes removes chlorines from hydrocarbons such as PCBs. NCSU does not have a working prototype yet, but is looking for companies interested in commercializing the idea. Details from: Dr. Michael Roe on +1 (919) 515-3771, or from Linda Abruzzini at the Triangle Universities Licensing Consortium on +1 (919) 549-9203. (Source: *Biotechnology Bulletin*, June 1994)

Structure of spider silk

In work that could give clues to the development of new fibres, scientists at Cornell University (Ithaca, NY) have determined the molecular structure of superstrong silk produced by certain spiders. The silk has the tensile strength of steel fibre of the same diameter, yet it can stretch and rebound from at least 10 times its original length and has better performance than metal or synthetic fibres, according to the Cornell researchers. The group says it used nuclear magnetic resonance analyses of the spider silk to unambiguously define the crystalline and amorphous regions of the material. (Source: *Chemical Week*, 12 October 1994)

Firefly genes enhance trout roe fertilization

A research team at Kinki University has produced transgenic rainbow trout using a new electrophoration technique that inoculates sperm with lightning bug luciferase genes to fertilize large quantities of roe with the new genetic code. Convention microinjection techniques insert genetic material into each egg individually through fine glass tubes. When sperm is placed in a solution with the genetic material and subjected to 1.2 kV electrophoration pulsed at 0.5 msec, a minute hole opens in the heads of the sperm to allow the entry of the genetic material. In experiments, about 80 per cent of the eggs were fertilized by the transgenic sperm as confirmed by light emissions from the resulting fry. (Source: *McGraw Hill's Biotechnology Newswatch*, 18 July 1994)

Killer cell line shown to cure leukaemia in mice

Scientists at the Wistar Institute (Philadelphia, PA) have demonstrated that a "killer" cell line they developed holds promise for the treatment of a variety of cancers, both of the blood and solid tumours. This line, known as TALL-104, has been shown to reverse and eradicate human acute myelogenous leukaemia, an aggressive form of blood cancer, in SCID mice. The cell line was derived from a child with a rare form of T-cell leukaemia by Daniela Santoli, Ph.D., at Wistar.

The researchers injected leukaemic mice with TALL-104 cells in conjunction with recombinant IL-2 or IL-12. To prevent proliferation of the TALL-104 killer cells in the mouse tissues and to allow them to die off after they had done their work of destroying the cancer cells, the killer cells were irradiated prior to being injected into the animals. A single injection of TALL-104 cells into the leukaemic mice significantly prolonged their life span; complete eradication of the transplanted leukaemia in the mice occurred when the cells were injected three times at close intervals.

If this method can be applied to humans, it has the potential to improve upon the adoptive transfer therapy approach developed by Dr. Steven A. Rosenberg of the National Institutes of Health. (Source: *Genetic Engineering News*, September 1994)

Newly discovered marine micro-organisms may be most abundant life form

The most common form of life on Earth may be a group of deep water microbes discovered by University of Southern California (Los Angeles) marine biologist Jed A. Fuhrman. The researcher used DNA analysis to detect the existence of numerous new species of micro-organisms in samples of sea water from various ocean locations. These micro-organisms fall outside of the known major divisions in the microbial group Archaea, to which they seem to belong.

In samples taken from deep ocean water, these new species made up about one-third of the life forms detected in the DNA analysis. Because there are so many cubic miles of this environment – which is nutrient poor and subject to high water pressures, and thus adverse to most life forms – it follows that "any organism common in this zone is likely to be one of the most abundant organisms on the planet", according to Dr. Fuhrman. (Source: *Genetic Engineering News*, 15 June 1994)

Transgenic mice support toxic waste theory of brain aging

Research using transgenic mice has provided support for the theory that the brain ages due to slow poisoning by its own toxic waste. It is believed that a lifetime's accumulation of free radical by-products that occasionally bypass the body's control systems could be the cause of degenerative changes seen in conditions such as Parkinson's disease, as well as the problems of normal aging.

Julie K. Andersen, Ph.D., an assistant professor at University of Southern California's (Los Angeles) Ethel Percy Andrus Gerontology Center, created mice whose neurons produce an average of four times the normal amount of the brain enzyme monoamine oxidase B (MAO-B), and in brain cells where it is not normally found. Normally, MAO-B breaks down serotonin in a reaction that produces hydrogen peroxide which, in the presence of iron, can give rise to free hydroxyl radicals.

The mice produced MAO-B in all nerve cells, including neurons that contain catecholamines. MAO-B can also break down catecholamines, and when it does, peroxides are produced. In all brain areas where catecholamines are not normally present, the cerebral material looked normal. However, in the sites where

catecholamines are present. Andersen found evidence of brain damage and atrophy comparable to a type seen in conditions such as Parkinson's disease. (Source: *Genetic Engineering News*, 15 June 1994)

Research on plant genes

Genetic engineering yields first pest-resistant seeds

Over the past decade, plant genetic engineers have racked up impressive successes in designing crop plants with improved resistance to insects and viruses. So far, that research has focused on endowing plants with genes that give them a survival edge in the field. But for many important crops, including cereal grains, beans and peas, the danger from pests does not end with the harvest. Weevils and other insects may cause losses just as great or greater during storage. The problem is particularly acute in developing countries, where farmers can rarely afford protective chemical fumigants.

A team of US and Australian researchers has shown how biotechnology can combat pests in the storage bin as well as in the field by creating a strain of garden pea that resists attack by two weevil species that damage stored crops. The genetic stratagem the researchers used involves inserting a foreign gene into the pea plants that triggers production of a protein that inhibits feeding by weevil larvae; the protein is expressed only in the pea seeds.

This achievement, which marks the first time that seeds have been genetically engineered for pest resistance, is expected to pave the way for new varieties of weevil-protected legumes, including some that are important sources of protein for people around the world, such as chickpeas, cowpeas (black-eyed peas), mung beans, and kidney and pinto beans. (Extracted from *Science*, Vol. 265, 5 August 1994)

HEAR oil gene from jojoba

Calgene Inc., an agricultural biotechnology company, has unveiled the first cloning and expression of a plant beta-ketoacyl-CoA synthase gene from jojoba. Mike Lassner, a Calgene scientist, explains that the "elongase" gene, isolated from jojoba, produces the long-chain condensing enzyme which is the key step in the production of the long-chain fatty acids used as precursors of wax biosynthesis. This enzyme is present in certain varieties of high erucic acid rape-seed (HEAR), which are naturally high in erucic acid, but is missing in low erucic acid rape-seed (LEAR or canola) varieties.

When Calgene scientists expressed the jojoba elongase gene in canola varieties normally having virtually no long-chain fatty acids, the transgenic varieties produced seeds with more than 50 per cent of the oil consisting of long-chain fatty acids.

HEAR oil is used in certain high performance lubricants, waterproofing agents, and as antislip and antiblocking agents in polyethylene plastic films. More than 100 million pounds of HEAR oil are consumed each year world-wide for these purposes.

In addition to the cloning, Calgene has succeeded in the purification of a lysophosphatidyl acyltransferase enzyme which controls the specific positioning of fatty acids in the triglyceride molecules of which plant oils are comprised. (Extracted from *Chemical Marketing Reporter*, 11 July 1994)

Trehalose expressed in plants

Calgene Inc. (Davis, CA) has successfully engineered the production of trehalose into plants via the expression of bacterial genes encoding enzymes that convert glucose into trehalose. The trehalose-synthesizing genes had been isolated and characterized by a research team led by Dr. Arne Strom, of the University of Tromso in Norway.

Trehalose has been shown to preserve the structure of membranes and proteins in the absence of water, and the flavour, colour and texture of dried foods associated with their fresh counterparts.

In a separate development, Calgene's Dr. Maelor Davies reported the successful purification of a lysophosphatidyl acyltransferase (LPAAT) enzyme, which controls the specific positioning of fatty acids in the triglyceride molecules of which plant oils are comprised. According to Dr. Davies, manipulation of this enzyme with Calgene's plant oils genetic engineering technology will enable control of composition of fatty acids in the No. 2 position in plant triglycerides.

When expressed in combination with the medium chain thioesterases responsible for the production of C10, C12 and C14 fatty acids, Calgene expects to achieve oils with super high fractions, greater than 70 per cent, of each fatty acid type. (Source: *Genetic Engineering News*, July 1994)

Researchers clone genes that confer resistance to plant diseases

Scientists at the University of California at Berkeley and the US Department of Agriculture have isolated and cloned two genes that are part of a close-knit family that confers resistance to a variety of plant diseases in a broad range of plants. A third gene reported at a scientific meeting in Scotland early in 1994 appears to be a member of the same family.

Brian J. Staskawicz and researchers at UC-Berkeley cloned a gene (RPS2) from a mustard-like plant called *Arabidopsis thaliana* that confers resistance to a common bacterial pathogen, *pseudomonas syringae*. The second team, led by UC-Berkeley professor Barbara Baker, found and cloned the N gene, which makes tobacco resistant to tobacco mosaic virus (TMV). The third team, lead by Jeffrey Ellis from the Commonwealth Scientific and Industrial Research Organization (Canberra, Australia), cloned the L-6 gene from flax that confers resistance to a rust disease caused by the fungus *Melampsora lini*.

"The amazing thing about these three genes is their similarity, considering how diverse the plants and pathogens are. This will help us understand the anatomy of disease resistance and bring us closer to inserting resistance genes into other species that suffer from similar diseases", says Baker. (Source: *Genetic Engineering News*, 15 October 1994)

Research on viral genes

Slowing down HIV infection with selenium

Using computer analysis of HIV genes, a team from the University of Georgia has found that selenium may be able to arrest HIV infection.

The HIV genes hold the information about the sequence of amino acids that the virus needs to be able to reproduce and spread the disease. Each amino acid corresponds to a codon, a set of three nucleotides that determines which amino acid is inserted into a protein.

Will Taylor found that HIV genes contain distinctive nucleotide sequences, which allow "slippage" in the way the gene is read before replicating. This means that a different set of codons is translated into proteins. But when selenium is around, it overrides the "stop" codon – which marks the end of the gene – so that the protein incorporates selenium as the amino acid selenocysteine, at this point in its sequence.

The resulting selenium-containing proteins resemble other proteins which control infection and they could be used to turn off HIV infection, says Taylor, but the infected person must have enough selenium in their system. However, he stresses that these results are purely theoretical (*Journal of Medicinal Chemistry*, 1994, 37, 2637).

Selenium is an essential nutrient, found in many antioxidant proteins. AIDS patients tend to have depressed levels of selenium in their blood plasma. Many of the groups that were initially most susceptible to AIDS, such as Africans and drug users, tend to be malnourished. In several studies selenium supplementation therapy has been reported to lead to some symptomatic improvements in such patients. (Source: *Chemistry & Industry*, 5 September 1994)

AIDS hope from baboon marrow

New treatments for diseases often come from very unlikely sources, and scientists from the University of Pittsburgh's transplant department are working on one of the oddest. The team is attempting to repair AIDS sufferers' damaged immune systems by transplanting bone marrow from baboons.

Baboons appear to have natural immunity to the human immunodeficiency virus (HIV), so a baboon marrow transplant should transfer this resistance. However, such cross-species transplants produce adverse reactions like graft-versus-host disease, when the transplanted immune system attacks the host.

The Pittsburgh team, led by Suzanne Ildstat, has discovered that mammals' bone marrow contains a "facilitating cell" which allows the transplant of purified stem cells from one species into another. Stem cells, a constituent of bone marrow, produce both the oxygen-carrying red blood cells and the white blood cells which form the backbone of the immune system. Transplanting just these parts of the marrow does not seem to cause rejection, claims Ildstat.

In addition, unlike in human-to-human transplants where the entire marrow is replaced, the recipient's marrow only has to be "partially ablated" rather than completely destroyed. It is a graft rather than a replacement so it gives better immune responses, and is a "less aggressive process", explains Ildstat.

Although the team has yet to attempt a baboon-to-human transplant, trials with other animals have been successful. "We have achieved engraftment even in highly genetically different animals", says Ildstat – most encouragingly, a human-to-baboon graft is among the successes. Baboon-to-human trials are "months away", Ildstat predicts. (Source: *Chemistry & Industry*, 1 August 1994)

Metals to fight cancer and viruses

New complexes developed by University of Buffalo researchers could provide a key to virus- or cancer-blocking drugs. Combining antisense genetic technology and transition metal catalysis, the complexes seek out and destroy the genetic equipment which viruses use to reproduce and cancers to spread, without damaging the host's DNA.

Antisense technology stops a virus from replicating inside a host cell. It works by binding a stretch of complementary DNA to the messenger RNA (mRNA) strands of the virus or cancer cell. This blocks the transfer of the strands' genetic information which is needed for the target to replicate and invade cells. The strands can then be destroyed.

The Buffalo team, led by Janet Morrow, has devised a complex in which a specific macrocyclic ligand encases a lanthanide ion. The metal ions catalyse the transesterification of nucleic acids – a reaction which breaks the sugar-phosphate backbones of DNA or RNA strands.

In previous antisense techniques using transition metals, the ion was released after reacting with the RNA and usually killed the infected cell's DNA. Morrow's ligand, however, keeps a tight grip on the lanthanide ion, letting it react but preventing it from escaping and wreaking havoc on the host's DNA.

The antisense nucleotide – a short stretch of DNA – is bound to the ligand. It is designed to attach to the mRNA strand in the correct position for the metal ion to react. The team can make specific nucleotides to attack different types of RNA, although the ligand stays the same.

The first targets will be the human papillovirus and herpes simplex. Morrow later hopes to tackle HIV and cancer-causing mutated *Ras* genes. (Source: *Chemistry & Industry*, 19 September 1994)

Scientists test insecticidal plant virus

Researchers at the Institute of Virology and Environmental Microbiology (Oxford, UK) are conducting field trials on a virus modified to hold an insecticidal gene for scorpion venom. The virus infects the alfalfa looper, a moth that produces widespread crop damage. (Source: *Chemical Week*, 27 July 1994)

Single-chain antibodies inhibit HIV replication

Using antibodies specifically altered to target an HIV protein, researchers at Thomas Jefferson University (Philadelphia, PA) have developed a potent tool for inhibiting replication of HIV in human cells. Roger Pomerantz, M.D., and co-workers developed intracellular single-chain antibodies that bind to the Rev protein, a key protein responsible for the replication of HIV. The intracellular antibodies were then introduced into human cells *in vitro*, where they bound to the Rev protein and rendered the cells resistant to HIV infection.

"One reason vaccines and viral drugs do not work well against AIDS is that they target the envelope around the virus, and the reverse transcriptase enzyme. This envelope changes so quickly, it is very difficult to get a single vaccine, but the regulatory proteins within the replicating virus do not change very much at all", explains Dr. Pomerantz. In addition to being highly effective in inhibiting HIV replication, this approach works against many different strains of the virus. (Source: *Genetic Engineering News*, 15 June 1994)

Enzyme inhibited to prevent HIV infection in lab cell culture

Scientists at Boston University School of Medicine have discovered that an enzyme called protein disulfide-

isomerase (PDI), which is found on the surface of some cells, breaks certain chemical bonds in the outer coat of HIV. By inhibiting this enzyme, HIV can be prevented from infecting cells grown in the laboratory, according to Hugues J.-P. Ryser and his colleagues.

Scientists have known for years that HIV binds to the CD4 protein found on the surfaces of some immune cells, but that binding to the CD4 receptor is not sufficient to trigger infection. Ryser believes he has found a second factor needed for HIV infection. Namely, by breaking the disulfide bonds that help form the shape of HIV's surface, PDI allows the virus to fuse with the cell membrane. His team inhibited the effects of PDI by using three drugs, one that blocks all enzymes at the cell surface, and two others that are specific for PDI. All three prevented HIV infection of cells, but did not affect the replication of HIV in previously infected cells. (Source: *Genetic Engineering News*, 1 June 1994)

Gene shuffling

A scientist in California has devised a technique called DNA shuffling which exploits the main advantage of sexual reproduction: it allows DNA to be broken up and recombined in a different order, generating mutations. This could be useful for designing industrial enzymes and therapeutic proteins.

In life, DNA shuffling produces the differences between successive generations which drive evolution, explains Willem Stemmer of Affymax. In the laboratory, it is a powerful technique for designing and improving any DNA sequence.

Stemmer explains it is a deceptively simple adaption of the polymerase chain reaction (PCR) – in PCR, small fragments of DNA are "amplified" – separating the strands, adding a small "primer" section designed to bond to one stretch of the strand, and extending this using the DNA polymerase enzyme. (Extracted from *Chemistry & Industry*, 15 August 1994)

Functional reconstruction of membrane fusion protein

The National Institute of Bioscience and Human Technology, the Agency of Industrial Science and Technology (AIST), is developing a new technology for artificially fusing lipid membranes using haemaglutinin glycoprotein on the surface of influenza virus to fuse the virus to a target cell allowing introduction of chemical substances such as drugs and DNA into the cell.

Membrane fusion protein taken from the virus is incorporated into liposome as glue, with the pH change in the ambient environment controlling the fusion functions.

The new technology will be the basis for R&D projects on microcell reactors to develop a proposed new material production system that imitates the efficient material production of the cell from intake of raw materials and energy to output of the final product, in contrast to existing bioreactors which use a single enzyme. The institute plans to use the new technology in the exocytosis process for final product extraction.

In the technology, the viral membrane is dissolved into lipid and protein in surfactant and is purified by sucrose density gradient centrifugal separation to isolate the protein. Phosphatidylcholine and lipid cholesterol are then added to the isolated protein to form a submicron-diameter liposome with haemaglutinin molecules embedded on the surface.

In the experiments, the resultant liposome was mixed with the membrane of red blood corpuscles to investigate the membrane fusion mechanism. The fusion occurred in a slightly acid environment with 70–80 per cent of the liposome working, while no fusion occurred when the acidity was neutral. This indicates the possibility of effective membrane fusion control.

A capsule can be produced by mixing the liposome with a drug agent and incorporating in another lipid membrane. The resulting capsule releases the drug, controlled by the acid change in the environment, so no release occurs when the environmental acidity is neutral. In the acid environment, the membrane fusion functions are activated to fuse the inner membrane with the outer for drug release, so the capsule can be used for the intelligent drug delivery system (DDS). Further details are available from the National Institute of Bioscience and Human Technology, AIST, 1-1, Higashi, Tsukuba City, Ibaraki Pref. 305; Tel.: +81-298-54-6053, Fax: +81-298-54-6005. (Source: *JETRO*, April 1994)

Detecting viruses

A seemingly simple combination of laser, microscope and computer is being hailed as a revolutionary development in detecting single molecules and virus-sized particles.

The remarkable detector was developed by Manfred Eigen at the Max Planck Institute for Biophysical Chemistry in Göttingen, together with Professor Rudolf Rigler of Sweden's Karolinskt Institute in Stockholm.

The idea of attaching a marker to target molecules so that they would fluoresce on floating through a laser beam occurred to Professor Rigler in 1967, but the technology available at the time was not sufficiently advanced to make this technique work in practice.

Since then there have been big improvements in computers and lasers, and now a Fluorescence Correlation Spectroscopy device has become a practical reality.

The sample of liquid is treated with a fluorescent marker which is specific to the particles being detected. A drop of this liquid is suspended under a microscope and illuminated by a laser beam. Any particles with the marker attached fluoresce, and a detector, linked to a computer, picks up the signal.

The number of detections is proportional to the concentration of the target molecule.

To make the device more sensitive, an electrical field can be used to drive more particles into the measurement zone.

According to Manfred Eigen, the method is so sensitive that the detector can be used to identify one single molecule.

At present the researchers at Gottingen are working on a technique to detect HIV in blood.

Detection of viruses is only one of the many possibilities opened up by the technique. Provided a fluorescent marker exists, any kind of molecules can be detected, and traced down to an incredibly low level of dilution. According to the researchers, the technique is so accurate that it could be used to identify traces of a sugar cube dissolved in the Baltic Sea. (Source: *Lab Tech*, April 1994)

Oligonucleotide compounds that inhibit HIV-1 activity found

Scientists at Triplex Pharmaceuticals Corporation have discovered a series of guanine-rich oligonucleotides that appear to inhibit the function of HIV (Human Immunodeficiency Virus), the virus that causes AIDS. This series of compounds, called guanine-thymine oligonucleotides (GTOs), was observed to prevent HIV-1 virus production in an *in vitro* acute assay system. They do not act through an antisense or "code-blocking" mechanism, but rather through a unique nucleic acid protein interaction.

"These compounds were capable of totally suppressing HIV-1 p24 production for more than seven days after their removal from an infected culture media", said Dr. James M. Chubb, the company's president. "Furthermore, the prolonged suppression of HIV-1 was determined to be a function of viral inhibition and not due to any toxic effect of the drug on the cell cultures."

Details from: Triplex Pharmaceutical Corporation, 9391 Grogan's Mill Road, The Woodlands, Texas 77380, USA or on +1 (713) 363-8761. (Source: *Biotechnology Bulletin*, July 1994)

Research on yeast and fungus genes

Biological pulping

Australian Biotech International Ltd. has applied for patent protection to cover two micro-organisms that enhance the pulping of wood and the bleaching of paper pulp. Biotech International has lodged separate patents for a fungus described as F425 and a bacterium described as B698 and has sought international patent coverage including Australia, USA, Europe, Japan and China.

The company's scientists isolated the two micro-organisms during a systematic screening programme as part of a project to develop biological pulping and biological bleaching products for the pulp and paper industry. Managing Director, Dr. Saliba Sassine, said that B698 produced an enzyme which was effective in bleaching kraft pulp at the laboratory stage. F425 had proved effective in enhancing the pulping of eucalyptus wood. He said the company's patent applications cover the pulping of wood, bleaching of paper pulp, the treatment of mill effluent, and for the decolorization of waste water. Dr. Sassine said the company's scientists were still investigating a number of other micro-organisms which have demonstrated encouraging enzyme activity for biological pulping and bleaching applications. In recent years chlorine-based wood pulping and bleaching techniques have come under attack from environmentalists. As a result, buyers have sought Totally Chlorine Free (TCF) pulp and this trend is expected to continue. TCF is commanding higher prices than chlorine bleached pulps. (Source: *Australasian Biotechnology*, Vol. 4, No. 3, June 1994)

Research on bacterial genes

"Mega-enzyme" key to new antibiotics

Scientists at the University of Cambridge are trying to exploit the synthetic ingenuity of bacteria to make new antibiotics. The research focuses on *Streptomyces*, a humble family of soil bacteria. These secrete many pharmaceutically active compounds, including the broad-spectrum antibiotic erythromycin, probably as a defence against predatory microbes.

The Cambridge teams, under chemist James Staunton and biochemist Peter Leadlay, searched the bacteria's genome until they located the genes responsible for the biosynthesis. They found three genes, which encoded three huge proteins. These twist together to make the largest protein structure ever discovered – a multi-functional enzyme with a molecular weight of slightly more than a million daltons.

This enzyme builds the main part of the erythromycin molecule (a 14-membered polyketide lactone) in only six steps; laboratory syntheses take more than 25. Each protein in the enzyme contains two active sites. The molecule is built up sequentially, being "passed around" the enzyme, until the last active site closes the lactone ring.

The goal of both teams is more effective drugs with fewer side-effects, but each team takes a different approach. One group synthesizes molecules that may be intermediates along the bacteria's pathway. Once they have found the right molecules, they will feed chemically modified versions of them to the bacteria to obtain new versions of the antibiotic. The other group is working on manipulating the genome to make a different enzyme which will assemble different antibiotics. (Source: *Chemistry & Industry*, 18 July 1994)

Spanish researchers find more proof of role for iron

Microbiologists in Spain have found further evidence of a new iron-scavenging molecule that bacteria use to scavenge metal from their host.

The scientists from the Universities of Santiago de Compostela and Valencia investigated the role of iron scavenging in *Pasteurella piscicida* and *Vibrio damsela*. Both bacteria cause disease in fish – pasteurellosis has caused major losses in the sea bass and sea bream industries in Europe – and *V. damsela* is often associated with wound infections in humans.

They found that *P. piscicida* uses a previously undiscovered siderophore to scavenge iron from iron-binding proteins such as transferrin and from other molecules like haemoglobin. The siderophore is neither hydroxamate nor phenolate – the two most common classes of natural iron chelator [*Appl. Environ. Microbiol.* **60**(8), 2990-2998 (1994)]. The team suggests that the siderophore may instead be a multocidin, a type discovered in *P. multocida* in 1986.

Siderophores normally work in conjunction with receptors on the cell surface, which take iron from the siderophore and transport it into the cell. Both pathogenic and nonpathogenic isolates of the bacterium contained three iron-regulated outer membrane proteins. The Spanish team found all three to be strongly immunogenic and candidates for vaccines against pasteurellosis. (Source: *Microbiology Europe*, Vol. 2, No. 5, September/October 1994)

Characterization and properties of the microbial biosurfactant produced by Bacillus licheniformis strain BS1

Biosurfactants are receiving increasing attention worldwide due to their specific advantages over the chemically synthesized counterparts. The properties include low toxicity, biodegradability, biological activity, a wide variety of possible structures, and ease of synthesis from inexpensive renewable sources. A broad range of surfactants is already known. As the list of biosurfactant-producing

organisms expands due to extensive research in the area, the spectrum of newer physical and chemical properties unravel leading to the discovery of novel surfactants suited for special applications. Recent research at the National Environmental Engineering Research Institute, Nagpur, India report on characterization and properties of the biosurfactant produced by *Bacillus licheniformis* strain BS1.

Most of the biologically produced tensides show outstanding advantages such as biodegradability and low toxicity as compared to the common synthetic surfactants. A surface active compound produced by *Bacillus licheniformis* strain BS1 in the study was characterized as a lipopeptide type of biosurfactant. Thin layer chromatography of the surfactant indicated the presence of three components of which the major constituent was lipopeptide as ascertained with infrared spectroscopy. Fast atom bombardment mass spectrum of the lipopeptide revealed an approximate molecular weight in the range of 1050–1150. The biosurfactant showed significant reduction in surface and interfacial tension, i.e. 27 dynes cm and less than 1 dyne cm respectively with a critical micelle concentration of 0.067 mg ml. These surface and interfacial properties of the lipopeptide biosurfactant encourage potential applications in various fields as an environmentally benign surface active compound. (Extracted from *Australasian Biotechnology*, Vol. 4, No. 2, October 1994)

Research instrumentation

Immobilized enzymes for better bioreactors

Chemists at Colorado State University (Fort Collins) have developed a way to immobilize enzymes by encapsulating them in polymeric materials. The work, say the researchers, could open the door to more efficient biosensors and bioreactors. The scientists produce dense arrays of hollow polymeric capsules that are sealed at one end. Enzymes can be placed inside these tubules, which are then sealed to form microcapsules. Small molecules can diffuse through the polymer wall, but the enzymes are too large to pass. (Source: *Chemical Week*, 1 June 1994)

High-throughput DNA detection technology

Hitachi Ltd. has developed the world's first high-throughput DNA detection technology that can analyse as many as 20,000 DNA base sequences in an hour, one-sixth of the time required by conventional systems.

The system is designed so DNA fragments from each sample flow through a capillary tube, a small bore glass tube, filled with a gelled substance, and as many as 100 samples can be analysed at once. The company has established this basic technology to promote the Human Genome Project intended to elucidate all the DNA base sequences of humans, which is presently being advanced as a global project.

The new sequencer uses a capillary tube with a diameter of 0.2 mm (inside diameter 0.1 mm) filled with a gelled substance for each sample when conducting electrophoresis, and the DNA fragment passes through the tube. The product is injected at the terminal part of the gelled substance, a voltage impressed, and the formed product starts migrating. Fragments with a smaller number of bases migrate faster, as well as at a higher impressed voltage.

The laser beam irradiation unit is a sensing unit that severs the capillary tube and temporarily discharges the DNA fragments into the buffer liquid, which then reflow into the capillary gel. The laser beam can irradiate a large quantity of samples, or DNA fragments, at once. A prism is fixed on the measuring camera to enable accurate measurements, while the electrolysis intensity has been increased to shorten the time for DNA fragment passage.

The Human Genome Project is currently being advanced under the leadership of the United States, Japan and Europe. The total number of DNA base sequences is about 30 billion, so the development of a sequencer capable of analysing roughly one million base sequences daily is needed. The company claims that this level can be attained by added automation improvements to the new sequencer. Further details are available from Hitachi Ltd., Public Relations Secretary's Office, 4-6, Kanda Surugadai, Chiyoda-ku, Tokyo 101; Tel.: +81-3-3258-1111, Fax: +81-3-3258-2375. (Source: *JETRO*, May 1994)

New range of applications found for high performance liquid chromatography

Biotechnologists and other scientists are finding new applications for high performance liquid chromatography (HPLC) in a variety of areas.

One recent use of HPLC involves the detection of material leached from packaging material into parenteral drug solutions. An example of a potential risk is the chemical DEHP (di-[2-ethylhexyl]phthalate), which is a plasticizing agent found in PVC packaging. This chemical is a carcinogen, and there is the potential that it might leach from the packaging into the drug solution and then into the patient's body. Although there is now no formal requirement, drug companies are making efforts to provide data about a drug's potential for leaching, and one of the key approaches they use is HPLC analysis.

HPLC might be used to provide a rapid, inexpensive and effective means of monitoring the presence of hazardous chemicals in toxic waste sites, where clean-up is accomplished by *in situ* stabilization rather than by active removal. According to the researchers, HPLC offers a number of advantages over traditional gas chromatography (GC) for this purpose, including the ability to use a direct liquid injection in HPLC and the avoidance of the extra steps of extraction, clean-up and derivatization that are necessary for GC. (Extracted from *Genetic Engineering News*, 1 May 1994)

General

New technique allows scientists to track microbes in the environment

Researchers at the University of Illinois (Urbana-Champaign) have developed a method to monitor genetically engineered micro-organisms after they have been released into the environment. Stephen Farrand, Ph.D., professor of plant pathology, and colleagues inserted genes for the catabolism of agropine from *Agrobacterium tumefaciens* into the chromosome of *Pseudomonas fluorescens*. The resulting genetically engineered bacterium is identifiable by the fused DNA sequences via PCR.

Dr. Farrand says the technique allows for easy detection of the gene-altered bacterium in any environment. The genes also provide a method for specifically isolating

the bacterium when it is present in environments containing many other bacterial types.

The technique offers a potential "fingerprint" for any genetically engineered bacterium, plant or animal, notes Dr. Farrand. "The detection strategy can be used in any gene-marker system in which there is a fusion of any two dissimilar pieces of DNA", he adds. (Source: *Genetic Engineering News*, 15 June 1994)

Genes introduced into cells using low-toxic cationic polymer as vector

Dr. T. Yamaoka, Professor Y. Kimura, and their research team of the Department of Polymer Science and Engineering, Kyoto Institute of Technology, have established a technique to introduce foreign genes into cultured cells by using a low-toxic new cationic polymer as a gene carrier (vector). Compared with the method of using conventional types of carriers such as a retrovirus or cationic liposome, the new technique is much safer and is expected to come into wide use as a new method for *in vivo* direct gene transfer in gene therapy.

The research team used a cationic polymer as a vector to introduce plasmid DNA with lac-*Z* gene into monkey kidney epithelial cell (COS-1). The gene introduction was conducted by the osmotic shock treatment using cationic polymers, by which foreign genes can be introduced into isolated non-phagocytic cells with ease.

The cationic polymer acted as a vector like cationic liposome which is widely examined *in vivo*. However liposome injected into the body is known to be mainly taken up by the reticuro endothelial system in the liver or spleen, while the soluble polymer can localize to the site of action. In the experiments, a polyion complex of cationic polymer and anionic DNA was formed, the solution further co-cultured with COS-1 cells, then a hypertonic solution was added and incubated for 10 minutes. The cells were washed, then cultured for 48 hours in a serum-free culture medium at 37° C. Subsequently, the X-gal staining was applied to measure the frequency of transient expression of lax-*Z* genes.

Various cationic polymers were used experimentally in attempts to develop low-toxic new gene carriers which can introduce genes into the cells, but gene expression was observed only with three types of polymer, poly (vinylalcohol) dimethyl-amino acetal (PVA-3), methyl glycolchitosan and conventional diethyl-aminoethyl (DEAE) dextran, all containing tertiary amino and hydro groups. Therefore, gene transfection is probably influenced by the type of cationic group and the characteristics of the polymer main chain. Tertiary or quaternary cations are essential, the polymer must have hydroxyl groups in the main chains, and the hydrophilicity retained even after the cationic polymer forms polyion complex with DNA. Appropriate molecular weight and cationic group density are required.

The newly synthesized PVA-3 shows much lower cell toxicity than conventional DEAE dextran and excellent gene expression, so the new technique using PVA-3 is a safe gene introduction method and may be also usable in the drug delivery system (DDS). Further details are available from the Kyoto Institute of Technology, Department of Polymer Science and Engineering, Goshokaido-cho, Matsugasaki, Sakyo-ku, Kyoto 606, Tel.: +81-75-724-7804, Fax: +81-75-712-3956. (Source: *JETRO*, December 1994)

Fullerenes may lead to novel drugs and diagnostics

Drug, imaging agent, photoactive compound, superconductive molecule, research reagent. These are just a few of the emerging uses for an extraordinary class of chemical compounds called fullerenes. Originally known as buckminsterfullerenes, they were named after the late Buckminster Fuller, who invented geodesic domes, which fullerenes resemble.

Fullerenes are a unique group of carbon-based compounds that form a spherical cage that resembles a soccer ball. Since they were first reported in 1985, the field has drawn the attention of a widening circle of researchers. The compounds show a host of fascinating properties that have led to a number of patents, including those covering uses as lubricants, fuel additives and as a component in many different kinds of polymer chemistry.

Fullerenes are denoted by the number of carbon atoms making up the spherical cage. The most common type is C-60. There is also C-70, plus several variations, including subfragment fullerenes and fullerene hybrid compounds. Most of the current biotechnology-related research is focused on C-60 compounds. Work on C-70 and other forms may appear later.

University research groups are investigating the use of fullerenes as drugs (see table). The idea of fullerene-based drugs has been circulating for more than a few years. However, not until recently has there been a body of information suggesting that these compounds could have therapeutic applications. Some researchers theorized that fullerenes may have toxic physiological effects. However, scientists at the University of Arizona (Tucson) reportedly did preliminary animal studies that showed no toxic effects when applied topically.

Another finding is that yet another solubilized version of C-60 does an efficient job of cleaving DNA when exposed to low-power visible light. This potential buckydrug binds to DNA but remains inactive until exposed to light. At that point, it cuts the guanosine base in the DNA to which it is bound. One theory holds that highly reactive oxygen free radicals are formed as a result.

If this phenomenon can somehow be harnessed to a "gene-specific" method of binding, it might have some therapeutic potential. If not, this finding suggests buckydrugs may yet turn out to be very toxic under some conditions. Researchers are looking at double helical forms of C-60 modified DNA to answer questions about the underlying mechanisms and about how it might be used in therapeutic applications.

The most startling finding about possible biological uses of fullerenes was arrived at by Simon Friedman at the University of California at San Francisco. He showed that a water-soluble C-60 fit nicely into the active site of an HIV-1 protease and completely inhibited the enzyme from functioning. The diameter of the C-60, it turns out, matches the size of the active-site cleft. Further testing will have to answer questions about what cellular receptors this compound might also interact with *in vivo*. In spite of the excitement engendered by these findings, there is much basic research about the biological activity of fullerene that has yet to be done.

Besides water-soluble forms of fullerenes, there are possible hybrids, such as the polyoxometallate-fullerenes which suggest potential antiviral activity.

Unmodified C-60 is a greasy compound that is virtually insoluble in water; thus C-60 is a fat-soluble compound. Besides water-soluble versions of C-60, other groups are studying unmodified C-60 compounds. They have done the original work on incorporating carbon-14 atoms into C-60. These were put into human keratinocyte and fibroblast cultures. Unmodified C-60 was readily taken up in the cell membranes. However, there are questions about whether these compounds might also be in other parts of the cell, such as the endoplasmic reticulum and even the nucleus of these cells.

The work above, taken together, points toward the emergence of a unique subgroup of fullerenes probably best termed "biofullerenes". One speculation is that as the number of analogues grows, there will be versions targeted for cell- or tissue-specific uses. Then the term biofullerenes will make more sense.

There is also research combining fullerenes and self-assembling monolayers. Lipid bilayers and fullerenes have also been looked at. These could contribute to one interesting area that could lead to self-assembling compounds fullerene subfragments like C-28. Fullerene subfragment research is new, but the possibility of linkage with various peptide analogues and nucleic acids would suggest possible uses in imaging in research and other areas of biotechnology. Fullerenes also show promise in diagnostics, reagent development and other areas involving biotechnology.

Groups researching biomedical uses of fullerenes

Organization	Researchers	Topic
University of California, San Francisco	Simon Friedman	HIV-1 protease inhibition
University of California, Santa Barbara	Fred Wudl	Development of water-soluble fullerenes
University of California, Los Angeles	Yves-Rubin	C-60 modified DNA; photochemistry
University of South Carolina, Dept. of Chemistry, Columbia	Jim Tutor William Scrivens	Cell culture research of unmodified fullerenes, uptake studies
Emory School of Medicine, Atlanta, GA, Dept. of Pediatrics	Ray Schinazi	Anti-viral screening
Emory University, Dept. of Chemistry	Craig Hill	Fullerene hybrids; poly oxo-metallate fullerenes
Dartmouth College, Hannover, NH, School of Engineering	Robert Richmond Ursula J. Gibson	Fullerene surface materials for cell culture; transfection
Burroughs-Wellcome, Research Triangle Park, NC	n.a.	Solubility studies of C-60 compounds

(Extracted from *Genetic Engineering News*, December 1994)

E. APPLICATIONS

Pharmaceutical and Medical Applications

Asahi develops T-cell removal systems

Asahi Chemical Industry Co. Ltd. has constructed a system for the removal of T lymphocytes for the treatment of such autoimmune neurological disorders as systemic lupus erythematosus, Guillain-Barre syndrome and multiple sclerosis.

The system, which reduces the T-cell count by 1/30th, is being developed for an external circulatory system. Autoimmune diseases develop when the patient's immune system identifies their proteins in the central and peripheral nervous systems as antigens and produces T-cells that attack target cells and antibodies. In experiments, the company produced an antibody that specifically reacts with CD4, a surface glycoprotein of T-cells using mice.

The antibody was applied to the bottom of a chemically treated flask. Then, a human blood fraction excluding red corpuscles and platelets in which T lymphocytes accounted for 30 per cent of the volume was introduced and in 45 minutes the volume of lymphocytes was reduced to 1 per cent.

The antibody removed 1 million T-cells per square centimetre. However, the antibody did not selectively remove the T-cells when whole blood was added. Researchers said that the red cells and platelets may have blocked the reaction between the antibody and T-cells, the major obstacle to commercializing the substance. (Source: *McGraw Hill's Biotechnology Newswatch*, 4 July 1994)

Centre finds GM-CSF blocker

Researchers at the Hanson Centre for Cancer Research in Adelaide, South Australia, have uncovered a genetically engineered drug which has the potential to cure some cancers and to stop allergies and inflammations in some common diseases. Adelaide-based biotechnology company Bresatec Ltd has licensed the patented product and begun collaborative research. The drug is based on a "molecular Key" which fits into the receptor or "locks" of specific human cells to influence their biological function. The "key" is a substance which acts as an antidote to a molecule involved in the formation of blood cells in the body and in the responses that produce inflammatory diseases. It has the effect of blocking specific actions of granulocyte-macrophage colony stimulating factor (GM-CSF), which induces the proliferation of white blood cells. Details from: Dr. Matthew Vadas on +61 8 228 7474. (Source: *Biotechnology Bulletin*, July 1994)

New "naked DNA" technology

France's Pasteur Mérieux Sérums et Vaccins has acquired exclusive licence options to a new "naked DNA" technology developed by the California-based biotechnology company Vical to be applied in the development of five new vaccines. The vaccines are against: cytomegalovirus (which causes congenital deficiencies), syncytial respiratory virus (cause of severe child pulmonary cases); Lyme's disease, *Helicobacter pylori* (related to gastric ulcers), and malaria. Vical's technology is based on direct intramuscular injection of genetic material. (Source: *European Chemical News*, 31 October 1994)

Laboratory-grown cartilage cells

A team of Swedish scientists successfully treated patients with knee cartilage injuries by transplanting laboratory-grown cartilage cells. The research is reportedly the first in humans to demonstrate cartilage repair with regenerated tissue.

The work resulted from a multidisciplinary collaboration among specialists in orthopaedic surgery and laboratory medicine within the University of Goteborg's Research Centre for Endocrinology and Metabolism and Sahlgrenska University Hospital (Gothenburg, Sweden). The surgical and cartilage cell culturing techniques and products are planned for further development for broader use in patients in collaboration with scientists at Bio-Surface Technology, Inc. (Cambridge, MA), which is involved in large-scale laboratory culture of normal human cells for therapeutic applications.

Cartilage tissue does not normally regenerate in the body and, as a result, deep injuries progress over time, resulting in debilitating osteoarthritis, which may lead to the need for a total knee replacement. Results from the five-year patient study indicate that one can repair cartilage defects using a patient's own cells. This treatment may ultimately arrest the progression of cartilage injuries to osteoarthritis. Currently, there are no effective long-term treatments for these injuries.

The hope is that treatment with cultured chondrocytes will significantly delay or eliminate the need for total joint replacement.

The transplant research introduces cultured cells into the knee defect; the cells subsequently adhere to the underlying bone and mature into normal cartilage. The 23 patients, aged 14 to 48 years, had cartilage defects in the knee joint, either on the end of the femoral condyle or on the patella. The defects resulted from trauma or from bone disorders (chondromalaciapatellae and osteochondritis dissecans). All of the patients had poor knee function and several had undergone prior treatment due to their disabling symptoms.

The researchers surgically removed a tiny amount of each patient's healthy cartilage and, through tissue culture techniques, expanded the cell population in their laboratory. They then surgically transplanted the cells back into the patient's defect and covered the injured area with a small flap of periosteum.

The patients were followed for periods ranging from 16 to 66 months, and in 14 of the 16 femoral transplants, the patients had "excellent" or "good" improvement in joint function. The transplants eliminated knee locking, and considerably reduced pain and swelling. Follow-up arthroscopic examinations of these patients also revealed that the transplanted cells regenerated into tissue that closely resembled healthy cartilage. In addition, the researchers conducted laboratory tests confirming that the transplanted cells produced cartilage similar to normal cartilage. (Source: *Genetic Engineering News*, 15 October 1994)

Gene switch technology aids gene therapy

Recent studies, reported in the 16 August issue of *Proceedings of the National Academy of Sciences* (PNAS), have demonstrated that GeneMedicine's proprietary "gene

switch" technology enables gene function to be selectively controlled using a drug which can be administered orally. In these studies, the gene switch functioned *in vivo* to provide drug-controlled expression of a gene medicine.

In the experiments, a tyrosine hydroxylase gene was combined with the gene switch and introduced into rats. When these rats were treated with a synthetic steroid drug, expression of the tyrosine hydroxylase gene was increased up to ten-fold as compared with untreated controls.

The gene switch is a genetically modified steroid receptor that is designed to be activated only by a certain class of synthetic steroid drugs (antiprogestins). When activated by the drug, the gene switch binds to a specific sequence incorporated within the gene medicine – a sequence not found anywhere else in the human genome – and turns on the expression of the therapeutic gene. Expression is turned off when the administered drug is naturally eliminated from the body. The drugs used to activate and control expression by the gene switch are clinically proven, and the doses reported in the PNAS paper are between 200 and 1,000 times lower than the doses commonly used for other clinical applications of these drugs. Target diseases include inflammatory conditions, cancers and neurodegenerative diseases, including Parkinson's and Alzheimer's. The technology was originally developed in the laboratories of Dr. Bert O'Malley, a scientific founder of the company and author of the PNAS paper. Details from: GeneMedicine Inc., 8080 North Stadium Drive, Suite 2100, Houston, TX 77054-1823, USA or on +1 (713) 796-2221. (Source: *Biotechnology Bulletin*, September 1994)

Malaria vaccine enters final phase of clinical trials

A malaria vaccine has passed the second phase of clinical trials, raising hopes that it could be in use by 1998.

The vaccine, called SPf66, was developed by the Colombian scientist Manual Patarroyo in 1988. It consists of a chemically synthesized polypeptide from *Plasmodium falciparum*, combined with aluminium hydroxide.

Dr. Patarroyo first tested the SPf66 vaccine on monkeys, then on humans in Colombia, where it achieved a 22–77 per cent reduction in malarial infection. The greatest protection was in the very young and the very old.

The World Health Organization (WHO) described the trials, which were in Kilombero, Tanzania, as "a much more severe test for the vaccine". Local inhabitants suffer an average of 300 bites a year from malaria-infected mosquitoes; in the rainy season this can amount to 20–25 infected bites a night – 100 times the rate in Colombia.

High infection rates are common in Africa, which accounts for 90 per cent of all clinical cases of malaria. WHO estimates that malaria claims 300–500 million victims world-wide every year, killing up to 3 million people.

The trial, in 18 adults and 25 children under five years old, revealed no major side effects and confirmed the vaccine's immunogenicity [*Vaccine* 12(4), 382]. This cleared the way for a phase III trial to test whether the vaccine reduces the number or severity of malaria cases. That trial is in more than 600 Tanzanian children aged 1–5 – the most vulnerable age group.

Other types of vaccine are also in development, including the so-called anti-transmission vaccine – a form of passive immunization using humans as a vehicle to get anti-plasmodium antibodies into the mosquitoes themselves. Patarroyo says SPf66 vaccination in Africa would be affordable with UNICEF and WHO help. (Source: *Microbiology Europe*, Vol. 2, No. 3, May/June 1994)

Swiss synthetic relative of Chinese herbal antimalarial

A new synthetic distant relative of an ancient Chinese plant-derived antimalarial looks promising against the challenging tropical disease. Scientists of Hoffmann-La Roche (Switzerland), long active in malaria research, say the drug acts rapidly and durably and combines well with standard agents as a deterrent against parasitic resistance.

Synthesis of the novel-structured Ro 42-1611 or arteflane was inspired by yingzhao-su, a cyclic peroxide isolated from an ornamental vine shrub, *Artabotrys uncinatus*. Researchers in Basel (Switzerland) synthesized about 60 related compounds and determined that it was the "front runner".

By chance they had noticed yingzhao-su in Chinese literature, mentioned as an "also-ran" of the legendary qinghao-su, obtained from another plant, a wormwood, *Artemesia annua L.* Qinghao-su and such derivatives as arteneether and arteether have recently shown remarkable therapeutic potential. A mass-producible synthetic analogue also would have clear advantages over a herbal, the company's scientists point out.

In early clinical trials, Ro 42-1611 appeared to offer a "decisive edge" among desperately needed new antimalarials, reports say. The lethal parasite *Plasmodium falciparum* has developed alarming, widespread multidrug resistance.

Pilot trials have been conducted in Cameroon and in Nigeria in collaboration with African researchers. Initial targets were young men with milder forms of the infection. The Roche drug has been well tolerated and is as effective as leading medicines. It has displayed particularly rapid onset and long duration of action. These attributes would be important in the two drug uses: treatment and prophylaxis.

The drug also appears not to be susceptible to cross-resistance and is "almost an ideal partner" in combination with standard drugs, as a measure to deter emergent resistance.

Initial clinical studies show that a dose of 1800 mg often rapidly reduces parasite count, fever and clinical signs and symptoms.

Researchers still want to determine the drug's value for either or both prophylaxis – suppressive action during the parasite's infective blood-stage – and treatment. In early work, it showed advantages over qinghao-su as a prophylactic agent – long duration of action – and over chloroquine in treatment – rapid onset of action, they said. Other peroxides, including derivatives of qinghao-su, have shorter biological half-lives than this Roche drug. The Swiss scientists are also searching for metabolites, breakdown products of this drug, which might be more effective.

But there has been concern about foetotoxicity of all these peroxides; many rodent embryos die. Roche scientists emphasize, however, that the new agent, Ro 42-1611, is not teratogenic, surviving newborns are normal. Also, toxicity in female rodents does not necessarily mean similar danger to human pregnancy. And, ultimately, even when new

drugs carry risks, health authorities must weigh them against the greater threat of malaria to mothers and infants. (Source: *Health Horizons*, No. 23, Autumn 1994)

Taxol® synthesized, approved for breast cancer

Bristol-Myers Squibb's drug Taxol® has been approved by the US Food and Drug Administration (FDA) for treatment of breast cancer where initial chemotherapy fails. It was approved earlier for similar use against ovarian cancer. Studies show that the drug shrinks or eliminates a third or more of tumours in severe breast cancer cases. Further work in Japan and the US, particularly as first-line therapy, will determine whether the drug prolongs life. Taxol® was first isolated from yew trees and environmentalists complained. Now, after almost 50 research teams have tried for more than 20 years, taxol has been synthesized, simultaneously and independently, by two teams, one at the Scripps Institute in La Jolla (CA), led by Kyriacou Nicolaou, and the other by Robert Holton and colleagues at Florida State University. (*Nature* 367: 593-95, 1994; *Science* 263: 911, 1994) (Source *Health Horizons*, No. 23, Autumn 1994)

Oestrogen blocks tumour growth and may protect against Alzheimer's

A natural oestrogen metabolite inhibits the growth of tumours and could be a drug candidate, a European research team reports. The German, Swiss and Finnish scientists found that 2-methoxyestradiol halted the formation of new blood vessels that nourish tumours.

"This potent inhibitor of vascular cell proliferation and migration strongly suppressed both neovascularization and solid tumour growth" in mice, the group concluded. The results bring further support for an antiangiogenic therapy of human diseases where new blood vessel formation is a "dominant feature". This compound, an endogenous oestrogen metabolite, is a novel antiangiogenic agent which might be used in the treatment of solid tumours and other angiogenic diseases, including diabetic retinopathy, rheumatoid arthritis, haemangiomas and psoriasis, the team said. The team includes Theodore Fotsis, Peter Paul Nawroth, Lothar Schweigerer and Youming Zhang of the University of Heidelberg, Michael Pepper and Roberto Montesano of the Geneva University Medical Center; and Herman Adlercreutz of the University of Helsinki.

They also found that unlike corticosteroids, this oestrogen metabolite did not require the co-administration of an anticoagulant like heparin for such activity. They conclude that again, oestrogen is proving to be more than simply an important player during a woman's reproductive cycle.

Neuroscientists are reporting evidence that oestrogen also plays a role in brain cell development and function throughout life. It may help to produce receptors that make the brain cells more sensitive to the stimulus of nerve growth factor. This should enrich the synaptic communications that govern memory, thinking and learning.

Theoretically, when oestrogen output falls in mature women, neurons may be more vulnerable to whatever kills them, causing Alzheimer's disease, scientists explain. Dr. C. Dominique Toran-Allerand and colleagues at Columbia University College of Physicians and Surgeons in New York (NY) postulate that oestrogen depletion could be just as important pathologically in the brain as it is in the bone, contributing to osteoporosis, and in the heart, facilitating atherosclerosis.

The team discovered that in rat brains oestrogen acted strongly on neurons in areas that are destroyed in Alzheimer's disease. The hormone apparently increased the neuron's ability to make receptors for nerve growth factor (NGF), that is, making brain cells more sensitive to NGF, thus maintaining and improving contact between neurons for normal thinking and even learning new things. A deficiency in oestrogen was dangerous.

Earlier Dr. Victor Henderson of the University of Southern California in Berkeley (CA) found an association: women receiving hormone replacement therapy (oestrogen) were 40 per cent less likely to develop Alzheimer's disease.

Others reported that the production of choline acetyl transferase that is involved in the synthesis of acetylcholine is induced by oestrogen. This neurotransmitter acts in the brain region and is associated with memory. Furthermore, it was found that Alzheimer's patients have a very low level of this enzyme. So oestrogen could be involved indirectly in this way, according to Dr. Bruce McEwen, neurobiologist of Rockefeller University in New York City. (*Nature* 368: 237-239, 1994; *Journal of Neuroscience* 14(2): 459-471, 1994.) (Source: *Health Horizons*, No. 23, Autumn 1994)

First success for gene therapy

An American research team recently published the first report of a successful gene therapy that led to a partial correction of an inherited, life-threatening disorder marked by extremely high cholesterol levels. Patients with such a disorder usually die very early of massive heart attacks.

The historic patient, a French Canadian woman in her late 20s suffered a heart attack at the age of 16, had bypass surgery at 26 and was still sinking when, in June 1992, she was the first recipient of liver-directed gene therapy.

Such patients with familial hypercholesterolaemia (FH) inherit mutant or missing versions of the gene that codes for a liver cell receptor. Their liver cells cannot clear low-density lipoprotein (LDL) cholesterol from the bloodstream. This 'bad' lipid adheres to arterial walls, narrowing the passages. Most in danger are patients, as this Canadian woman, who have inherited two copies of the defective gene because their dyslipidemia are refractory to conventional therapies.

Pioneer Dr. James M. Wilson and colleagues of the University of Pennsylvania, Institute for Human Gene Therapy, in Philadelphia, have presented their successful experience with the first recipient of an *ex vivo* gene therapy directed to the liver where a reduction of blood cholesterol levels was maintained for almost two years.

In the Wilson procedure, a portion (15 per cent) of the patient's liver is removed and cells cultured. A disabled retrovirus is used as vector to insert normal copies of the human low-density lipoprotein (LDL) cholesterol-lowering receptor gene into the cultured liver cells that are then injected back to the liver by infusion in the portal circulation.

Some genetically corrected cells established themselves in the women's liver, and the inserted genes turned on and directed production of the normal lipid-clearing receptor. The woman's LDL serum levels significantly fell from 482 mg dl to 404 mg dl. Gene therapy allowed the patient to respond to conventional therapy as a further improvement in the patient's LDL level (356 mg dl) was achieved.

when on a widely used cholesterol-lowering drug, lovastatin.

Most significantly, the woman's LDL HDL ratio – a good indicator of coronary risk – declined from 10 13 before gene therapy to 5 8 following gene therapy.

After a follow-up of 18 months, the engrafted cells still expressed LDL receptor with a sustained improvement of lipid profile. Furthermore, X-rays of her arteries did suggest that atherosclerosis had not progressed since the gene therapy.

Several other patients have also reportedly been treated by this research group. Dr. David Weatherall of Oxford University, UK, sees a "genuine step forward in the slow road to successful somatic gene therapy", suggesting that "ultimately it will be possible to correct genetic diseases that are expressed primarily in liver cells".

Other successes in correcting the code will be published soon in the scientific literature, professional sources said. Before Wilson's first case, other researchers had received official permission to try gene therapy to correct the ADA (adenosine deaminase) gene to combat a severe inherited immunodeficiency. *Nature Genetics* 6: 335-341; editorial: 323-324, 1994. (Source: *Health Horizons*, No. 23, Autumn 1994)

Lupus disease corrected in mice

Gene therapy has corrected and cured a lupus-like autoimmune disorder in mice. Researchers say the research could lead to more effective treatment of patients suffering from systemic lupus erythematosus (SLE). A defective gene is clearly responsible for the mouse form.

This destructive disorder can cause inflammation and injury to the joints, skin, kidneys, lungs, blood vessels and central nervous system. The victims produce antibodies that widely attack healthy body tissue, sometimes fatally.

John D. Mountz and colleagues at the University of Alabama, Birmingham, used mice presenting a defective Fas gene that develop a similar disease, marked by kidney, lung and arthritic joint disease. They suspected that the mutant gene and its protein product might cause the massive autoimmune disorder.

They inserted a normal Fas gene into single-cell embryos that had inherited two defective copies, one from each parent, and re-inserted the embryos into the fallopian tubes of female mice.

Less than three weeks later, the newborn pups were tested. The inserted genes had turned on in T-cells, and the young mice were making healthy amounts of normal Fas protein. After six months, there were no signs of the disorder, kidney or lung disease or arthritis, nor overproduction of antibodies that attack the tissues. The team believes the normal Fas gene directs production of a protein receptor that is essential to apoptosis or programmed cell suicide. In this way the body destroys immune cells that would attack healthy tissue, as a defence against autoimmune disease.

Mountz suggests that immune cells with a faulty Fas gene and receptor persist in attacking tissues. This could explain lupus (SLE). Some SLE patients have a Fas gene defect, he says, but other genes as well probably regulate apoptosis. Conventional SLE drug therapy is steroids, which may control symptoms by provoking apoptosis. New gene therapy might one day do it better. *Proc. Natl. Acad. Sci.* 91: 2344-2348, 1994. (Source: *Health Horizons*, No. 23, Autumn 1994)

Industry consortium begins testing drug combinations for AIDS

A consortium of 16 research-based companies, the Intercompany Collaboration on AIDS Drug Development,* has launched a study initiative designed to evaluate rapidly a series of powerful triple-drug combination regimens for the treatment of HIV infection. The new study design, a consensus protocol called the continuous cohort variable regimen (CCVR), "builds up drug combination concepts that led to the successful control of leprosy, tuberculosis and certain cancers", said Dr. Jurgen Drews, head of international R&D at Hoffmann-La Roche and chairman of the Scientific Panel of the consortium, when he spoke earlier to the US National Task Force for AIDS Drug Development.

Led by Dr. David Barry of Burroughs-Wellcome (UK), this new protocol development effort should act as a rapid screen for those combination regimens with impressive *in vitro* antiviral activities, of drugs of non-overlapping toxicities. The study calls for a group of 100 patients to be sequentially enrolled and followed at intervals for up to one year. Each group of 100 patients will receive a different triple-drug regimen and each triple combination will be graded after participants have completed one year in the study. The interaction of chemotherapy agents on HIV is extremely complex. Rapid mutation of the virus leads to the development of resistance to single drugs and even to two-drug combinations. *In vitro* evidence points to the distinct possibility that development resistance can be circumvented with the proper combination of agents. Firstly, resistant strains exposed to additional agents have shown increased sensitivity to the initial agent. Secondly, several *in vitro* studies with three drugs combinations have shown "complete suppression of all virus replication".

"The rapid identification of the best combinations of antiretroviral agents, which can completely suppress viral replication and development of resistance over an extended period is therefore not only possible but urgently needed", Dr. Drew declared. There are currently seven FDA-approved drugs with known *in vitro* anti-HIV activities: AZT, DDI, DDC, D4T, interferon, foscarnet and ribavirin, plus 3TC, in parallel track status. The study will rapidly evaluate current three-drug combinations and allow the addition of new agents as they become available. Although these protocols function as pilot Phase II studies, "it is conceivable that they could become the basis for widespread use within the parallel track system if the results are sufficiently impressive", said Dr. Drew. The clinical trial subcommittee also is in discussions with the (US) National Institutes of Health (NIH), the Food and Drug Administration (FDA) and academia for a possible joint venture in the development of a common database on end-point measurements.

The original 15 pharmaceutical companies teamed up in April 1993 to establish the Intercompany Collaboration on AIDS Drug Development. A 16th company joined later.

---

* Current participation in the Intercompany Collaboration: Ajl Pharma USA, Astra Biochemicer Ingelheim, Bristol-Myers Squibb, Burroughs-Wellcome, DuPont-Merck, Glaxo, Hoechst, Hoffman-La Roche, Eli Lilly, Merck, Miles (Bayer AG), Pfizer, Sigma-Tau, SmithKline Beecham and Syntex.

Membership in the Intercompany Collaboration is open to all companies with active compounds to test. The goal of this collaboration is to "develop mechanisms to facilitate the initiation and the conduct of combination as well as comparative drug studies by individual companies or by companies working together".

The Intercompany Collaboration is not a legal entity but an "organized effort to provide a forum for member companies to share relevant scientific data and drug supply and agree on standard preclinical assays and procedures. All of these activities should facilitate clinical trials on AIDS drugs and help avoid duplication of effort", according to Dr. Drew. (Source: *Health Horizons*, No. 23, Autumn 1994)

Untangling Alzheimer's

Glaxo is to collaborate with a team from Duke University in North Carolina to develop a drug that could delay the onset of Alzheimer's disease for up to 20 years.

Allen Roses, of the University's Joseph and Kathleen Bryan Alzheimer's Disease Research Center, is to lead the research. Teams from Duke and Glaxo will try to find molecules that mimic the function of a form of the blood protein apolipoprotein E (apoE), which may stop nerve cells in the brain from dying and forming the "tangles" characteristic to Alzheimer's disease.

Two years ago, Roses discovered a link between an inherited form of Alzheimer's disease and the presence of an abnormal form of apoE. These proteins were known to shuttle cholesterol in and out of blood cells, but Roses found that they are also involved in nerve cells, which move molecules around through microtubules. These are stabilized by a protein known as "tau"; apoE proteins seem to stop tau strands from sticking together.

There are three forms of apoE, however, and one of them – apoE-4 – does not work as well as the others. When two copies of the gene encoding apoE-4 are inherited, Roses found that the tau strands tangle, leading to Alzheimer's. People with the genes for another form, apoE-2, either do not suffer from the disease or develop it much later. Roses believes that if a way can be found to "get the right apoE mimic into nerve cells", people with the apoE-4 gene could hold off Alzheimer's for "at least two decades".

Roses and colleagues are to work with Glaxo's Institute for Molecular Biology in Geneva, which is also carrying out basic research into the disease's mechanisms, to develop an apoE-2 mimic. The company's London laboratories will also be involved, screening possible drug targets. (Source: *European Chemical News*, 3 October 1994)

Mouthwash screening

A cystic fibrosis screening test using gene amplification technology has been launched by Zeneca's Cellmark Diagnostics and Kodak Clinical Diagnostics.

The test uses genetic material from mouthwash samples and provides answers in about six hours.

The tests are being manufactured at Cellmark's new facility at Abingdon in Oxford and will be marketed by the Kodak sales force.

The link-up is part of a wider strategic agreement between the two companies to make and market novel genetic testing products in Europe. (Source: *Manufacturing Chemist*, September 1994)

Blood tests identify MI rapidly

Scientists say they have developed a new blood test that quickly helps determine whether a patient with chest pain in the emergency room has had an actual heart attack. The test, which compares two levels of an enzyme produced by the heart, tells doctors within six hours if a myocardial infarction (MI) has occurred – not the 12–24 hours normally required by enzyme tests – according to researchers at the Baylor College of Medicine (Houston, TX).

And an even faster test by a Toronto biotechnology firm is expected to be available by mid-1995.

Electrocardiogram irregularities generally tell ER specialists if chest pain is due to a heart attack, but when these readings are inconclusive, they must wait until blood enzymes reveal the truth. In about 70 per cent of cases, severe chest pain turns out to result from angina or other heart disorders or non-cardiac causes such as indigestion or pulmonary hypertension.

The test is based on the difference in the amounts of two variations of creatine kinase MB, which the heart continually releases into the bloodstream in small amounts. Levels rise gradually after a heart attack, taking a day or so before they are high enough to ascertain that a heart attack has occurred.

As the enzyme breaks down in the bloodstream, the test can measure changes in the ratio between freshly released creatine kinase and that which was already circulating in the blood. The results are clear within six hours after symptoms began. The Baylor group tested the new technique on 1,100 ER patients. They found that among the 118 who had suffered an MI, the test correctly identified 114, or nearly 97 per cent. Also, the test identified 98.9 per cent of those who did not have an MI.

The Baylor group reported their results in 1 September *New England Journal of Medicine*.

Spectral Diagnostics Inc., a Toronto-based biotechnology company, has combined myoglobin, creatine kinase MB, troponin I and another cardiac protein, myosin light chain-I, into its assay. The credit card-sized Chest Pain Panel Test is expected to reach the US market by mid-1995.

Since they found no individual marker to be as effective as a spectrum of markers in diagnosis, the researchers named their company Spectral.

Using only several drops of whole blood – rather than plasma, as is employed in the Baylor test – the dye-linked markers can differentiate non-cardiac chest pain, unstable angina and an acute MI within eight minutes. "The test was found to be 100 per cent sensitive and 95 per cent specific to MI in retrospective studies", reports Yehia Gawad, M.D., Spectral's clinical director. "It is fully diagnostic in the emergency room."

The results of Spectral's retrospective studies on 485 hospital patients have been submitted for FDA 510k and Canadian Government approval. In addition, prospective controlled trials with the chest pain panel on more than 12,000 hospital patients are proceeding. (Extracted from *Genetic Engineering News*, 15 September 1994)

Polymer based drug delivery systems for organ targeting

A project funded under the EC BRITE EURAM programme has developed particulate carrier systems that can

deliver drugs to specific target sites in the body. By understanding the way in which particulate systems are handled by the body, colloidal particles have been engineered to target specific sites. Now microspheres, emulsions and liposomes can be used as diagnostic agents, to deliver drugs and to carry vaccines.

For information in the first instance, please contact: Phil O'Leary, BioResearch Ireland, Forbairt, Glasnevin, Dublin 9, Ireland. Tel.: 353-1-8370177; Fax: 353-1-8370176.

Recombinant products from yeast

The yeast *Saccharomyces cerevisiae*, which has been traditionally used in the brewing, baking and wine making industries for centuries, has been developed as an important host for the production of a potentially wide range of industrially important proteins.

Research funded under the EU BRIDGE programme has isolated *Saccharomyces* mutants with interesting properties. The project has addressed the problems of yeast cell wall breakage for the release of cytoplasmically expressed proteins, and also of improving the efficiency of secretion of proteins that can be recovered via the secretion pathway.

One aspect of the project investigated the secretion pathway of *Saccharomyces*. This pathway is suitable for many of the naturally secreted proteins, such as hormones. Many foreign proteins are inefficiently expressed by yeast, however this research group have isolated mutants that exhibit an enhanced secretion phenotype without an associated increase in expression. The mutations are chromosomally located and are currently being identified. One set of mutants were selected for their ability to secrete enhanced levels of mini-proinsulin, indicating that they could be used to increase recombinant insulin production from yeast.

The second aspect of this project deals with cytoplasmically expressed proteins, such as viral-like particles for vaccines, which need to be recovered via cell breakage. A number of mutants have been isolated which have a temperature-sensitive lysis phenotype. This opens the possibility of providing an effective strategy for protein release. The genes involved in three of these mutants have been cloned and analysed. In addition, fermenter systems have been developed to study the release of the recombinant protein. Further studies on the molecular characteristics of these mutants will provide the basis to further manipulate cell-integrity control and to further develop the protein release system.

Saccharomyces cerevisiae is a food-grade organism so applications will include the production of industrial grade, food grade and medical grade enzymes. The production of proteins for vaccines is a possible application. In addition, the production of authentic human proteins from yeast will be a key application for the pharmaceutical industry. For further information, in the first instance, contact: Phil O'Leary, BioResearch Ireland, Forbairt, Glasnevin, Dublin 9, Ireland. Tel.: 353-1-8370177; Fax: 353-1-8370176.

Victorious sponge

Marine creatures have long been a focus for anticancer drug discovery programmes. This, explains a team from Arizona State University in Tempe, is because many marine animals have survived virtually unchanged for millions of years, and they hardly ever get cancer.

The Arizona team has been studying one of the longest-surviving complex life-forms on the planet – marine sponges. Fossil sponges over a billion years old have been found which are identical to today's animals, and some species have yielded minute amounts of compounds which are effective against a few tumours. Now, however, the team has found a compound which works against at least 20 cancers.

The compound, dubbed spongistatin, was extracted from a member of the *Spongia* family found in the eastern Indian Ocean. The team extracted 400 kg of sponge with methanol, followed by an ethylene chloride methanol mixture, then purified the extract by chromatography. This yielded only 13.8 mg of spongistatin, whose structure was found by infrared, ultraviolet and nmr spectroscopy.

The team ran spongistatin through the US National Cancer Institute's series of tests against 60 human tumour cells. To their surprise, they found it has "phenomenally potent activity" against 20 of them: three leukaemias, two small cell and four non-small cell lung cancers, five colon cancers, three melanomas, two ovarian cancers and one renal tumour. (Source: *Chemistry & Industry*, 5 September 1994)

Regulatory approval given for novel in vitro test technique

The US Department of Transportation (DOT) has approved the use of Advanced Tissue Sciences Inc.'s (ATS, La Jolla, CA) Skin2 TM *in vitro* laboratory test kit as an alternative to live animal testing of potentially corrosive materials. The product contains living human skin tissue that is cultured using ATS' tissue engineering technology, which is based on techniques initially developed at Procter & Gamble (Cincinnati, OH).

ATS officials say the approval marks the first time a government regulatory agency has granted an approval for an *in vitro* test method containing cultured human tissue.

According to ATS, the approval came about as a result of the DOT's implementation of a United Nations directive that requires all transported hazardous materials to be tested, labelled and packaged based on their level of potential corrosivity. Corrosive materials are those that cause visible, irreversible destruction or alternation of human skin. The approval granted for ATS' kits applies to the testing of specific types of hazardous materials which are transported in interstate commerce. (Source: *Genetic Engineering News*, July 1994)

Livestock applications

Jockey club changes to DNA typing

The US Jockey Club is switching from blood-typing to DNA-typing to verify parentage of all newborn foals.

Starting in 1995, no foal can be registered (allowed to race) until their parentage has been verified by DNA. Most stallions have been DNA-typed already, and the Jockey Club is moving to type all mares under 15 by the end of the year.

The Jockey Club oversees the breeding of thoroughbred racehorses. Today, foals are registered only after a laboratory verifies the blood sample and physical markings with those of the parents.

The Jockey Club mandated blood-typing of all newborns in the mid-1980s. But only last year did the other breeds (quarter horses, Arabians, Appaloosas) adopt a blood-typing standard. (Source: *McGraw Hill's Biotechnology Newswatch*, 15 August 1994)

Genetic engineered rabies vaccine

Researchers at McMaster University, Canada, have developed a possible counterstrike to the threat of raccoon-specific rabies, a strain that has been working its way to Ontario from the mid-eastern USA for the past four decades. It is the first time genetic engineering has been harnessed in Canada to fight the problem.

The Ontario government operates an effective catch-and-release programme to inoculate wild animals with a vaccine based on live rabies virus. While the method works with all species of animals, it fails when used as air-dropped baits in wilderness areas. Foxes develop an immunity when they eat the vaccine, but the method has proved ineffective with raccoons.

To solve the problem, researchers took a rabies virus gene known to cause an immune response and spliced it into human adenovirus, a harmless virus that causes symptoms similar to the common cold. Preliminary tests indicate the modified adenovirus is effective in combating rabies in raccoons, foxes and skunks.

MicroBix Biosystems of Toronto is working with the researchers to commercialize the vaccine. Further testing is required before Agriculture Canada approval, but if the vaccine continues to perform well, it could be air-dropped to inoculate wild animals in the next three years - and be made available for domestic dogs and cats. (Source: *The AgBiotech Bulletin*, Vol. 2, Issue 5, September 1994)

New developments to detect latent porcine viral infections

Aujeszky's disease is a major cause of economic loss in the swine industry, affecting mainly the sensory and central neurons of affected animals. This disease is caused by a virus belonging to the alpha herpes virus family, the pseudorabies virus (PRV). The virus can exist latently in the animal (i.e. in an inactive state), which means it is one of the more difficult viruses to eradicate from a population of pigs. Animals carrying the virus in its latent form will not be subjected to the disease, until the virus reactivates under new conditions.

The Polymerase Chain Reaction (PCR) was a major development in molecular biology. Researchers have adopted this new technique to develop a highly specific and sensitive PCR assay to identify minute amounts of PRV virus, which may be present latently in different tissues. Briefly, the assay involves an internal standard with a sequence similar to PRV which is added to the PCR reaction. The products of this reaction are detected and analysed by a sequencer. The assay is highly reproducible with a detection limit of just one copy of PRV DNA. This assay can be used to distinguish different strains of PRV and is also valuable for monitoring vaccine efficiency.

The PRV Genes specific for latency, known as the Latency Associated Transcript (LAT) have been sequenced and cloned. Researchers now are working on a latency-marker for PRV-infection to develop a diagnostic kit to determine if and when PRV is present latently in pigs.

This investigation is attempting to reduce the pathogenicity of recombinant PRV following recent work by Sambhi *et al.* (1991, *Proc. Natl. Acad. Sci. USA* 88, 4025-4029) which has shown that porcine tumour necrosis factor alpha (TNFα) has antiviral effects using recombinant vaccinia virus in a mouse model. A similar approach is being used by this group who developed a recombinant PRV carrying the porcine TNFα gene under the control of selected viral promoters. These recombinant PRV viruses with modified pathogenicity will be investigated in pigs by analysing their organ tropism and latency characteristics.

These results will be of particular interest to companies involved in the development of veterinary pharmaceuticals. An opportunity exists for a license agreement or joint venture with a view to the development of a commercial diagnostic kit for the detection of latent PRV virus in pigs. For further information, please contact: Phil O'Leary, BioResearch Ireland, Forbairt, Glasnevin, Dublin 9, Ireland. Tel.: 353-1-8370177; Fax: 353-1-837017o.

New tick vaccine launched

The development of tick strains resistant to all major chemical groups is a problem of major concern to cattlemen. Increasingly, both beef and dairy farmers are struggling to produce meat and milk free of chemical residues whilst maintaining an acceptable level of tick control. Cattle ticks cause productivity losses in Australia also estimated at over $A 100 million per annum. The new vaccine, called TickGARD, is the world's first genetically engineered anti-parasite vaccine to be registered for commercial use. The vaccine is effective against all acaricide resistant cattle strains.

More than ten years of collaborative research between the CSIRO Division of Tropical Animal Production and Biotech Australia, a member of the Hoechst group, has culminated in the production of TickGARD. TickGARD has been evaluated in extensive field trials on beef and dairy properties during the last five years. Widespread use on commercial and research properties has demonstrated the safety and efficacy of TickGARD as part of an integrated tick control programme.

TickGARD contains Bm86, a tick gut protein produced by genetic engineering. It has been purified and incorporated into an oil adjuvanted vaccine (similar to the adjuvant of the bovine vibriosis vaccine). Cattle vaccinated with TickGARD produce specific antibodies against the gut of the cattle tick. When a cattle tick feeds on a vaccinated animal, it will take up these antibodies which bind to and damage the gut of the tick. The most significant result of this is a reduction of up to 70 per cent in the fertility of the ticks. Damaged ticks lay fewer eggs, fewer of these eggs hatch successfully and fewer of those larvae (seed ticks) that do hatch are viable. Therefore, vaccination of a group of cattle will reduce the build-up of ticks in the paddock. It is the tick population in the paddock, not on the individual cattle, that is the prime target of the vaccine.

Use of the vaccine every 6-10 weeks during the tick season will maintain continuous effective antibody levels which will reduce the fertility of ticks on cattle throughout the season. The effects of vaccination will become evident after the first two months of use, with fewer chemical treatments being needed for the control of ticks. (Extracted from *Australasian Biotechnology*, Vol. 4, No. 3, June 1994)

Chicken anaemia virus (CAV)

One of the killers of young chicks is Chicken Anaemia Virus, or CAV as it is known. Strange as it may sound,

chickens suffer from anaemia with similar symptoms to those of humans, their skin bruises, they are stressed and fatigued and they either die from the disease, are crushed in a chicken stampede, or if they survive, have extremely poor growth.

The Rural Biomedical Research Group at Charles Stuart University in Australia has just begun to research and develop a test for CAV in meat producing birds with world-wide potential for control of the disease.

In charge of the research is microbiology lecturer in the School of Science and Technology Dr. Geoff Crawford, who estimates that CAV costs the Australian chicken meat industry at least $17 million per annum.

CAV was first discovered by Japanese researchers in 1979 and it was found to infect laying hens, which pass the virus to chicks through the egg. The disease grows in the young birds' bone marrow disrupting the normal production of red and white blood cells, which in turn affects the immune system. UK research has found that if older birds are infected by the virus they are unlikely to die or even show signs of the disease, but their growth is restricted.

Dr. Crawford has received a major research grant to produce an ELISA (enzyme linked immunosorbent assay), a test used to diagnose many human and animal diseases. The project is to produce a test to detect whether a chicken is infected with CAV so outbreaks can be identified and also to tell whether a chicken is immune to CAV either naturally or by vaccination.

In conjunction with the CSIRO Division of Animal Health, Dr. Crawford and his team aim to clone the antigen for CAV using *Escherichia coli*. The *E. coli* will become the factory to produce the antigen cheaply. The CSIRO researchers are working on increasing the efficiency of this technique.

It is envisaged this work will be complete by June 1995 and then an ELISA test will be produced by the Rural Biomedical Research Group at CSU to be manufactured and marketed by JCU Tropical Biotechnology Pty Ltd., a Queensland company that specializes in launching Australian inventions. (Source: *Australasian Biotechnology*, Vol. 4, No. 4, August 1994)

Agricultural Applications

Rescue of Latin American maize progresses

An international panel of experts on maize genetic resources conservation recently praised the work of 13 national seed banks in Latin America and the Caribbean that have been cooperating to regenerate endangered holdings of maize landraces. The landraces were gathered in farmers' fields and in markets across the Americas as part of a Rockefeller Foundation initiative undertaken during the 1940s to 1960s. Prior to the cooperative rescue effort, the national banks lacked the money to store and regenerate the seed, some of which had already lost the ability to germinate.

Coordinated by the Mexico-based International Maize and Wheat Improvement Center (CIMMYT) and supported by the US Agency for International Development (USAID) through Project Noah and the US National Seed Storage Laboratory (NSSL) of the US Department of Agriculture (USDA), the rescue effort has restored seed of more than 3,000 endangered accessions and partially regenerated nearly 3,000 more since September 1991. In addition, the panel's report states that "... the project has laid the groundwork for future cooperative international activities related to the conservation and utilization of maize germplasm".

More than two dozen maize specialists from some 15 countries attended the review meetings held at CIMMYT in April 1994 to assess this landmark regeneration effort. Representatives of cooperating genebanks reported on progress to date and discussed technical problems – such as poor germination, crop failure, or poor adaptation of accessions to regeneration locations – which have sometimes kept them from obtaining the 100-ear minimum per accession required for a successful regeneration.

Regeneration for more than 7,900 accessions was supposed to be completed in September 1994. However, due to the above problems and the lag between the project's fiscal schedule and southern hemisphere growing seasons, only half the projected growing cycles will have been planted by that time. Since funds are disbursed for work completed, the review panel recommended that regeneration continue through 1996, drawing on yet unused reserves to plant the remaining cycles. Other major suggestions by the panel included:

- Organizing future meetings among cooperators to review progress and strengthen the network;
- Offering short, practical courses on seed handling at CIMMYT for regeneration cooperators; and
- Forming core subsets of major race complexes in cooperating banks.

In addition, to improve the handling and exchange of regenerated seed, USDA through NSSL will provide new seed dryers for participating countries. Besides representing an important heritage, the landraces constitute a vital reservoir of traits that breeders can use to improve maize. Each participating genebank is planting, harvesting and processing its own endangered holdings. The banks are keeping the collections they renew. As an added safety net against catastrophic loss, backup samples are stored at CIMMYT and NSSL. The inventory will be updated periodically with new samples coming from the regeneration project. A report is currently being written.

For additional information, contact: Dr. Suketoshi Taba, CIMMYT, Apartado Postal 6-641, 06600 Mexico D.F., Mexico. Fax: 52-595-41069. E-mail: S.Taba@alphac.cimmyt.mx. (Source: *Diversity*, Vol. 10, No. 4, 1994)

New maize varieties

The International Centre for Insect Physiology and Ecology (ICIPE) has developed two maize populations and four elite sorghum hybrids that combine resistance to the spotted stemborer, *Chilo partellus*. The centre has also launched research on developing varieties with multiple resistance to different borers in maize and strengthened its work on developing sorghum genotypes with combined resistance to stemborers and shootfly. In addition, more than 30 diverse banana cultivars were added to the ICIPE germplasm collection at Ungoye in Western Kenya. For additional information, contact: The International Centre of Insect Physiology and Ecology, P.O. Box 30772, Nairobi, Kenya. Tel: 254-2-802501. Fax: 254-2-803360. E-mail: CG0063

International Maize and Wheat Improvement Centre (CIMMYT) maize breeders have been able to develop drought-tolerant tropical maize varieties after noticing that

maize deprived of water around flowering time produces its female flowers (silks) several days later than usual because the male flower (pollen producing tassel) apparently monopolizes the limited supply of plant carbohydrates, leaving little for silks and ears. CIMMYT physiologist Gregory Edmeades and his team placed eight successive generations of maize under extreme drought at flowering and selected only those plants in which silks appeared soon after male flowers. This reduced "anthesis to silking interval" (ASI) of the flower proved to be a clear indicator for selecting tolerance to mid-season drought in tropical maize. CIMMYT's applied molecular genetics laboratory is now developing markers that will enable selection for reduced ASI even in the absence of drought. For additional information, contact: Dr. Gregory Edmeades, CIMMYT, Lisboa 27, Apartado Postal 6-641, 06600 Mexico, D.F., Mexico. Tel.: 52-5954-2100; Fax: 52-5-954-1069; E-mail: CIMMYT *@* alphac.cimmyt.mx.(Source: *Diversity*, Vol. 10, No. 4, 1994)

New potato virus test saves times

Researchers in Fredricton, New Brunswick, Canada, have discovered a new bioassay host that cuts a time-consuming step when testing for PVYn potato virus. According to a report in *AGvance*, the virus does not actually harm potato plants. However, it is seen as a threat to other commercial crops. This chases away buyers, particularly for seed potatoes.

Testing for the virus has been further complicated because it is part of a larger group of generally benign viruses. The presence of one of these "cousins" can cause inconclusive test results. The current test, called the tobacco bioassay, is also time-consuming. A tobacco plant is inoculated with samples from the suspect potato crop. If the disease is present, symptoms develop in the tobacco in 10 to 21 days. However, because several different "cousin" viruses also cause symptoms in tobacco, the virus must be extracted to accurately determine if it is PVYn. This adds another two to three weeks to the testing process.

The Fredricton researchers' new bioassay host – a type of wild potato – is susceptible to PVYn. So susceptible, in fact, that the virus kills the plant within 10 days – an excellent indicator of the presence of the virus. Further information from Dr. Doug McBeath, Fredricton Research Centre, (506) 452-3260 or Fax: 452-3316. (Source: *The IGBiotech Bulletin*, Vol. 2, Issue 6, October 1994)

Controlling flower development

In the cut flower industry the shape, colour and number of flowers are all critically important. The mechanisms which control the production and development of flowers have been a central concern for plant research for many years. Cut flowers and flowering plants are a huge industry in Europe and it is one where the quality of the blooms is of paramount importance.

The quality of flowering plants is affected by diseases that blemish foliage and blooms, this can reduce the shelf-life of the product. Quality is also associated with novelty. The possibility of altering flower shape and colour by genetic engineering promises exciting new developments. New, unusually coloured varieties of flowering plants by the modification of genes controlling enzymes in pigment biosynthetic pathways is an example of how flowering plants can be altered. Petunia and tobacco flower colours have already been modified by the insertion of a gene from maize which interferes with normal pigment production.

EU funded research is helping to contribute to the isolation of key plant genes and to our understanding of flower development. This project is isolating and studying the key flowering genes in *Antirrhinum* (snapdragon). This plant grows throughout Europe, has a good genetic map, well characterized transposons and mutations, in addition to a large flower.

To facilitate gene cloning and analysis, a range of areas are being investigated.

A "library" of transposons has been established each transposing to different areas of the chromosomal map, these short segments of DNA can move around the plant genome and help isolate key genes.

The construction of a combined restriction fragment length polymorphism and genetic map has been carried out.

By studying mutations that cause *Antirrhinum* flowers to develop abnormally, they have been able to start unravelling how genes control the development of flowers. Other species, such as pea are being looked at to establish which events are common to all plant species.

The ability to modify and introduce genes into plants is an essential tool in analysing gene function. Initial work has seen the development of a protocol of transformation and regeneration in *Antirrhinum*.

Commercial plant breeders and plant developmental and reproductive biologists will find this project of interest. The flower is of major agronomic importance in ensuring efficient breeding of crops and because many plant products are derived from flower fruits and seeds. For further information on this work, please contact: Phil O'Leary, BioResearch Ireland, Forbairt, Glasnevin, Dublin 9, Ireland. Tel.: 353-1-8370177; Fax: 353-1-8370176

Garlic to the rescue

Garlic has for centuries been used by people all over the world as a key ingredient in all sorts of home remedies – in addition, of course, to its usefulness in the culinary arts.

According to S. D. Singh, Senior Scientist (Crop Protection), it also works against plant disease. Singh used a spray made from garlic extract in greenhouse and field experiments at ICRISAT Asia Centre with astounding success against ergot, a deadly fungal disease that wreaks havoc on sorghum crops in India and Africa. Plant breeders have thus far had little success developing cultivars resistant to ergot.

The possibility of using garlic as a fungicide is welcome news to farmers and environmentalists concerned with overuse of dangerous chemicals to control plant diseases, since it poses no danger to spray operators or consumers.

The main problem with garlic extract is that rain washes it off the plants. Also, preparing the extract is hard work. It takes 40 kg of garlic to create 500 litres of spray – sufficient to spray a hectare of sorghum. The cost of garlic is not low, but it is cheaper than the most effective fungicides, says Singh, and if a technology can be developed that reduces the labour required to prepare the extract, adoption will be widespread. (Source: *SAT News*, No. 16, 1994)

Plantain improvement

Research at the International Institute of Tropical Agriculture (IITA) indicates that genetic improvement of plantains is on the horizon. Three IITA scientists in Nigeria are exploring techniques for developing durable host resistance to black sigatoka disease which is seriously threatening the plantain in sub-Saharan Africa, home of 50 per cent of the world's production. Germplasm enhancement scientist D. Vuylsteke, breeder-geneticist R. Ortiz, and agronomist breeder R. Swennen have been working on the project for six years. Their results will also be applicable in the tropical humid forest areas of America. For additional information, contact: D. Vuylsteke, IITA, Oyo Road, PMB 5320, Ibadan, Nigeria. Tel.: 234-22-400300 318; Fax: 234-1-611896; E-mail: iita *a* cgnet.com. (Source: *Diversity*, Vol. 10, No. 2, 1994)

Fungicides

Spanish scientists have come to the rescue of fruit suffering from mould infections. They have made a new fungicide which could save the Spanish wine industry grapes and money.

Botrytis is a grey mould fungus which attacks grapes, strawberries, bulbs and forest tree seedlings, and inflicts significant commercial damage on the wine industry, in particular. Dr. Isidro Collado and his team at the University of Cadiz have made a selective fungicide which inhibits the growth of a species of the mould, *Botrytis cinerea*.

Although there are a number of fungicides on the market which are used to protect plants against attack by *B. cinerea* and related species, there are worrying signs that the fungi are developing resistance to these compounds. This has led to increased use, and there is concern that the compounds may persist in the soil and accumulate in the food chain.

Collado's research suggests that a toxin, botrydial, synthesized by the fungi, is probably responsible for the typical tissue damage that destroys the plant once infection has set in (*Journal of Natural Products*, in press). The biosynthetic pathway to botrydial is well-known and Collado has been able to synthesize analogues to some of its precursors.

Some of these analogues show marked inhibition of the growth of *B. cinerea*. This is presumably because they bind to enzymes which catalyse the steps of the botrydial synthetic pathway in place of the correct precursors. Collado is now concentrating on isolating and characterizing these enzymes, with the aim of targeting the biosynthesis of the toxin more precisely and producing even more effective fungicides. He is hoping to move towards field trials, in collaboration with industrial partners in the wine industry. (Source: *Chemistry & Industry*, 1 August 1994)

New pheromone developed

A new pheromone developed by Oxford Asymmetry Ltd., an English-based chiral chemicals company, may address the UK's problem with the woodworm, an insect that causes devastating damage to dwellings and furnishings.

Oxford scientists have synthesized the pheromones (sex hormones used by females to attract male partners) of the woodworm, and recreated them in the laboratory. The pheromones can, in turn, be released into homes to confuse the male, or placed in traps for easy capture.

The new treatment is based on the use of stegobinone, a naturally occurring chiral pheromone. Stegobinone has both a right- and left-handed form, making it very difficult to synthesize in the laboratory. However, using a new synthetic route, Oxford has produced commercial quantities of highly pure material which has been shown to be as effective as naturally occurring stegobinone.

Trials by Oxford, thus far, are confirming the approach to be a viable alternative to insecticides. If put into commercial use, stegobinone will reduce the need for insecticide spraying, thus eliminating exposure to dangerous chemicals, the company says.

Woodworms account for between 70 and 80 per cent of boring insect-caused wood damage in the UK. (Source: *Chemical Marketing Reporter*, 15 August 1994)

New developments for tomato growers

All plants encode a huge variety of interesting and important genes but they are known only by the phenotype they confer and their map position. Disease resistance, growth habit, fruit ripening, hormone synthesis and flowering time are just some of the genes of interest to commercial growers of tomato plants. These genes can be targeted and used to improve the range of commercially available varieties in addition to strengthening academic knowledge available in this area. Extracting such genetically defined genes from plant genomes is difficult in practice. Transposon tagging and map based cloning are the two major technologies available for this task.

A set of tomato genotypes has been obtained with mapped transposon inserts and now stocks are available with a transposable element for each tomato chromosome. This research group are now positioned to use this technology to isolate interesting genes both by non-targeted and targeted tagging.

In research funded under the CEC BRIDGE scheme to improve procedures for cloning and targeting the wide variety of important plant genes and to investigate disease resistance, targeted transposon tagging experiments were done to investigate Alternaria Stem Canker Disease followed by characterizing transposon induced mutations. This technology is also being used to isolate the gene Cf-9, which confers resistance to some species from the leaf mould pathogen, *Cladosporium fulvum*.

In studying plant development, researchers have isolated the genes that initiate and or control apical and lateral meristems. Targeted transposon tagging experiments have been carried out on specific genes, in addition to untargeted transposon tagging experiments which were done to find new developmental mutants.

In the area of hormone biosynthesis transposon induced mutants for the genes encoding enzymes involved in biosynthesis of the plant hormone ABA are being investigated.

Commercial breeders of tomato cultivars will be interested in this research. The potential exists now to clone specific genes by targeted transposon tagging and to isolate interesting traits in tomato. In fact in the US Calgene's Flavr Savr tomato was the first transgenic whole food to get FDA approval and has been on sale since 21 May 1994. This development paves the way for consumer acceptance of the use of these technologies in food products. Ultimately development of improved strains by tailoring plant development, hormone biosynthesis and disease

resistance genes to improve commercial performance, is possible. European organizations and companies interested in establishing links in order to benefit from these developments should, in the first instance, contact: Phil O'Leary, BioResearch Ireland, Forbairt, Glasnevin, Dublin 9, Ireland. Tel.: +353-1-8370177; Fax: +353-1-8370176.

Wheat transformation project

A new project under the UK Biotechnology and Biological Sciences Research Council's "Collaboration with Industry Scheme" and the Ministry of Agriculture, Fisheries and Food's Crop Molecular Genetics programme is focusing on the genetic engineering of wheat. Among the goals: to enhance nutrient uptake and increase natural resistance to pests and disease, as well as to modify the starch, lipid and protein composition of the grain.

An important factor which has held back transformation technology in wheat and barley is that they are harder to regenerate from tissue culture than rice or maize. Dr. Paul Lazzeri, project leader at Rothamsted Experimental Station, believes that he and colleagues have recently produced what are believed to be the first cereals genetically transformed in the UK using both a wheat X barley hybrid (fertile amphiploid) called tritordeum and "model" wheat cultivars amenable to manipulation in culture.

The success so far draws on two pieces of technology: a helium particle gun to shoot gold pellets coated with DNA into plant tissue; and the use of highly regenerable cultures of immature inflorescence tissue. Lazzeri and his colleague Dr. Pilar Barcelo developed the culture system when working on tritordeum at the University of Hamburg, Germany. A key element in the design of effective gene transfer techniques for wheat will be the identification of cell types which will tolerate particle bombardment and be able to proliferate and regenerate at high efficiency. Details are available from: Biotechnology and Biological Sciences Research Council, Polaris House, North Star Avenue, Swindon SN2 1UH or on 0793-413200. (Source: *Biotechnology Bulletin*, August 1994)

Extraction Industry Applications

Biotechnology desulphurization

Energy BioSystems (The Woodlands, TX) and partner Petrolite have begun building a $1.5-million pilot plant using a biotechnology process to remove sulphur from petroleum streams. The companies say it will be the first such continuous unit to use a biological process. The pilot plant is located at Petrolite's research laboratories in St. Louis and is being built by M. W. Kellogg. The companies expect construction of a commercial-scale plant to begin in the second half of 1995. (Source: *ChemicalWeek*, 1 June 1994)

Institute develops coal bioleaching

Japan's Central Research Institute of the Electric Power Industry has developed a practical [illegible] of a continuous coal leaching process for coal-[illegible] stations using microbes. The sulphur in coal [illegible] organic sulphur bound to carbon and inorganic sulphur bound to iron as iron sulphide. Iron oxidizing bacteria, which have an affinity for the iron sulphide, were found to cause the inorganic compound to precipitate out into water in a coal slurry. Air bubbles then carry the coal particles to the top leaving the inorganic sulphur on the bottom. (Source: *McGraw Hill's Biotechnology Newswatch*, 1 August 1994)

High-yield extraction of oil from microalgae

The National Institute for Resources and Environment of the Agency of Industrial Science and Technology of Japan has established a new technology for effectively recovering liquid fuels from microalgae which convert carbon dioxide (CO_2), the cause of global warming, into the liquid fuels.

With this new technology, the microalgae are treated by a high-temperature, high-pressure process for recovering the liquid fuel, which is usable as an alternative to petroleum-alternative oil, and extraction is possible at a yield that is 15 per cent higher than by conventional methods. Research is still in the basic stage, but the technology may pave the way for the mass production of microalgae liquid fuel.

The microalgae is *Botryococcus braunii* of the Chlorophyceae algae. It consumes CO_2 as its nutrient and can store liquid hydrocarbons called botryococcine to roughly one-half of its weight. These hydrocarbons are usable as boiler fuel, and are usable as gasoline by cracking the hydrocarbons.

These hydrocarbons are recovered by first freeze-drying *Botryococcus braunii*, then extracting the oil with an organic solvent such as hexane or acetone during ultrasonic irradiation. This method enables the entire volume of botryococcine to be recovered, but is not suitable for mass production since complex processes are involved.

By contrast, with the new technology, the liquid fuel can be extracted at a high yield of 65 per cent simply by placing *Botryococcus braunii* inside a reactor and raising the temperature and pressure. This high recovery rate depends on applying a high temperature and pressure, by which other organic substances comprising *Botryococcus braunii* are converted into hydrocarbons. The research team observed that the proteins and sugars existing inside the microalgae are converted into hydrocarbons in the process.

In experiments, *Botryococcus braunii* and a catalyst (sodium carbonate) were fed into a reactor and reaction advanced at 300 °C and 10 Mpa. The ratio of *Botryococcus braunii* and sodium carbonate was 100:5. Liquid fuel up to 65 per cent of the algae weight was generated, a yield 15 per cent higher than the recovery of liquid fuel by conventional processes. Further details are available from: National Institute for Resources and Environment, AIST, 16-3, Onogawa, Tsukuba City, Ibaraki Pref. 305. Tel.: +81-298-58-8111; Fax: +81-298-58-8118. (Source: *JETRO*, December 1993)

Chemical Applications

Antimicrobial fibre

Hoechst Celanese, in conjunction with Microban Products (Huntersville, NC), has introduced a new antimicrobial acetate staple and filament fibre. The fibre, MicroSafe AM, provides control of the growth of a wide range of gram-positive and gram-negative bacteria as well as fungi, mould, mildew and yeast, the company says. Potential applications for the product are in clothing, homes, health care facilities, laboratories, food service units, public transportation and education and correctional institutions. (Source: *ChemicalWeek*, 1 August 1994)

Cosmetic companies move to adopting biotechnology techniques

The cosmetics industry is inching towards biotechnology. Although the market is currently too small for biotechnology or cosmetics analysts to track, there are indications that a biocosmetics industry will emerge as companies become increasingly concerned about the purity, availability or ethics of current ingredients.

In response, biotechnology companies have developed active ingredients that in cosmetics provide more than mere colour or surface protection.

Anti-aging compounds, sun blocks, tanning agents, skin creams, shampoos, moisturizers, hair dyes and fragrances are all being developed using biotechnology-based ingredients, and some of them are manufactured by major companies.

These "cosmeceuticals" are accepted somewhat more readily by cosmetics firms in Japan and Europe than by those in the U.S.

Because the regulations governing the disclosure of ingredients are much looser in cosmetics than is the case for health care, it is difficult to know what is in a given product by reading the advertisements or the label.

Currently, many ingredients in cosmetics sound like substances found in medieval apothecaries. For example, hyaluronic acid, which is used extensively as a moisturizer, is extracted from a cock's comb, which hardly conjures up the elegant image of modern beauty products. Its biotechnology-based version was produced as early as 1990 by Fermentech Ltd (Edinburgh, Scotland) and, at least initially, had only limited market success. Shiseido, in Japan, is now pursuing the biotechnology version for its product line.

Another ingredient, the pigment shikonin, is developed from the now-rare root of the perennial *Lithospermum erythrorizon*, which only develops its colour after the plant is several years old. Cell culture technology, however, allows cultures to be grown in the thousands and saves the plant in the process. The technology and the products are available. The challenge now is to interest more cosmetics firms.

At Novo Nordisk (Bagsvaerd, Denmark), they plan to examine all possible biological ingredients that can be made using their biotechnology methods so that, by the end of this decade, it will become a leading supplier of biotechnology-based ingredients for personal care products. For cosmetics, that includes enzymes, glycolipids, protein derivatives and structured lipids.

Initially, the company plans to expand its enzyme market from the lens care and dental care segments to skin care, using enzymes to replace harsh ingredients. Novo Nordisk is testing proteolytic enzymes to remove particles of dead skin during facial peeling and is testing superoxide dismutase as part of an anti-aging compound to remove free radicals from the skin surface. For hair care, Novo Nordisk is hoping to use enzymes and a class of biological surfactants known as glycolipids as milder alternatives to the harsh chemicals currently used. (Extracted from *Chemical Week*, 14 September 1994.)

Food Production and Processing

Advances in food processing

Although biotechnology is now taken for granted in medicine, pharmaceuticals and agriculture, food biotechnology has up to now focused on yield and nutrition rather than processing. Over the next few years, however, food experts expect advances in genetics, enzymology and contaminant detection to change the way food is processed as well.

Unlike pharmaceuticals or medicine, where biotechnology can do things that were impossible just a few years ago, food processors are ultimately limited by what consumers like and what they will buy. The enormous volume and intense competition in the food industry has resulted, to a large degree, from efficient, low-cost processing techniques that will be difficult to change.

Bioengineering wheat with 50 per cent more protein is one thing, yet tinkering with a leavening process that has changed little in 50 years is quite another.

As the chemical engines of living systems, enzymes are natural to food processing. Enzymes that make or break chemical bonds in fats, peptides and carbohydrates are already used, either as extracts or in live microbes, to process all types of food.

Over half of the world's enzymes are consumed by the food industry; proteases, lipases, pectinases, cellulases, amylases and isomerases are extensively used to process the nutritional components of foods. Chymosin, a protease used to make cheese, was originally extracted from the stomachs of veal calves. Since an identical form of chymosin expressed in *E. coli* was approved for cheese making in 1990, over 15 billion pounds of cheese have been made in 17 countries using the recombinant enzyme.

Novo Nordisk (Bagsvaerd, Denmark) currently supplies about 60 per cent of all enzymes used by the food industry, 60 per cent of which are recombinant.

Novo Nordisk is primarily involved in identifying and expressing natural enzymes in yeast and bacteria. NovaMyl, an amylase, retards spoilage in bread and reduces the need for chemical anti-staling agents.

E. coli-produced chymosin costs about half as much as the calf enzyme, but this has had little if any effect on the price of cheese. Rather, the recombinant protein offers cheese-makers stable price and availability, as well as purer enzyme. The protein from calves only met about 30 per cent of the demand for cheese-processing enzymes, the rest came from microbial proteases that resemble chymosin but are not as efficient. Also, only about 5 per cent of the calf protein extract was actually chymosin, compared with 90 per cent from *E. coli*.

Every food group includes fermented products processed with enzymes from live, intact organisms. Fermented foods are a natural target for designed processability, since organisms carrying out fermentation could be programmed to produce such ingredients as amino acids, vitamins, pigments, flavours, sweeteners, thickeners or other ingredients normally added later on in food processing.

Although regulators and the public are generally quite accepting of food processing biotechnology, the adoption of genetically altered microbes for processing or processability is not problem-free. The food industry is concerned about the introduction of allergens, antigens or foreign genes into humans, but this should not be a problem where targeted, specific changes are introduced into microbial genomes. At any rate the genetic changes introduced through bioengineering are minute compared with those induced through chemical mutagenesis, radiation or even traditional selective breeding.

Enzymes altered chemically or through base substitution on genes that code for them could become an important part of the food processing industry. Chemical modification shows some promise but is limited since it operates only on existing protein and involves these additional chemical and purification steps:

- Alpha amylase acetylated with p-nitrophenyl acetate with improved thermal stability;
- Acetylation or iodination of carboxypeptidase A shows enhanced esterase activity while turning off peptidase activity;
- Acylation of chymosin has up to twice the milk-coagulating activity of native protein;
- Acylation of thermolysin with amino acid N-hydroxysuccinimide esters increases enzymatic activity up to 70-fold.

Genetic manipulation has even greater potential for producing enzymes that carry out specific, narrowly defined processes in foods. Researchers are particularly interested in enzymes that:

- Function at higher or lower temperature than normal, affording a simple means to turn enzymatic activity on and off;
- Withstand great fluctuations in pH;
- Have altered substrate specificity, useful in limiting or broadening the utility of an enzyme;
- Have started cultures that are more phage resistant.

The distinction between altering foods for nutrition or yield and changing them for greater processability is often blurry. Both goals may be possible with one genetic manipulation. Antisense technology could play a significant role in designing processability into foods.

Another item on the wish-list for food processors is food diagnostics: rapid, reliable, inexpensive diagnostic tests for food pathogens, nutrients and contaminants. In many cases, the technology, the immunoassay, in particular, is already developed for other markets and would simply have to be adapted to the particular needs of food processors.

In the dairy industry, for example, milk is tested for nutritional content and microbes at the processing plant after an entire tanker car is filled. If there was a simple dipstick test for the most common bacterial problems in milk, a test that a farmer or tank car operators could perform at the point of collection, the dairy industry would have to destroy many fewer tank-loads of milk.

Recombinant food processing enzymes confer a modest regulatory burden to processors but no added labeling burden as long as they are identical to the natural proteins. Cheese made with chymosin expressed in *E. coli*, for example, need not carry a label indicating that the enzyme was not derived from calves.

So far, there has been no public outcry over the use of recombinant food processing enzymes, certainly nothing approaching the controversy on bovine somatotropin. For some reason, the public views chymosin as a processing adjunct and BST as an additive. (Source: *Genetic Engineering News*, 1 May 1994)

Plants show promise as sources of food dyes

In the University of Illinois (Urbana) laboratory of food chemist M. Dolores Berber-Jiminez, researchers are looking at various anthocyanins (reddish or blue pigments in many flowers and plants) as sources of stable, natural pigments that can be extracted and produced in sufficient quantities. The scientists found that under normal growth conditions, *tradescantia* (known as the wandering Jew, and known for its purple flowers), produces the most stable red pigment in comparative tests with ajuga, grape and cabbage. When tested *in vitro*, with tissues artificially produced in a horticulture laboratory, the pigments in ajuga (also called bugleweed) fared the best. The pigments in both plants appear to be more stable than those found in regular fruit, such as commonly used cranberries, cherries and grapes, according to the researchers.

The scientists used nuclear magnetic resonance, enzymatic analysis and mass spectrometry to study the molecular makeup, location of protons and the stability of the pigments in ajuga and *tradescantia*. They also used a light-exposure test to accelerate grocery-store lighting conditions, which tend to break down the stability of anthocyanins. (Source: *Genetic Engineering News*, 15 June 1994)

Antibiotic markers questioned

A panel which advises the UK Ministry of Agriculture has expressed concerns on the use of antibiotic resistance markers in genetically modified food organisms.

The panel, the Advisory Committee on Novel Foods and Processes, feels that the possibility of antibiotic resistance being transferred from the food to humans cannot be ruled out. Such markers are used in developing genetically modified crops to indicate whether the genetic change has occurred successfully.

The panel's reservations cast doubt on future UK marketing approvals for products such as the genetically modified fresh tomato, now on sale in the US.

Genetically modified processed foods, like the tomato products being developed by Zeneca, are not affected by the issue, because of denaturing during processing, a spokeswomen for Zeneca Seeds explained. (Source: *European Chemical News*, 8 August 1994)

Antibody fortified foods could block salmonella

An agricultural life sciences research laboratory at Tokyo University and the Japanese National Institute of Health have confirmed at the cellular level that when antigens attach to intestinal walls, they prevent pathogens from penetrating cell walls. In experiments, researchers used human intestinal cells prepared with antibodies from chicken eggs which prevented salmonella organisms from reaching the bloodstream. Since it is thought that pathogens enter the bloodstream opportunistically as the intestine absorbs nutrients, the findings suggest that by including antibodies in food such opportunistic infections could be curtailed. Leading candidates for fortification include milk and eggs. (Source: *McGraw Hill's Biotechnology Newswatch*, 6 June 1994)

DNA gene probes "unreliable"

DNA gene probes are an unreliable way of detecting bacteria in food, claims the UK Institute of Food Research (IFR). The Institute says messenger RNA (mRNA) is a much more reliable guide.

DNA probes, usually coupled with the polymerase chain reaction (PCR), are now available for detecting a wide range of bacteria. The problem is that while they are very sensitive, they cannot distinguish live and dead bacteria.

IFR says it has shown that there is no simple relationship between cell death and the detection of *Listeria monocytogenes* and *Escherichia coli* by PCR. It claims that mRNA is a better indicator of viable organisms, because it has a half-life (the time taken for 50 per cent to disappear) of only 1–2 minutes.

The Institute is developing a method of detecting mRNAs from *E. coli* and *L. monocytogenes*, which it says would allow detection during all stages of growth and after starvation. It claims these would give a real-time indicator of cell health.

According to Ian Masters, who is leading the research, the new technique is at least two years away from commercial application. It still uses PCR, but the extra step of first producing DNA from the mRNA using reverse transcriptase is causing problems.

Getting the RNA out in a usable form is another problem, because it is liable to be destroyed by cellular RNase.

Work to date is based on pure bacterial cultures, but once the method is refined, Dr. Masters will have to test it on "sick" bacterial cells before applying it to bacteria in food. (Source: *Microbiology Europe*, Vol. 2, No. 4, July/August 1994)

Industrial Microbiology

Easier ethanol

The process for making ethanol from biomass is currently not efficient enough to make ethanol a truly competitive additive for petrol. As a possible prelude to cheaper ethanol, researchers at the US Department of Energy's National Renewable Energy Laboratory (NREL) have announced they have genetically engineered a bacterium which promises to make the process quicker and cheaper.

Ethanol can be obtained from materials such as sugar cane, corn, wood and waste paper. The most common method uses yeast to ferment glucose, the major component of most biomass feedstocks. In order to produce as much ethanol as possible from the material, a second processing step is often added to break down xylose, which can make up 25–40 per cent of biomass.

The process of converting glucose can be made more efficient by replacing yeast with the bacterium *Zymomonas mobilis*. But xylose still remains in one piece. The NREL researchers say they have solved this problem by genetically engineering a new strain of the *Zymomonas* bacterium which can simultaneously ferment both glucose and xylose.

Use of the new bacterium, combined with other changes such as switching to cheaper feedstocks (for example, agriculture residues or sawdust) is expected to lower the cost of producing ethanol from approximately $1.20/gal to around $0.60–0.70/gal. The process is still being tested on a laboratory scale but the engineers expect to expand to bench scale in six months and hope to open a pilot plant in about a year. (Source: *Chemistry & Industry*, 5 September 1994)

The maths of making ethanol

Producing ethanol from renewable sources appears economically feasible, according to new research. With some adjustments, a Swedish chemical engineering team believes that this ethanol could cost 22c/l, today's market price is 35c/l.

Ethanol has aroused much environmental interest, but some financial doubts, as a replacement for liquid fossil fuels. It can be obtained from materials such as sugar cane, corn, wood and waste paper. The most established technique uses starch (corn in the US, wheat in Sweden).

Scientists have questioned whether hardwoods like willow could prove an economical source of ethanol. The problem is that hardwoods produce a sugar mix that is pentose-rich and fermenting pentoses can be expensive. As the price of the raw material dominates process costs, using all of it is crucial.

The Swedish team analysed ethanol production from willow wood, broken down into fibres by steam. After hydrolysing the cellulose fibres, they fermented the resulting sugars – hexoses and pentoses – producing ethanol for distilling.

The team chose recombinant *Escherichia coli* for its fermentation because it is the best known organism for fermenting pentoses. *Saccharomyces cerevisiae*, the most frequently used organism in ethanol fermentation, is not able to deal with pentoses. They found that producing ethanol from fermenting pentoses costs 48c/l compared with 50c/l when only hexoses are fermented.

Fermentation is the most expensive part of dealing with pentoses, followed by detoxification – the removal of potential fermentation inhibitors from the sugar solution. This process accounts for 22 per cent of the total cost. If scientists could hit on a micro-organism that ferments at the same yield and productivity but without the need to detoxify, the cost could be squeezed to 38c/l. Plus if they cannot use the pentose fraction, selling it as a by-product could knock off a further 6.3c/l.

Developing the technical process so that either the pentoses and hexoses are fermented simultaneously, or the pentoses are fermented separately and the fermentation broth is recirculated to the hydrolysis step, would bring the cost down by 6.3c/l. Reusing the secondary steam from the pentose fermentation plant would reduce the cost by 3.8c/l. (Source: *Chemistry & Industry*, 19 September 1994)

Alternative approach for alcohol production

Yeast has traditionally been used in fermenting grains, rice and fruit to produce alcohol all over the world. The CEC BAP programme has funded research to investigate other alternative approaches. In doing so researchers have studied *Zymomonas mobilis*, a gram-negative anaerobe which can produce alcohol five to six times faster than yeast. However this organism can only utilize glucose, fructose and sucrose as carbon sources and so an increase in the range of metabolizable carbohydrates was essential if *Z. mobilis* was to be used at an industrial level. Genetic improvement was approached through classical genetics and genetic engineering.

A combination of chemical mutagenesis, transposon mutagenesis, gene transfer by aided conjugation, construction of recombinant expression vectors and transfer into *Z. mobilis* genes responsible for xylose metabolism were established and can now be applied to increase the substrate range of *Z. mobilis*.

Recombinant plasmids were constructed by subcloning fragments of native *Z. mobilis* plasmids in known vectors. These were transferred into *Z. mobilis* by aided conjugation and were stably inherited. New expression vectors were constructed using subcloned *Z. mobilis* plasmid sequences which could be transferred into *Z. mobilis* and induce

expression of the xylose catabolism genes xylA and xylB. However these engineered strains could not ferment xylose. To overcome this, conjugal transfer of transposon bearing plasmids was carried out to attain transposon mutagenesis. Both Pseudomonas and *Escherichia coli* were used as the transposon bearing plasmid donors for *Z. mobilis*. All *Z. mobilis* strains tested were able to ferment extracts of various fruits, such as apples, oranges, peaches, watermelons, etc.

Moreover, recent research shows that Zymomonas can be used as a source for the production of hopanoids, Sterol-like compounds which are not commercially available, as well as a source for the production of heterologous ice-nucleation protein with many applications in the frozen food industry, artificial snow, etc.

This work is of interest to those engaged in industrial manufacturing technologies and has substantial market applications in the areas of fine chemicals, biotechnology, fermentation technology and genetic and protein engineering. For further information, contact: Phil O'Leary, BioResearch Ireland, Forbairt, Glasnevin, Dublin 9, Ireland. Tel.: 353-1-8370177; Fax: 353-1-8370176.

Super cheap biopolymers

Early in the 21st century genetically altered oilseed rape plants may be yielding biodegradable polymers at about one-tenth the price of petroleum-based polymers, say researchers at the University of Warwick (Coventry, UK), but Zeneca Biopolymers, which is conducting similar research in association with Zeneca Seeds (Bracknell, UK), says the prices of the biopolymers will initially be "roughly similar" to those of conventional polymers.

Zeneca (London) produces 600 m.t. year of its biodegradable polyhydroxybutyrate (PHB) resin, Biopol, by fermenting sugar with a naturally occurring bacteria at a cost of £5-£12 ($7.50-$18) kg, about 15–20 times the price of conventional polymers.

Researchers at Warwick's Department of Biological Sciences, headed by Malcolm Bennett, say that if the genetic techniques being tested there work they will be able to produce PHB at about £0.07 kg. Bennett's team, funded by the UK's Biotechnology Directorate and using ger - provided by Zeneca, is using the protein GAL4 to regulate and coordinate the activation of genes in the oilseed rape plant. Because GAL4 is in a separate plant line from those used in making PHB in oilseed rape, the "transgenic plastic producing ability is bred out of the plant within one generation, thus easing fears about the introduction of transgenic plants into the environment", the researchers say.

Oilseed rape is a non-food crop widely grown in Europe on land set aside from food production because of reforms of the Common Agricultural Policy. Warwick researchers say they have not yet created an entire PHB-producing plant and that commercial production will not be possible until the next century. (Source: *Chemical Week*, 15 June 1994)

Sensors

Two companies, AromaScan and Neotronics, have both developed artificial electronic noses. These devices are laboratory equipment – gas chromatograph-sized gadgets which mimic the function of the human nose. Unlike the natural nose, however, these robonoses provide reproducible, digital readouts.

Both AromaScan's and Neotronics' robonoses derive from original research by George Dodd at the University of Warwick's Institute of Olfactory Studies. Dodd acts as a consultant to Neotronics, while AromaScan's scientific consultant, Krishna Persaud of UMIST, is a former Ph.D. student of Dodd's.

The robonoses use an array of polymer sensors to detect smells. These sensors are made of semiconducting polypyrroles, whose conductivity changes when odour-carrying substances adsorb onto their surfaces. With several sensors, each sensitive to different smell components, the robonoses build up "smell profiles" unique to each substance. The polypyrroles are most sensitive to polar compounds, especially amines; the nose can hardly sniff out halogenated hydrocarbons like freons at all.

So how good is a robonose. A wine critic recently found to his chagrin that AromaScan's machine can match a human in a blind sniffing, distinguishing easily between three chardonnays it had only sniffed once before. It could not tell apart two reds from neighbouring villages, but the expert made the same mistake. Human sniffers are not the only ones threatened – in field (or rather forest) trials, the machine was 25 per cent better at finding truffles than a trained truffle hound.

Both companies are working on improvements to their systems.

AromaScan's clients include the US Food and Drug Administration, which is using the nose to sniff out bad fish; Coca-Cola which is testing the nose's ability to find contaminated plastic bottles; and a hospital in Manchester has shown that the nose can detect early signs of wound infection and can even distinguish between different infections. Other customers include Deutsche Aerospace, which plans to send a robonose on the Russian Mira spacecraft to sniff the cosmonauts' environment, and Sumitomo, which is developing a personal halitosis detector.

Perhaps the biggest potential use for robonoses is in quality control, enabling perfumers to check scents against a computer-stored standard profile, and brewers, wine-makers and distillers to ensure consistent flavours. (Extracted from *Chemistry & Industry*, 1 August 1994)

Opportunities in and alternative strategies for biomanufacturing success

The biotechnology industry has moved forward by seizing the opportunities for biotherapeutic development – from growth hormone and insulin to targeted monoclonal antibodies and gene therapy. In contrast, the biomanufacturing segment of the business has been overshadowed by these rapid advances. Its story is one of slower advance and less rapid innovation.

However, with greater numbers of companies now reaching the stage where their biotherapeutics must be produced, understanding various biomanufacturing opportunities has become increasingly important. Also, since biomanufacturing is more expensive than traditional chemical therapeutic synthesis, these opportunities are being carefully examined for cost-effectiveness in light of the current emphasis on health care reform.

In this environment, three questions arise: what are the opportunities for innovation in biomanufacturing; what is the likelihood that these opportunities can be capitalized on by setting objectives that will advance the technology, aiming towards the ultimate goal of commercialization; and

will the commercial goal be a cost-effective one, either directly or indirectly?

In spite of the current outlook, which suggests a slow advance in process technology improvement, what would be the likely manufacturing cost savings if these advances did occur? Table 1 presents a generalized breakdown of estimated bioprocessing costs associated with a biomanufacturing operation averaging $15-20 million in direct annual operating costs.

Table 1. Estimated bioprocessing costs

	Biomanufacturing type		
	Bacterial	Mammalian	Ideal
Materials	1.5-2.0*	3.0-4.0*	1.2-1.6*
Upstream	0.3-0.4	2.1-2.8	0.3-0.4
Down-stream	1.2-1.6	0.9-1.2	0.9-1.2
Labour	3.0-4.0	1.5-2.0	1.5-2.0
Total	4.5-6.0	4.5-6.0	2.7-3.6

Note: Assumes an average of $15-20 million in direct annual operating costs.
* Cost (millions of dollars)
Source: ISRB Associates

Frustration with the current status of biomanufacturing and the slow pace of bioprocessing advance has led to the pursuit of alternative strategies that reflect two opposing themes of technological advance. Transgenic biomanufacturing attempts to capitalize on the advancement of technology in genetic manipulation of cells and animals. Synthetic biomanufacturing tries to build on the understanding of complex biomolecular structure to partially return to an older chemical synthesis strategy.

Transgenic technology promises to allow both animals and plants to be used as living bioreactors. Recent advances in the basic technique of foreign-gene insertion into farm animals, and targeting expression of these genes to the mammary gland have led to the ability to express the product of these foreign genes in milk at concentrations of 1-3 grams/litre. Although further behind technologically, the commercially useful expression of biotherapeutics in transgenic plants is also possible.

However, some overly optimistic statements have been made about the potential of this technology to revolutionize biomanufacturing.

Even in an optimistic scenario, where bioactive therapeutic proteins are expressed at high levels in transgenics, the manufacturing cost per gram of material will still be comparable to that seen currently with standard technology (table 2).

Synthetic biomanufacturing now centres on the production of small oligopeptides and oligonucleotides of specific sequences. The technology used to produce these materials is just beginning to develop. However, current production requires painstaking step-by-step synthesis of one residue at a time, a process that is not easily streamlined. As a result, commercially significant production is limited to a few grams of short-sequence protein or nucleic acid, whose cost is in the tens of thousands of dollars per gram (table 2).

Table 2. Estimated Manufacturing Costs

Manufacturing Type	Cost per gram
Hybridomas	$ 3,000 - 5,000
Bacteria	1,000 - 4,000
Transgenic animals	2,500 - 4,000*
Transgenic plants	3,500 - 4,500*
Oligopeptides	10,000 - 40,000
Oligonucleotides	30,000 - 50,000
Chemical synthesis	100 - 1,000

Note: *Indicates an expression level of 3 g/l in the milk of transgenic animals and 5 per cent of tuber protein in transgenic potatoes is assumed.
Source: ISRB Associates

The hope for the future is that knowledge about the specific interactions of biomolecules will advance sufficiently that small peptides, or even relatively simple chemical compounds, can be substituted for full-size effector proteins. While truncated biomolecules and small peptides (such as antigen-binding regions of immunoglobulins) are increasingly being studied and used therapeutically, the dream of biomolecular synthesis at a cost approaching that of chemical synthesis remains a distant goal.

Advancement of current biomanufacturing technology will be evolutionary, not revolutionary. However, the potential is great for market encroachment by alternative strategies, such as transgenics and partial chemical synthesis of small peptides from the active-site regions of larger biomolecules. (Extracted from *Genetic Engineering News*, August 1994)

Energy and Environmental Applications

Zeneca biosensor to protect sewage works

Zeneca's Brixham Environmental Laboratory in South Devon, UK, is working with the University of Luton to develop a biosensor to detect and monitor toxicity levels at sewage works.

The device – in theory very simple – should allow the detection of a toxicant within seconds or minutes, giving a prompt alert of any potential upset to the sewage works. This would offer a significant advantage over conventional time-consuming sampling techniques, which take hours to analyse.

The device is based on the immobilization of whole microbial cells on a microelectrode (round 5 mm in diameter). The degree of inhibition of metabolic rate of micro-organisms in the sewage works – as interrogated by

a chemical mediator and the resultant electron flux converted by the sensor microelectronics into an electrical signal – is proportional to the toxicity of the test sample. However, the device does not identify the nature of the toxicant.

Work on [illegible]effluent samples is currently under way at Brixham [illegible]g static systems, while the Luton effort is focusing on the development of a continuous on-line system as envisaged for placing upstream of a sewage works.

If all goes well, a commercial diagnostic device may be developed for the protection of sewage plants. As with all biosensors, much remains to be done in terms of stability, not just of the signal but also of the cells on the instrument.

While the protection of sewage plant has been identified as the prime market, other opportunities abound. (Source: *European Chemical News*, 8 August 1994)

Soil bioremediation success in laboratory

A soil bioremediation consortium of nine companies led by the Japan Research Institute Ltd. and organized in 1991, recently demonstrated at the laboratory level the ability to restore polluted soils using methane-assimilating bacteria. Soils polluted with trichloroethylene were collected from three sites and placed in flasks with methane-oxygen enriched cultures to break the trichloroethylene down. After two days, the concentration of trichloroethylene was reduced from 4 ppm to 0.8 ppm in one case, from 4.7 ppm to 1.1 ppm in the second case, and from 1.0 ppm to 0.6 ppm in the third case. In columns, it was demonstrated that from 20 per cent to 40 per cent of the trichloroethylene was broken down within eight hours. The consortium plans to conduct field trials of the technology in the near future. (Source: *McGraw Hill's Biotechnology Newswatch*, 18 July 1994)

Bioreactor degrades trichloroethylene

Ebara Corporation and the Japanese National Institute of the Environment have jointly developed a bioreactor that uses strain M methylocystis microbes derived from methane-assimilating bacteria to reduce trichloroethylene concentration from 1 ppm to 0.1 ppm. Investigators from the organizations are trying a variety of ways to stabilize the micro-organisms, such as inclusion in gels for bioremediating contaminated groundwater. The most successful experiments to date include the M strain in sodium alginate gel packed in a 20-litre glass vessel into which 130 cc min of trichloroethylene-contaminated water is fed from the bottom together with a 1:9 mixture of methane and air, to nurture the microbes, fed at a rate of 100 cc min. The gel stabilizes the M strain as if it were in an aqueous suspension while it degrades the trichloroethylene. The apparatus can process 187 Litres per day. Research is continuing to develop more robust systems with higher capacity. (Source: *McGraw Hill's Biotechnology Newswatch*, 1 August 1994)

Plant cells to purify liquids of pollutants

Paul Jackson, a microbiologist at Los Alamos National Laboratory (New Mexico), is using plant cells to purify liquids of heavy metal contaminants, such as barium and uranium, and of explosives' residue, such as that from TNT. He runs contaminated liquid through a silica-based powder containing cells from citrus, corn, jimsonweed and other plants. Certain plants take up some minerals better than others; thus, the mixture of cells can be tailored to the particular contaminants. Microscopic hooks on the outside of the plant cells grab the toxins from the liquid. According to Jackson, laboratory studies show that contaminant levels are reduced to below federal standards at a rate of a gallon every three minutes. Acids strip metals from the sand and concentrate them in commercial quantities. (Source: *Genetic Engineering News*, 15 June 1994)

"Orange peel" in bio-cleaning

Pronatur Products, the Liverpool-based specialist in "orange peel" solvents, has developed an accelerated bioremediation system to clean up waste oils, tars and other unwanted hydrocarbons. Recent trials, carried out at a British Railways' regional depot in Birmingham, UK, are claimed to have achieved breakdown of hydrocarbon contamination within 20 days.

The system is based on Pronatur's recently developed "orange peel"-based solvent and a special culture of naturally occurring bacteria. The key to the process lies in dissolving the bacteria in the non-toxic solvent, making the bacteria more accessible to the hydrocarbon.

The Birmingham trials involved the use of the system to clean tracks at a refuelling depot, where the ground was heavily contaminated with diesel fuels and antifreeze, together with detergent from platform cleaning operations.

According to Pronatur, the original chemical oxygen demand (COD) was 12,144 mg l – more than 20 times the consent level. By spraying with the solvent and water, to dissolve the hydrocarbon, then adding bacteria, the COD level dropped to 4,286 mg l after one week, and 88 mg l after three weeks. The hydrocarbon content fell from 470 to 54 mg l over the same period. Ethylene glycol readings fell from 7,610 mg l to less than 1 mg l in six days, while pH fell from 12 to 6.8. (Source: *European Chemical News*, 3 October 1994)

Recovering heavy metals for recycling

A combination of biology and physics promises to boost the prospects of efficiently recovering toxic heavy metals from industrial effluents. An international team of scientists have managed to remove cadmium from laboratory-scale liquid wastes by first using microbes to trap the metal – a process known as biosorption – and then separating the metal-loaded biomass by flotation. This is the first time the two processes have been combined, they claim.

Biosorption makes use of compounds such as chitin found in the cell walls of fungi and bacteria to bind heavy metal ions. Both live and dead microbes can be used in biosorption, sidestepping any problems with toxicity of the waste stream. This also means that the process can save costs by using waste biomass from processes such as antibiotic production.

However, although biosorption can remove a wide range of heavy metals from liquid wastes, its commercial potential is limited by drawbacks with current methods of separating the metal-loaded biomass. Filtration leads to clogging, sedimentation is slow, while centrifugation pushes up costs.

Flotation is a separation technique with a wide range of industrial applications, such as separating minerals from low-grade ores. Simply, it involves aerating a mixture of solids in water, causing suspended particles to cling to air bubbles and float to the surface of the mixture where they can be skimmed off.

Anastasios Zouboulis of Aristotle University in Thessaloniki, Greece, and colleagues from the University of Newcastle-upon-Tyne showed that biosorptive flotation (biosorption followed by flotation) was highly effective at removing cadmium from experimental waste streams. Cadmium, which is toxic to both animals and plants, is widely used in corrosion protection and the manufacture of batteries.

Zouboulis is collaborating with a number of industrial companies on electrochemical techniques, such as metal plating, for recovery of the metal once it is washed off the separated biomass. (Source: *Chemistry & Industry*, 1 August 1994)

Slime light

Any system using large volumes of water as a cooling system is vulnerable to bacterial slime; the biggest victims are pulp and paper mills, and power stations. Bacteria breed in the water, and as their numbers multiply their gelatinous protein coats stick together, creating a greasy mess, which gradually clogs up the system. To control the slime, the bacteria must be killed. There are many ways to do this, but they invariably involve dangerous or difficult-to-store substances such as chlorine gas, chlorinated phenols, organobromines or organosulphurs.

Wilson Whitekettle and Deborah Donofrio of Betz Europe in Pennsylvania have discovered that combining two "fairly common" biocides, 2-(2-bromo-2-nitroethenyl)furan (BNEF) and decylthioethanamine hydrochloride (DTEA), has a synergistic effect. A 160:1 mixture of the two is three times as effective as using the same amount of either biocide alone, they claim. Because of this, the amount of biocide needed to treat a water system can be dramatically reduced; this, in turn, reduces the risks associated with these chemicals.

Moreover, say the researchers, this mixture is effective on *Klebsiella pneumoniae* species. These bacteria can grow under both aerobic and anaerobic conditions, meaning that the biocide mixture is likely to be effective on a "wide range" of fungal, algal and bacterial slimes, they claim. (Source: *Chemistry & Industry*, 3 October 1994)

New R&D group aims at bioremediation

Six companies – DuPont, Monsanto, General Electric, Ciba-Geigy, Dow Chemical and Zeneca – are to establish an R&D consortium to develop soil remediation processes that accelerate the *in situ* biodegradation of chlorinated solvents. The process could be up to ten times cheaper than traditional "dig and burn" technologies, according to Philip Palmer, remediation technology programmes leader at DuPont Specialty Chemicals.

The project is scheduled to run four years, with initial funding of $12 million. The consortium – which expects to work with the Environmental Protection Agency (EPA), the Department of Energy, and the Department of Defense – will function in parallel with a related R&D consortium established in 1993 by Monsanto, DuPont and General Electric. Both projects were developed through the EPA's Remediation Technology Development Forum, established in 1992.

The new consortium, to be managed by DuPont, will focus on three aspects of the biodegradation of chlorinated solvents: natural attenuation, accelerated anaerobic bioremediation, and bioventing. It will involve extensive laboratory work and field testing.

To date, DuPont is the only one of the consortium's members to successfully field-test a process – now patented – for biodegrading chlorinated solvents *in situ*, which it carried out in a contaminated aquifer under a plant near Victoria, TX.

"Results have demonstrated the *in situ* biotransformation of tetrachloroethene, trichloroethene, 1,2-dichloroethene, chloroethane and vinyl chloride to ethane and ethene using microbial reductive dehalogenation", according to DuPont. It adds that the microbial reductive dechlorination was accomplished by pumping either a benzoate or sulphate solution into the circulating groundwater. (Source: *ChemicalWeek*, 14 September 1994)

Worms surface as soil guide

The humble earthworm is being used to provide a "snapshot" of soil pollution. Scientists from the Natural Environment Research Council in the UK have devised what they describe as a relatively simple but highly effective "biomarker" technique to detect contaminants such as heavy metals and dioxins. The technique cuts out chemical analysis in an initial screening stage.

The method involves taking body fluid cells from earthworms in contaminated areas, in much the same way as blood samples are taken from humans, and exposing them to a neutral red dye that is absorbed by sub-cellular organelles. In cells taken from normal earthworms, the dye is released only slowly. However, if the earthworm cells have been stressed by pollutants, the dye is released rapidly (because the cells have been working to eliminate the poisons).

Jason Weeks of the NERC's Institute of Terrestrial Ecology in Huntingdon says there is a definite dose-response relationship, though the technique does not allow identification of specific pollutants. Work is continuing to establish the relationship in more detail.

The technique has been used over the past year to screen several contaminated land locations in the UK, concentrating mainly on spillage or fire sites, including the pollution impact two years after a small fire at a plastics factory. The technique has also been used in the assessment of the environmental impacts of waste from gold mining in Africa.

Weeks says NERC plans to develop the technology as a "kit", to be used as a simple tool to allow monitoring in the field. Longer term, the technique could be combined with other analysis procedures, such as nuclear magnetic resonance, to provide a more detailed fingerprint of the biochemistry taking place. (Source: *European Chemical News*, 25 July 1994)

Micro-organisms degrading aliphatic polycarbonate

Japan's National Institute of Bioscience and Human Technology, Agency of Industrial Science and Technology (AIST), JSP Corp. and a research team headed by Professor Y. Yoshida at the Department of Applied Chemistry, Faculty of Engineering, Tokyo University, have discovered micro-organisms that degrade aliphatic polycarbonate (PC), a plastic material. The research is now attempting to degrade types of aliphatic PC with very high molecular weights. The micro-organisms, however, have already proved able to degrade an aliphatic PC with a molecular weight of 2,000.

Aliphatic PC, a new type of plastic material, is produced from carbon dioxide (CO_2) which causes global warming. However, there is only one biodegradable plastic material, aliphatic polyester. The new PC is another biodegradable material, and the design of biodegradable plastics will become more flexible.

The seven micro-organisms were found by the clear zone method. Diluted samples were applied individually to an agar containing emulsified and suspended PC. Each medium was kept at 30° C for two weeks and then examined to see whether a clear zone exists or not, which is caused by a colony decomposing the PC around. The samples were collected from lakes and rivers in the Kanto Area, Japan. The species and genera have yet to be identified. The highest performance achieved was to reduce 80 mg of aliphatic PC (molecular weight: 2,000) to about a quarter in 200 hours. The research will continue with aliphatic PC of greater molecular weights.

Aliphatic PC can be used as plastic, but may be a source of polyurethane. Biodegradable polyurethane may therefore be developed. Unlike aromatic PC, a conventional engineering plastic material, aliphatic PC has the advantage of being produced from CO_2. Applications range widely from an intermediate product in the polyurethane process, to films and fine chemicals. With a melting point higher than those of polyesters, aliphatic PC may be exploited in industries.

Aliphatic PC decomposes in rats. The biodegradability of the polymer by micro-organisms, however, has been established for the first time. All biodegradable plastic materials previously known were aliphatic polyesters, such as polyhydroxybutyric acid (PHB) and polycaprolactone. Further details are available from the National Institute of Bioscience and Human Technology, AIST, 1-1, Higashi, Tsukuba City, Ibaraki Pref., 305; Tel.: +81-298-54-6089; Fax: +81-298-54-6009. (Source: *JETRO*, May 1994)

Team develops cotton bio-scouring method

Kurabo Industries Ltd. and the University of Osaka Prefecture (Japan) are undertaking research to develop a practical cotton fibre bio-scouring technology which uses enzymes rather than environmentally harmful chemicals including caustic soda.

Two objectives of the new technology would be to dispense with the need for waste treatment facilities and to produce textiles with a better finish. The researchers will also investigate enzyme production methods that could reduce scouring costs. The academic partner began investigations two years ago on a single-step bio-scouring starch removal process that reduced the cost of processing effluents. In addition, experimental production yielded tighter, faster-dying fabrics with a softer surface texture.

With support from Kurabo, researchers will attempt to increase the production of five types of bacteria and yeasts extracted from enzymes by a factor of 100 by exploring recombinant gene technology and mutations. The team will also investigate the possibilities for recycling the enzymes. (Source: *McGraw Hill's Biotechnology Newswatch*, 16 May 1994)

Bioremediation

Whales could play a role in oil clean-up, claim scientists in the US. The anaerobic bacteria in a whale's stomach may prove more versatile and useful than aerobic bacteria used in conventional bioremediation. Meanwhile, other researchers are using anaerobic bacteria as a cheap, simple way of breaking down contaminants such as polychlorinated biphenyls (PCBs).

Whales can eat up to 2,000 lbs of polluted plankton per day and survive, reports Morrie Craig of Oregon State University (OSU). The anaerobic bacteria in their stomach break down not only PCBs but also anthracene and naphthalene – two chemicals released during oil spills, he says.

OSU researchers had already discovered that a group of six bacteria in a sheep's rumen – the first of its four stomachs – performs similarly, breaking down trinitrotoluene (TNT) by taking the amines off the toluene ring and leaving it harmless.

At the Michigan Biotechnology Institute (MBI), researchers have applied for a patent on a "consortium" of bacteria that can work under water and without oxygen to break down the PCBs into carbon dioxide and methane. Several microbes band together to form granules which sink to the bottom.

The scientists can seed the microbes directly into sediments in lakes or rivers. Cutting out oxygen, dredging and off-site treatment makes the microbial mixtures much cheaper than current techniques such as heat or chemical treatment, landfilling and incineration which can be expensive and disruptive.

The MBI bacteria are related to a strain developed by General Electric. However, the GE bacteria need oxygen to perform their task.

In tests in the laboratory, the bacteria cleaned soil to meet the Environmental Protection Agency standard of less than 2 ppm. (Source: *Chemistry & Industry*, 20 June 1994)

F. PATENTS & INTELLECTUAL PROPERTY RIGHTS

Korea to establish a Patent Court

Following amendments passed by the National Assembly on 14 July 1994, the Republic of Korea will establish a Patent Court as of 1 March 1998, as a Court of Appeals. The Court will have panels of three judges each, and the judges will be supported by judicial assistants, who have appropriate technical expertise in various fields. At the same time, the present Trial Board and Appellate Trial Board of the Korea Industrial Property Office will be incorporated into a "Board of Trials" which will operate as a tribunal of first instance. The Patent Court will handle appeals from decision of the Board of Trials, or from the Examining Divisions of the Korea Industrial Property Office. Appeal from the Patent Court will be to the highest court in Korea, the Supreme Court.

The Patent, Utility Model, Design and Trademark Acts are being reviewed in preparation for the establishment of the Patent Court, and it is likely that amendments to these Acts will be introduced during the September session of the National Assembly. (Source: *Australasian Biotechnology*, Vol. 4, No. 5, October 1994)

New Zealand Patents Act to be amended

Legislation has been introduced into the New Zealand Parliament to give effect to the TRIPS Agreement of the General Agreement on Tariffs and Trade. The amendments will bring the Patents Act into line with New Zealand's major trading partners, and include extension of the term of a patent from 16 years to 20 years. However, the provisions for extension of term will be repealed. This is despite the fact that in most of the major industrialized countries, including those of the European Patent Convention, extension of the patent term or a supplementary protection certificate is available in recognition that a fixed 20-year term does not provide adequate length of protection for technologies subject to rigorous regulatory scrutiny which results in long delays, such as pharmaceutical inventions. Amendment is also proposed to reverse the burden of proof of alleged infringement of a process patent, so that the same product produced by a party other than the patentee or its licensee will be assumed to have been produced by the patented process, unless the defendant proves the contrary. Changes to Crown use provisions are also proposed. (Source: *Australasian Biotechnology*, Vol. 4, No. 5, October 1994)

Indigenous peoples from Central and South America meet on intellectual property rights

In September 1994, representatives from indigenous people's organizations in 12 Central and South American countries gathered in Santa Cruz, Bolivia, for a conference on "Biodiversity, Intellectual Property Rights and Indigenous Peoples". The meeting was coordinated by COICA (the Coordinating Body for Indigenous Peoples' Organization of the Amazon) and CIDOB (the Indigenous Confederation of Orient, Chaco and Amazonia of Bolivia), with financial support from UNDP. The principal reference document for the meeting was a newly released UNDP study entitled (in English) *Conserving indigenous knowledge: Integrating two systems of innovation*, prepared by RAFI, the Canadian-based Rural Advancement Foundation International.

In three days of intensive meetings, delegates considered the implications of western systems of intellectual property for indigenous peoples. They concluded that "the concepts of individual and monopolistic intellectual property over knowledge, and over life, are based on a world view which is antagonistic, and incomprehensible to indigenous thinking". They affirmed that indigenous knowledge about "genetic resources" could not be separated from the "resources" themselves, or from the lands and the cultures of which they are part. Most importantly, the delegates agreed upon short- and longer-term strategies: to develop their own thinking on the issues; to gather and share information about corporate "bio-prospecting" and relevant legal structures in each country; to plan education programmes for indigenous leaders and communities; and to participate in relevant discussion fora at the national, regional and international levels — to make known the views, and defend the interests of indigenous peoples.

Conserving indigenous knowledge: Integrating two systems of innovation is now available in English and Spanish, from Mr. Marcel Viergever, Programme Officer, Bureau for Programme and Policy Evaluation, UNDP, 1 UN Plaza, New York, NY 10017, USA. (Source: *African Diversity*, No. 10, October 1994)

Validity in Canada of inventions relating to the human body

Since a court decision in 1974, inventions in respect of methods relating to the human body, and in particular inventions for medical treatment of the human body, have mostly been regarded as unpatentable. However, four successful appeals to the Patent Appeal Board of the Canadian Patent Office suggests that the Board is now adopting a consistent approach, and is interpreting very narrowly the finding of the Supreme Court of Canada that "patents for medical treatment in the strict sense must be excluded" (Tennessee Eastman's application, 1974). Thus, provided that the normal requirements of patentability, i.e. novelty, inventive step, and industrial applicability, are satisfied, a method relating to the human body will be patentable if it can be performed without the use of professional medical skills.

Thus for diagnosing the capacity and strength of lungs (Application No. 016962), a method of making the presence of disease causing foreign matter in the oral cavity of a living human visible to the naked eye (Application No. 880719), a method for detecting and localizing a tumour, involving injecting a subject with various substances (Application No. 372233), and a method of evaluating the mechanical condition of a human heart, the applications involve measurements in which diagnosis of the results does not form part of the process, so that the process does not depend upon professional skills, in which no step of medical or surgical treatment is set out in the claims, which are reproducible and controllable to produce the desired result whenever it is worked or used, which are non-invasive and produce only diagnostic information, or

which will produce the claimed results when used by a normally skilled practitioner in the assessment of various patients.

Thus it appears that provided that the process is non-invasive, and it is possible to obtain a claimed result which is reproducible without the necessity to use any distinct professional medical skill, an invention relating to, or which is performed on, the human body is likely to be patentable in Canada. (Source: *Australasian Biotechnology*, Vol. 4, No. 4, August 1994)

European Council Directive on Biotechnological Inventions

In the latest episode of the long-running saga of the proposed European Council directive, the first draft of which was presented by the European Commission to the Council in October 1988, the Council of the European Union has adopted a common position on the Directive for the legal protection of biotechnological inventions. Denmark, Spain and Luxembourg voted against the proposal, and the United Kingdom's vote in favour was subject to examination of the directive, a subcommittee of the House of Lords. The Directive will ultimately be binding on members of the European Union; however, Member States are also members of the European Patent Convention, so that implementation will require amendment of the Convention. Alternatively, some independent prediction must be made available under the Directive, and it is difficult to see how this could be achieved.

Unfortunately the latest version of the Directive is unclear in many areas, and the preliminary recitals appear in some respects to contradict the articles of the Directive.

The text of the biotechnology Directive was considered by the legal affairs of the Committee of the European Parliament at the end of March 1994, which proposed a number of major changes from the common position previously adopted by the Commission and the Council. The report of the Laws and Institutions Subcommittee of the House of Lords, while generally in support of the common position, has recognized that there are many problems inherent in the current Directive.

There appears to be wide concern that the biotechnology directive, particularly in the form proposed by the Rapporteur of the Legal Affairs Committee of the European Parliament, would cause major problems for the pharmaceutical and biotechnology industries, and would be in significant conflict with the European Patent Convention. A detailed discussion of the directive may be found in Pharma Law Report No. 9, Biotechnology Products, March 1994, and in *European Intellectual Property Review*, 1994 5 191-194. (Source: *Australasian Biotechnology*, Vol. 4, No. 4, August 1994)

Patent law amendment in Andean Pact countries

The patent law of countries of the Andean Pact, Bolivia, Colombia, Ecuador, Peru and Venezuela has been amended by Decision 344 of the Cartagena Agreement. The decision came into effect in Colombia, Ecuador, Peru and Venezuela on 1 January 1994, but is not yet effective in Bolivia. Prohibitions on the grant of patents for biotechnological inventions have been abolished, and provision has been made for the use of deposit of biological materials to provide full disclosure of the invention (Source: *Australasian Biotechnology*, Vol. 4, No. 4, August 1994)

New Patent Law in Taiwan

The amended Taiwanese Patent Law, which was passed on 28 December 1993, came into effect on 23 January 1994. The amended law now provides for patents for foods and beverages, and for new uses of known articles. Although the law also contains a provision allowing repeal of the prohibition on patents for new micro-organism strains, this will only be implemented when Taiwan has been admitted to the General Agreement on Tariffs and Trade, and one year after the TRIPS Agreement comes into effect. However, the repeal of the prohibition may be effected on the basis of reciprocity for inventions originating from countries which have a bilateral agreement with Taiwan on the patenting of micro-organisms. If a micro-organism is not readily available, a sample must be deposited in a culture collection in Taiwan which is recognized by the Taiwan Patent Office, apparently before lodgement of the application in Taiwan. The term "micro-organism" will include microbes, including viruses, recombinant cells, whether prokaryotic or eukaryotic; and DNA vectors such as plasmids.

The term of a patent will be 20 years from the date of filing in Taiwan, with an extension of up to five years for patents for medicines, agricultural chemicals or methods of synthesis thereof whose marketing requires a licence from the relevant national ministry. The extended term may be two to five years, but cannot exceed the period of regulatory delay. An extension of term will only be available for patentees which are citizens of Taiwan, or of a country having appropriate agreements with Taiwan.

Hitherto it has not been possible to claim priority of an application in another country when filing in Taiwan. However, the new law provides for a priority period of one year for applications by nationals of countries which have a reciprocal arrangement with Taiwan regarding priority.

Although patents may not be granted in respect of micro-organisms until one year following commencement of the TRIPS Agreement, it is possible to lodge applications in respect of micro-organisms immediately. Grant will be delayed until the appropriate provision comes into effect. (Source: *Australasian Biotechnology*, Vol. 4, No. 4, August 1994)

Intellectual property rights and biotechnology in developing countries

Intellectual property rights are important for biotechnology in Egypt and other nations with substantial biotechnology programmes because they can provide incentives for local researchers and firms, they have come to be required by international law, and they can assist in the international transfer of technology.

The intended purpose of an intellectual property system is to create incentives for research by giving the successful researcher an opportunity to protect its market against imitators for a reasonable term of protection. Thus, with a plant breeders' rights system, the breeder can keep others from selling its variety without its permission.

Protection of a variety in this way or through the regular patent systems is an important part of encouraging the evolution of a private seed industry. If private firms are able to breed their own varieties, they clearly need protection against copying. Even if they simply buy varieties produced by the Government, the possibility of exclusive rights permits them to be more confident in such desirable marketing expenditures as providing training to

farmers or conducting additional tests to ensure that a variety is adapted to a particular region.

As a nation moves toward genetic engineering, it needs to ensure that the developer of a novel gene can obtain appropriate protection and thus needs more than plant breeders' rights. The major research effort in this form of biotechnology is in identifying the gene and in learning how to insert it into crop plants. If another breeder can simply transfer the gene to another variety, as through backcrossing, the genetic engineer loses the benefit of its research investment.

Thus, if the private sector (local or international) is to do genetic engineering oriented to the nation's needs, it must be able to patent the use of a gene identified and transferred through biotechnology. Not only is an intellectual property system likely to be useful to the nation, it is also becoming required by international law. The new Uruguay Round "Agreement on Trade-related Aspects of Intellectual Property Rights, Including Trade in Counterfeit Goods", defines minimum standards for intellectual property law in a number of areas including biotechnology. In particular, it requires that patents be available in all fields of technology. This is clearly meant to include pharmaceuticals and agricultural chemicals; it covers genes as well.

The agreement goes on to say that plants and animals (except for micro-organisms) and essentially biological processes for their production, can be excluded from patentability, but that there must be protection for plant varieties, either through patents or through a *sui generis* system such as plant breeders' rights.

These obligations, however, can be substantially postponed. A developing nation need not enact the patent law changes for five years or certain of the product patent law changes for ten years (and the provisions on plants and animals are to be reviewed four years after the agreement enters into force). The least developed nations have another ten years. Egypt, for example, is already moving to strengthen its laws. Under its old law, Law No. 132 of 1949 on patents, there is no food or pharmaceutical product protection, but only a possibility of ten-year process protection. According to the law's explanatory memorandum, food products are excluded on the ground that they do not constitute an invention and that a monopoly over producing such products is harmful to the public's health.

Under a new draft law, agriculture, foodstuffs, medical drugs, pharmaceutical compounds, plant and animal species, and microbiological organisms and products are included as patentable subject-matter. This is a significant strengthening from the current law and brings Egypt into line with international standards as set forth in the GATT text discussed above.

In other provisions, the new draft increases the patent term to the new international norm of 20 years from filing. It includes a pipeline provision stating that, for a one-year period from the effective date of the law, a firm will be able to obtain protection for a medical drug, pharmaceutical, agricultural or chemical product that was not protectable under the old law if (a) the product has not been marketed in Egypt prior to the effective date of the new patent law, and (b) the product is the subject of an unexpired patent elsewhere. In such a case, the term of protection will be equal to the term remaining in the other country.

The draft also deletes a provision in existing law that permits the Government to expropriate patents for public utility and instead permits only compulsory licences, in certain cases, with fair remuneration. It widens the rights of employers vis-à-vis employees and creates a new utility model provision permitting coverage of innovations that are not great enough to be patentable, such as a new shape or composition for a tool or implement.

New laws such as this, and expanded understanding of intellectual property, should assist Egypt to acquire technology more readily and to enter into more effective scientific strategic alliances that will help in developing new technologies and in strengthening local research capabilities. Agreements, for example, between a developed world university and an Egyptian research centre such as the Agricultural Genetic Engineering Research Institute (AGERI) are becoming increasingly complex, as they have to consider issues such as inventions made cooperatively, the expense of filing patent applications, the allocation of decision-making with respect to future inventions and the participation of international and possibly of national firms in the research.

Looking into the future, Egypt will have to confront further issues in a world that is both privatizing and looking more to intellectual property. It is already exploring technology transfer questions and plant variety protection. As AGERI completes new transgenic varieties and as a private seed industry evolves in Egypt, it will have to consider the terms and procedures for the release of the new varieties to the private sector and, with the Biodiversity Convention now in force, it will have to define appropriate terms and provisions for the transfer of genetic material newly identified within the nation. (Source: *BioLink*, 1994)

Patentability of biotechnological inventions in countries of the Pacific rim

The boom in biotechnology and its potential to meet world market demands for goods ranging from new breeds or varieties of agricultural animals and plants to vaccines has led biotechnology corporations and academic researchers to seek protection for their inventions. Since there is no such thing as a "world patent" which would provide a patentee with uniform, world-wide rights to an invention, separate national patent rights have to be sought. The extent of protection available varies with the intellectual property law and regulations of each country, particularly since the legislation in some countries has not caught up with the development of biotechnology.

Patent laws pertaining to biotechnological subject-matter in countries of the Pacific rim essentially fall into four different categories, namely:

(i) They may not include specific provisions for biotechnological inventions, but inventions that are novel, involve an inventive step and have industrial applicability are patentable (e.g. Australia, USA, Japan).

(ii) They are undergoing extensive revision whereby existing laws are likely to be replaced with new laws which include provisions for the patenting of biotechnological subject-matter (e.g. Taiwan).

(iii) They provide for re-registration of United Kingdom patents or European patents designating the United Kingdom. Thus the provisions of the United

Kingdom legislation prevail in those countries (e.g. Hong Kong, Singapore); or

(iv) There is no patent law at all (e.g. Papua New Guinea, Cambodia and Laos).

Many of the Pacific rim countries follow the model law recommended by the World Intellectual Property Organization, which, like the European Patent Convention, excludes plant or animal varieties, biological processes for their production, and methods of medical or surgical treatment of humans or animals.

The article aims to provide a summary of the patentability of biotechnological inventions in countries around the Pacific rim. The countries considered are listed in table 1. Countries with no patent law are not considered further.

The inventions referred to in the article are assumed to satisfy the criteria for patentability, namely novelty, inventive step and industrial applicability. Micro-organisms, proteins, enzymes etc. that occur in nature are assumed to have been isolated and purified through human intervention.

Biotechnological inventions can be protected by patents in most countries of the Pacific rim. However, the scope of protection available for such inventions varies. In some countries a particular product may not be patentable, whereas the process of producing or using that product may be patentable. Research and development in the biotechnological industry is advancing at a rapid pace. Governments in countries throughout the Pacific rim are continually revising and updating their policies on the patentability of biotechnological inventions. What is unpatentable today may be patentable tomorrow. It is therefore important when considering patent protection or when entering commercial ventures with companies that hold patent rights in one or more of the Pacific rim countries to consider the scope of protection, present and future, that each country will allow for such inventions.

Important note: The information in this article has been collected from patent attorneys in the countries concerned. Whilst all care has been taken to ensure that the foregoing information is as accurate as possible, readers are warned that it is not a substitute for specific legal advice on the patentability of individual biotechnology-related inventions.

(Abstracted from an article written by Gary B. Cox, Wray & Associates, Susan S.H. Wong, Shelston Waters and Vivien B. Santer, Griffith Hack & Co., which appeared in Australasian Biotechnology, Vol. 4, No. 5, October 1994)

Table 1. Patentability of biotechnology subject-matter in Pacific rim countries

Patentable Subject Matter	DNA Sequences	Vectors	Purified Proteins	Recombinant Proteins	Microorganism Produced by Human Intervention	Use of a Microorganism	Animal Varieties	Plant Varieties	Diagnostic Methods	Vaccines	Pharmaceuticals	Methods of Treatment	Member of Budapest Treaty
Australia	•	•	•	•	•	•	•	•	•	•	•	•	•
[illegible]	•	•	•	•	•	•				•	•		
Canada	•	•	•	•	•	•			•	•	•		
China	•			•	•	•					•		•
[illegible]	•	•	•	•	•	•				•	•		
Hong Kong	•	•	•	•	•	•			•	•	•		•
[illegible]					•	•							
Japan	•	•	•	•	•	•	•	•	•	•	•		•
Malaysia			•	•	•	•			•	•	•	•	
New Zealand	•	•	•	•	•	•	•	•	•	•	•	•	
[illegible]	•	•	•	•	•	•				•	•		
Philippines	•	•	•	•	•	•	•	•	•	•	•		•
Singapore	•	•	•	•	•	•			•	•	•		•
[illegible]	•	•	•	•	•	•	•	•	•	•	•		•
[illegible]			•	•		•			•	•	•		
[illegible]	•	•	•	•	•	•			•	•	•		
[illegible]	•	•	•	•	•	•	•	•	•	•	•	•	•
[illegible]	•	•	•	•		•				•			

[illegible] … human beings per se are not patentable.
[illegible]
[illegible]
[illegible] … animals are patentable.
[illegible] … chemicals.
[illegible]
[illegible]
[illegible]
[illegible]

Patent protection in biotechnology

Patent rights are typically justified as a means of encouraging investment in research and development that might not be profitable if firms that had not shared in the initial risk and cost were free to copy successful new inventions. A patent confers the right to exclude others from making, using and selling the invention within the territory of the nation granting the patent for a limited term 17 years from the date the patent issues under US law, and 20 years from the date the application is filed in many other countries. In some circumstances, a patent on a process also confers a right to exclude sales within the nation of a product manufactured abroad through the use of the patented process. In order to obtain a patent, the inventor must file an application that includes a full description of the invention and of how to make and use it. In Europe and Japan, this disclosure is made public 18 months after the application is filed; in the US, it is made public as soon as the patent is issued. The extent to which patent systems achieve their goals of inducing the development of new inventions and promoting disclosure to the public is an empirical question with no clear answers. Patent systems involve certain costs that must be weighed against their benefits, including increased prices and reduced supply of products covered by patents as well as administrative costs.

The basic requirements for patent protection are novelty, utility or industrial applicability, and non-obviousness or inventive step. Determining whether an invention is new and non-obvious requires searching through certain categories of prior art, including prior patents, publications, and public uses of inventions to determine the state of knowledge in the field at the time the invention was made or the patent application filed. An invention that already existed in the prior art is unpatentable for lack of novelty. A new invention might still be unpatentable if it would have been obvious to a person of ordinary skill in the field in light of prior art. The utility requirement limits patent protection to inventions with practical applications.

The range of biotechnology inventions qualifying for patent protection has expanded tremendously in the past 15 years, particularly in the US. In 1980, the US Supreme Court upheld the patentability of a living, genetically-engineered micro-organism. Since that time the US utility patents have been issued on plants, animals and DNA sequences. Claims to such inventions must be carefully drafted so as to distinguish them from any naturally occurring products. The range of biotechnology inventions falling within patentable subject-matter is somewhat more restricted outside the US.

The commercial value and significance of a patent depends on the scope of the patent claims, which in turn depends on the breadth of the disclosure in the patent specification. The disclosure must be adequate to enable a skilled person reading the patent application to make and use the invention as broadly as it is claimed without undue experimentation. This determination varies according to the background knowledge of other skilled people working in the field at the time of the disclosure and is specific to the facts of a particular case. US courts have used the enabling disclosure to hold invalid broad claims in a number of recent biotechnology patent cases. At other times the US Patent and Trademark Office has issued biotechnology patents of extremely broad scope.

The technological scope of a patent monopoly is determined by the language of the patent claims. Ordinarily, if the defendant's product or process includes each of the elements of a patent claim, infringement will be found. Sometimes a court will find infringement even though the defendant's product or process falls outside the literal scope of a patent claim under the doctrine of equivalents, if the defendant's device does the same work in substantially the same way to accomplish substantially the same result as the patented product or process.

The doctrine of prosecution history estoppel limits the doctrine of equivalents by holding that a patent owner may not use the doctrine of equivalents so as to recapture subject-matter deliberately surrendered in response to a rejection of broad claims by the patent office in light of prior art.

Defences to patent infringement action include invalidity of the patent, inequitable conduct or fraud during patent prosecution, misuse of a patent to violate anti-trust laws, experimental use of the invention and unreasonable delays in bringing suit. Remedies for proven infringement include preliminary and permanent injunction, compensatory damages in the amount of lost profits, established royalty or reasonable royalty, increased damages up to treble the amount of compensatory damages in the discretion of the court for wilful infringement, interest and attorney fees.

The Paris Convention for the Protection of Industrial Property requires that signatory nations allow nationals of any country in the Union the same rights that they extend to their own nationals under their patent laws. The Patent Cooperation Treaty streamlines filing procedures where an applicant seeks patent protection in multiple countries that are parties to that treaty. (Source: *Biotech*, 1994)

Intellectual property and plant breeders' rights

In addition to patents, plant breeders' rights are often available and provide an intellectual property system designed specifically for breeders. Under this system, a farmer is, in general, able to reuse harvested crop from a protected variety as seed; this is probably not the case for a variety protected under the regular patent law. Moreover, a breeder can freely use another's protected variety in breeding. This freedom is slightly restricted in a new international version of plant breeders' rights under which a breeder may not market a variety that is "essentially derived" from another's variety. Typical examples include a variety in which one gene is changed, as by genetic engineering or backcrossing.

In general, for conventional breeding, plant variety protection is adequate. For biotechnology-based breeding, however, the right to protect a gene under the regular patent system is essential; otherwise, the benefit of protection can be lost to another breeder who breeds the inserted gene into his or her varieties.

In understanding the implications of a regular patent, it is important to distinguish the specification, which describes and discloses the invention, from the claims, which define the actual legal monopoly. In a patent of a gene, for instance, the specification will cover the sequence of the gene or otherwise describe how to obtain it. The claim will typically cover an isolated DNA fragment containing the sequence of a plasmid containing it, a plant that has been transformed with it, and the seed or progeny of such a plant that contain the relevant gene. Thus, the

patent does not cover conventional breeding with the gene as found in its natural background, because such breeding never isolates the DNA or creates a plasmid or transformed plant. In addition to gene patents, some in the United States have patented varieties under the regular patent system, presumably to provide stronger protection. There are also a variety of process patents relevant to biotechnology, e.g. the original Cohen-Boyer patent on the process of genetic engineering.

A number of important international treaties create a framework for intellectual property systems. Traditionally, the most important were the Paris Convention, governing regular patents and UPOV (International Union for the Protection of New Varieties of Plants) governing breeders' rights. The Paris Convention has an international secretariat called WIPO (World Intellectual Property Organization) in Geneva, Switzerland. The UPOV secretariat is also called UPOV and is located in Geneva. Recently, intellectual property has become coupled with trade. The result has been not only a number of international disputes about the use of unilateral trade sanctions in the intellectual property area but also a new Uruguay Round agreement on intellectual property. This agreement requires protection of pharmaceuticals and genes; it does permit exclusion of living plants and animals from patentability, but requires use of a *sui generis* system such as plant breeders' rights for plants. These obligations, however, need not be enacted into law (save for certain pipeline provisions) for 10 years for a developing nation that does not currently protect such products and for 20 years for the least developed nations.

Entities license intellectual property and materials for a number of reasons. They license out technology in order to market it; the Agricultural Genetic Engineering Research Institute (AGERI) in Egypt, for example, may soon be able to license the technology contained in a new seed to an Egyptian firm for distribution to the farmer. They license in technology that they may not have themselves or as part of a cooperative development process, such as that between AGERI and Michigan State University. In these agreements it is important to describe the technology (and to deal with the issue of technologies that may be derived from the transferred technology or material) or technology for research or commercial purposes and, in appropriate cases, to define royalty obligations. Agreements will typically, also, have provisions governing such issues as liabilities in the event that a patent is invalid, obligations and liabilities respecting biosafety and arrangements for dispute settlement and termination. With the new Biodiversity Convention, the global community has recognized the sovereign rights of source nations over genetic materials located within their boundaries; transfers of these materials will probably be under new forms of licence or material transfer agreements still to be negotiated. (Source: *BioLink*, 1994)

Intellectual property and licensing agreement

An institutional intellectual properties policy describes how these properties are handled and, most importantly, who owns them. Establishing ownership is very important in patenting and licensing of inventions. Without clear ownership, patenting may be impossible and licensing very difficult. The policy also provides the researcher with guidance in the handling of his/her inventions and what reward can be expected for inventing.

Three terms or components of a licence agreement need considerable attention. One is the definition of the licensed materials or process. This definition includes the concerned patents and or pending patent applications and know-how. It must also include a complete description of the biological material which is being licensed. The other two components are grant of licence and royalties. Both need considerable review and study to determine the appropriate terms for each. For example, for the particular material or process being licensed it may be best to do this under a non-exclusive or exclusive licence or a variation of an exclusive licence. Also, the royalty rate determination depends on a number of factors including sponsor of the research, stage of development and cost of commercialization. Most of the other components of a licence can be handled routinely. (Source: *BioLink*, 1994)

European Council adopts a common position on the Draft Directive on Legal Protection of Biotechnological Inventions

After over five years of tortuous progression through the European Community legislative procedure, a common position on this draft directive has finally been adopted by qualified majority. The December 1993 issue of *ECJ Update* (Issue 12) reported on the basis of the proposed legislation and here we examine the main changes that have been introduced to the European Commission's amended proposal.

The common position retains the European Parliament's amendment excluding from patentability any invention "the publication or exploitation of which would be contrary to public policy or morality". However, it omits the qualification that processes for modifying the genetic identity of humans which are "contrary to the dignity of man" should be for a non-therapeutic purpose in order to be unpatentable, as was included in the amended proposal, and now includes a provision that animals resulting from processes to modify their genetic identity which are likely to inflict suffering or physical handicap upon them without any substantial benefit to man or animals shall be unpatentable, as well as such processes themselves.

The common position omits the provision contained in the amended proposal that methods for the treatment of the human or animal body by surgery or therapy and diagnostic methods practised on the human or animal body shall not be patentable. However, the provision that a process comprising a succession of steps shall not be excluded for the reason only that one or more of the steps involves a surgical, therapeutic or diagnostic methods practised on the animal body, although the treatment or diagnostic method shall not be protected, *per se*, remains.

The European Parliament controversial "farmers' privilege" provision, by which a farmer is permitted to use the product of his harvest for multiplication or propagation by himself on his own farm, is retained. However, the common position does not utilize the wording for the exception as proposed by the European Parliament, which in particular granted to farmers (rearing livestock protected by patents) the right to use it for multiplication purposes on their own farms to renew their stock.

The common position introduces into the provisions for granting of compulsory licences the requirement that such licences should be granted only to the extent that they are necessary for exploitation of the invention protected plant

variety where the invention plant variety represents a technically significant progress and also provides that Member States may allow for the right to a reciprocal licence to use the invention protected plant variety when such compulsory licences are granted.

Member States will have until the end of 1996 to transpose the directive into national law. Spain, Italy and Denmark all voted against the text for various ethical reasons. Among other reasons, Denmark considered it artificial to make a distinction between animals and animal breeds, and Spain argued that all processes for modifying human genetic identity should be unpatentable in principle, considering it impossible to distinguish between processes which violate human dignity and those which do not.

Eur-Lex Intl. European Law Bulletin, Bird & Bird, 90 Fetter Lane, London EC4A 1PJ, UK. Tel: 071 242 6681 Fax: 071 242 3643 (Source: *The Genetic Engineer and Biotechnologist*, Vol. 14, No. 3, 1994)

Patenting plants: The implications for developing countries

Global interest in biological diversity ("biodiversity") and its conservation has grown rapidly in recent years. Farmers have a role, particularly in less developed countries (LDCs), in maintaining biodiversity among the plant genetic resources used for food and agriculture. The growth of the biotechnology industry means that certain plant genetic resources are becoming commercially more valuable, so stimulating agriculture-related research by private companies and giving rise to demands from the developers of new plant varieties for more effective intellectual property protection over their inventions and the genetic resources they contain. The subject played an important role in the GATT talks.

The large investments being made in plant genetic research by biotechnology companies are part of a global trend towards the commercialization and privatization of research into genetic resources. In order to safeguard the returns on their investments, companies are pressing for intellectual property protection over their inventions, including those that consist of life forms.

Whilst inventors in most fields of industry have long been granted a degree of monopoly on their inventions, in return for making their knowledge available to society and as an incentive to further innovation, systems of intellectual property protection vary greatly around the world, being tailored to match cultural differences in attitudes to property rights as well as to meet the needs of nations at different stages of economic development. In many nations, and especially in the agricultural sector, informal innovation (i.e. without the protection of intellectual property rights (IPRs)) is still very important.

Biotechnology companies and some Governments in industrialized countries are calling not merely for the introduction of some kind of IPR, but for "harmonization", i.e. for all countries to adopt the types of IPR system currently operating in industrialized countries. For instance, the USA was exerting pressure in this direction as part of wider multilateral trade negotiations, particularly in the Uruguay Round and bilaterally, for example through the "Super 301" trade legislation, which applies sanctions to trading partners who refuse to recognize patents on US intellectual property.

While IPRs are not new, their extension to biological products raises new economic, political and ethical questions. Two forms of intellectual property protection are relevant to plant genetic resources: patents and plant breeders' rights.

A patent protects a product or process which is the result of an inventive step and which is new, useful and non-obvious. In return for patent protection, the invention must be disclosed to the public. Patents usually permit the holder to forbid commercial use, sale or manufacture of the protected product or process by others for a period of 17-20 years. Patent systems are determined by national legislation and vary from one country to another in, for example, the length of the period of monopoly rights and in coverage. Many Governments exclude pharmaceutical and food products, primarily so that their nationals can benefit from existing technologies.

Rules to protect public interest

Countries with patent systems have developed safeguards to ensure that the system serves the public interest by balancing the rights and obligations of patent holders. In addition to more general anti-trust laws, some countries have compulsory licensing measures to ensure that society can benefit from important innovations even if an inventor is reluctant to work a patent.

The number and proportion of inventions formally patented tends to be higher in industrialized rather than in developing countries. However, it is only relatively recently that plant and animal varieties, and the genetic resources that they contain, have fallen under the patent system.

The extension of patent systems to include living things is coincident with the globalization of patent systems. Though national, most patent systems operate under the framework of the 1883 Paris Convention which is administered by the UN World Intellectual Property Organization (WIPO). This flexible framework is likely to be replaced soon: WIPO is preparing a draft treaty on patent harmonization which stipulates that all inventions be patentable. More significantly, an agreement on Trade-Related Intellectual Property Rights (TRIPs) has been negotiated as part of the Uruguay Round of GATT. The draft agreement on TRIPs requires signatories to extend patents, or other IPRs, to all inventions, including plant and animal varieties, to limit compulsory licensing, and to provide a monopoly period of at least 20 years.

Plant breeders' rights

Many countries have judged patent systems to be an unsuitable form of IPR for living things such as plant varieties because of restrictions on access that they impose. Therefore, in order to provide less exclusive intellectual property protection for plant varieties, national systems of plant breeders' rights (PBRs) have developed. Most of the industrialized countries which have PBRs are members of the International Union for the Protection of New Varieties of Plants (UPOV), an intergovernmental association outside the UN system. The UPOV Convention, agreed in 1961, provides a framework for national PBR legislation. Although others cannot commercialize a protected variety without permission from the PBR holder and payment of a royalty, the genetic material contained within that variety is freely available for the purpose of breeding other varieties, under the "breeders' exemption". Similarly, a "farmers' privilege" allows farmers to resow seed harvested from protected varieties for their own use. There are two important differences from the patent system:

The UPOV Convention was revised in 1991 and now Member States do not have to guarantee the breeders' exemption or the farmers' privilege. Also, the protection provided by PBRs has been extended from the propagating part of the variety (the seed) to the whole plant, including grain for food in the case of cereal crops. Together, these changes make the PBR system more similar to the patent system.

It is unlikely that any new IPR regimes would be enforced rapidly and widely, particularly amongst farmers in developing countries, but the existence of more extensive intellectual property protection for plant genetic resources could, in the long run, have a substantial impact on global biological diversity, on developing country agriculture and on plant genetic research in the long run.

Biodiversity, plant genetic resources and peasant farmers

At the 1992 UN Conference on Environment and Development (UNCED) a comprehensive Convention on Biological Diversity was agreed to promote both the conservation and the utilization of biological diversity at three levels: ecosystems, species and genes. The implicit intention is that sharing the benefits of biodiversity use will promote conservation: that conservation will be encouraged by providing incentives, and enabled by providing the technological and financial means. The Convention came into force on 29 December 1993.

The Convention addresses IPRs on genetic resources in its Article 16, but only in a general way: on the one hand it recognizes IPRs, on the other, calls for mechanisms, which it does not specify, to be developed to ensure that IPRs do not prove a barrier to technology transfer. Further, it calls for cooperation to ensure that IPRs are supportive of and do not run counter to the wider objectives of the Convention.

Plant genetic resources for food and agriculture (PGRFA) comprise the range of plants which have long been managed by humans in farms and forests as well as the wild relatives of these plants. PGRs provide resistance to pests and disease in plants, tolerance to environmental extremes, and specific culinary and nutritional qualities. Their value to agriculture is already well known, and their potential as a "raw material" for the biotechnology industry is increasingly being recognized.

Rapid decline in genetic diversity

There has been an increase in genetic diversity from the birth of agriculture until recent times as a result of the human management of plant genetic resources on farms, such as crossing different cultivars, and saving seed from spontaneous mutations and wild relatives of food crops. In recent years this genetic diversity has declined rapidly. The loss of PGRFA is closely bound up with agricultural development itself, particularly with the introduction of modern varieties. Biotechnology is likely to accelerate genetic erosion by facilitating the breeding of modern varieties.

The "Green Revolution" from the 1960s onwards provided new short-straw, fertilizer-responsive varieties of rice, wheat and maize which greatly increased yields where water supply was reliable and contributed to an increase in world food production. But as farmers replaced their many traditional varieties with a few introduced ones, valuable genetic resources were lost. A handful of rice varieties now cover the majority of rice lands in Asia where once thousands of varieties were grown. In Zimbabwe, two hybrid varieties account for 90 per cent of all maize seed planted, and have displaced many traditional varieties of millet and sorghum.

Small-scale farmers outside the limited high-potential agricultural areas constitute about 80 per cent of the total in developing countries. The areas which they farm are characterized by complex interactions among a wide range of plant and animal species in agro-ecological conditions which are diverse and risk-prone. Modern varieties are generally less resilient than local varieties ("landraces") under these conditions, and perform poorly unless inputs designed to enhance their performance can be supplied (fertilizer, pesticide, irrigation). In the majority of peasant farming areas such inputs are difficult and expensive to obtain, and they represent a high risk strategy since their use increases the financial loss that crop failure would incur.

An alternative strategy has been for peasant farmers, as informal plant breeders, to adapt crops to the specific requirements of their agro-ecological environment and socio-economic situation. The wide range of traditional landraces maintained on farms is the result of this work and more than 85 per cent of seed in most developing countries is produced by farmers themselves. Farmers therefore both depend on genetic diversity as the "pool" from which their landraces are drawn, but also contribute to the maintenance of diversity by their very strategies of growing a wide range of cultivars which interbreed among themselves and, in some cases, with wild relatives.

Importance of private plant breeders

Historically, agricultural development in industrial countries has been dependent on public-sector plant genetic research rather than on private companies. The same was true of the Green Revolution in the 1960s and 1970s, and private plant breeding companies, focusing on the small areas of highly commercial agriculture, are only recently beginning to emerge. Nowadays, whether a developing country will benefit from the introduction of PBR or patent legislation depends on the extent to which a private plant-breeding sector is present in the country. PBRs promote local private-sector plant breeding oriented to the needs of local commercial agriculture.

In the few developing countries where there is a high level of research and development in biotechnology, patent legislation may promote the availability of patented biotechnology innovation, and increase cooperation between foreign and local companies. Set against this, the granting of patents on plants involves the risk that access to a common pool of plant genetic resources, essential to plant breeding, is likely to become restricted. Experience shows that most foreign countries registering their patents in LDCs do so in order to protect the import of their products, rather than to initiate local production. Furthermore, the international seed market now, unlike the seed market at the time when industrialized countries adopted their PBR laws, is dominated by a few seed companies poised to achieve market dominance in individual developing countries. Under these conditions, patents or PBR will mainly facilitate the introduction into developing countries of foreign varieties with a narrow genetic base.

The commercialization of plant breeding promoted by IPRs has led to intensive breeding of new varieties with a

limited genetic base. These varieties do not always meet the needs of small farmers. The adoption of intellectual property protection for plant material may therefore speed up the marginalization of low-input farmers. They are less likely to benefit from the seeds produced commercially, while the extension of private seed companies may lead to erosion of the role of public-sector breeders and undermine informal seed exchange mechanisms.

Increased intellectual property protection will also affect the biodiversity conservation activities of peasant farmers. This is perhaps the biggest threat of IPRs to biodiversity. In the long run the maintenance of global plant genetic diversity depends less on the relatively small number of formal plant breeders producing improved varieties for the marketplace, than on the vast number of peasant farmers who develop and maintain varieties to meet the needs of agriculture in highly variable environments.

Local varieties need to be enhanced using modern plant-breeding techniques, and farmers themselves need to be able to develop locally adapted varieties using enhanced germplasm produced by plant breeders. Progress in agricultural development consistent with conservation of PGRFA will require the formal and informal sectors to work together, but intellectual property protection may drive a wedge between them. Under patent law, farmers or local public-sector plant breeders cannot develop or maintain varieties for local distribution by re-sowing and crossing seed saved from the harvest of a protected variety, without permission and without the payment of royalties. In patenting applications, protection can be claimed even for individual genetic characteristics. A situation could arise where, if a protected gene finds its way into another variety (whether by deliberate or accidental crossing, or natural introgression), the patent holder could exercise their claims over the resulting variety. Thus a seed company could have a legal right to claim as its own all plants, with, for example, a high level of commercially valuable compound. Such restrictions would be likely to limit both the flow of acceptable varieties to farmers and their contribution to biodiversity. So domestic patent and IPR legislation, particularly in developing countries, should include provisions to maintain the "farmers' privilege" of permitting farmers to plant saved seed in successive seasons.

The issue of equity

There are also wider political and economic issues surrounding the extension of intellectual property rights to plants and their genetic components. Developing countries are being asked to introduce systems which will ensure that their farmers pay for improved germplasm while their own valuable contributions of genetic resources to the world community remain unrewarded. Many developing countries now emphasize that they have sovereign rights over PGRFA in their territories. Increasing attention is being placed on possible mechanisms to ensure that LDCs receive a share of the benefits derived from biodiversity. This is more than simply a matter of equity between LDCs and industrialized countries. If LDCs – or their farmers – are not receiving due compensation for their role in the development and conservation of PGRFA, then the incentives for conservation are likely to be sub-optimal. Solutions to this problem are now being sought in FAO and under the umbrella of the Convention on Biological Diversity. Such solutions may also require re-examination of the Paris Convention on patents, the UPOV Convention and the draft WIPO treaty on patent harmonization.

Reprinted in abridged version from a Briefing Paper published in November 1993 by the Overseas Development Institute, London. (Source *Development and Cooperation*, 1994 2)

G. BIO INFORMATICS

Intellectual Property Rights for Indigenous Peoples: A Source Book. Tor Greaves, Editor. Society for Applied Anthropology. Norman, OK, USA. 1994. 270 pp. $10.25 paperback.

This book is a useful and timely introduction to a topic of fiendish complexity. *Intellectual Property Rights for Indigenous Peoples* is academic writing at its best: rigorous and clear, focused on a substantive topic of great consequence, thoroughly and creatively documented. If the prospects for the successful extension of intellectual property rights (IPR) to indigenous peoples in defence of their genetic resources, traditional knowledge and cultural identities remain dim, the contributors to this volume effectively raise awareness of IPR issues and pose a number of promising new avenues for policy.

The common motivation of many of those contributors is well summarized in the spirited closing essay by Darrell Posey of St. Anthony's College, Oxford, and the Museu Paraense Emilio Goeldi in Belem, Brazil:

> "IPR developed as a Western concept that was essentially established to protect individual, technological, and industrial inventions ... Many think, as I do on some occasions, that IPR is not an appropriate mechanism to strengthen and empower traditional and indigenous peoples. Yet I continue to pursue the nebulous and incorrigibly difficult precepts upon which IPR is based for one principal reason: it is a subject that challenges every category of thinker and thereby stimulates dialogue."

Editor Greaves and his contributors have assembled a book commensurate with the challenge. It will prove useful to anyone interested in IPR as these rights bear on genetic resources, ethnobotanical knowledge, or the efforts of indigenous peoples to achieve full self-determination.

While the book's goal is to help tribal peoples (and others who work on their behalf) to secure some tangible benefit from the contribution of their knowledge or materials harvested from their lands to the world economy, its contributors do not advocate a single approach. Rather they explore the advantages and disadvantages of IPR as these rights are articulated in western law, and suggest approaches to a legally defensible concept of intellectual property better suited to the cultural and social circumstances of indigenous peoples. This is an evolving concept, and a work in progress.

To order a copy of *Intellectual Property Rights for Indigenous Peoples*, send a cheque in U.S. dollars drawn on a U.S. bank, for $10.25 plus $1.75 shipping and handling in the United States and Canada, or $2.75 in other countries, to: The Society for Applied Anthropology, PO Box 24083, Oklahoma City, OK 73124, USA.

Singapore Biotech Directory

The Singapore Society for Biochemistry and Molecular Biology has released the first edition (1994) of the *Singapore Biotechnology Directory*. The book, sponsored by the National Biotechnology Program of the Economic Development Board of Singapore, is available free of charge.

Contact: Gregory Chow, National Biotechnology Program, Economic Development Board, #27-00 Raffles City Tower, North Bridge Road, Singapore.

Malaysian Biotechnology Journal

A new publication (established last December) offers a window on the state of the biotech industry in Malaysia. *Asia-Pacific Journal of Molecular Biology and Biotechnology* is published jointly by the Malaysian Society for Molecular Biology and Biotechnology and the National Working Group on Biotechnology in Malaysia.

For information, contact Professor Tikki Pang, Editor, University of Malaysia, Kuala Lumpur, Malaysia.

Microbial Biotech "Bible" coming

Industry and academia will have a valuable new resource with the release of *Food Biotechnology - Micro-organisms*. The 1,000-page compendium includes submissions from 47 distinguished scientists from nine different countries. It covers three broad areas: principles of food biotechnology with examples of general applications; production of enzymes and food ingredients; and manufacture of fermented foods.

Dr. George Khachatourians, Professor of Applied Microbiology and Food Science at the U of S, co-edited the book with Dr. Y.H. Hui, Head of the American Food and Nutrition Centre in California. Khachatourians says the book is "the bible for looking at micro-organisms", giving both the state of the art in the field as well as future trends as seen by a wide range of experts.

Food Biotechnology - Micro-organisms is available from VCH Publishers Inc. of New York, USA.

Chinese Biotechnology Directory published

An English language Chinese biotechnology directory has been published. It is divided into three parts: the first part covers an overview on Chinese biotechnology, including government policy and regulation environment. The second part lists all government agencies and societies involved in biotechnology. The third part lists research institutes, university departments and companies in biotechnology. Information includes the organization names, full address, telephone, fax and telex numbers, activities and services offered. (256 pp., US$ 199.)

Pharmacopoeia of the People's Republic of China 1992

An English language *Pharmacopoeia of the People's Republic of China 1992*, English edition compiled by the Ministry of Public Health, has been published. It covers 784 traditional Chinese medicines, and 967 western medicines and preparations, giving information on the standards of purity, description, test, dosage, precaution, storage and the strength for each drug included. (1,100 pp. hardback, ISBN 7-5359-0945-0, US$ 298.)

Both books are available from: Han Bao Consultants Inc., PO Box 71006, Wuhan, Hubei 430071, People's Republic of China. Fax: +86-27-718345.

Highly selective separations in biotechnology

Ed. G. Street. London, Chapman & Hall 1994. Pp. 1-334. £65. ISBN 0-7514-0051-3.

Success in exploiting the products of biotechnology depends, in no small part, on the availability of effective separation technology. Typically, biotechnology products

are made in dilute solution and have to be separated from very complex mixtures of impurities.

Developing cost-effective processes which can recover products at high yield is a major challenge. This is especially true for therapeutic products, where exceptionally high levels of purity are typically required. This book examines a number of approaches which are currently being developed to improve the selectivity of separation processes. It is an edited volume, with chapters contributed by experts in their respective fields.

The focus of the book is mainly on proteins, and there are contributions on affinity partitioning in two-phase aqueous systems, the application of reverse micelles, affinity chromatography and the use of protein fusions to design molecules with improved properties in separation processes. Chapters on molecular imprinting and chiral separations describe approaches to the highly selective separation of small molecules.

The volume will be a useful reference for all biotechnologists and chemical engineers who are interested in the development of separation processes.

Membranes in bioprocessing: theory and applications

Eds J. Howell, V. Sanchez & R. Field
London: Chapman & Hall 1993
Pp. 1-336, £85, ISBN 0-7514-0149-8

The complexity and cost of downstream processing of biological materials has long been recognized, and efforts have been made to improve this aspect of production. One much studied area of downstream processing is membranes, particularly cross-flow micro-filtration and ultra-filtration. This research effort has resulted in the evolution of many small companies, often producing systems based on specific membrane materials and configurations for application in downstream processing. However, there has not been a systematic review of membranes in bioprocessing.

This book addresses the basic principles of membrane science in relation to the specific problems of downstream processing of biological materials.

The book is well referenced and full of practical information which, together with the various exercises, make it a useful source of information for those working on membrane applications in bioprocessing.

"Growing Diversity" now available in Spanish and Portuguese

Growing Diversity: Genetic Resources and Local Food Security (edited by GRAIN, published by IT Publications, London, 1992) is now available in Spanish and Portuguese versions.

Farmers throughout the world, but especially those in the gene-rich South, have always nurtured that part of genetic resources which feeds all of us: agricultural biological diversity. That nurturing implies conscious use, selection and management of those varieties best adapted to local physical and cultural realities. In recent decades, the "Green Revolution" shift towards industrialized agriculture, highly dependent on external energy and chemical inputs, has been responsible for the massive loss of thousands of traditional varieties. Together with that genetic erosion comes the loss of the knowledge systems and cultural resources associated with them.

Growing Diversity, originally published in English, documents farmer and community approaches to plant genetic conservation and management in Asia, Africa and Latin America. Written mainly by NGOs and supportive scientists, this book has now been translated for broader use in Latin America.

Cultivando Diversidad is the Spanish language version and includes a special prologue and introduction. Published by Comision de Coordinacion de Tecnologia Andina and ITDG Tecnologia Intermedia in Lima, 1994, 209 pp. Available from CCTA, Casilla Postal 14-0426, Lima, Peru. Fax: (51-14) 22 99 23. Sells for US$ 15, plus shipping.

Cultivando a Diversidade is a Brazilian translation and expansion of the original work. Aside from new chapters on farmers' work with traditional maize varieties in Brazil, it includes potato conservation in Chile, traditional livestock breeding in Nicaragua, agricultural biodiversity in Colombia, and local seed banks in Peru. Published by Assoria e Servicos a Projetos em Agricultura Alternativa in Rio de Janeiro, 1994, 205 pp. Available from AS PTA, Rua de Candelaira 9, 5° andar, 20091.020, Rio de Janeiro - RJ, Brazil. Fax: (55-21) 233 83 63. Sells for 25 URVs in Brazil and US$ 35 abroad, including shipping.

Grain briefing papers for the Convention on Biological Diversity

An Intergovernmental Committee for the Convention on Biological Diversity (ICCBD) was set up to handle interim developments related to the Convention prior to the first meeting of the Conference of the Parties (Bahamas, 28 November - 1 December 1994). GRAIN prepared a set of briefing documents for the government delegates and NGOs present at the last ICCBD meeting in Nairobi. Although these papers focus on that particular event, the information, arguments and policy positions espoused may be of interest to many who are working the same issues.

GRAIN Biobriefing, No. 4, June 1994 is a set of four separate issue sheets:

- Part 1: Agricultural Biodiversity in the Convention;
- Part 2: Intellectual Property Rights for Whom?;
- Part 3: In-Situ, Ex-Situ: Forgetting the Farmers?
- Part 4: Threats from the Test-Tubes: Towards a Protocol on Biosafety

Additionally, Dan Leskien of the European Coordination of Friends of the Earth (CEAI) and GRAIN prepared together a briefing paper on biosafety for the ICCBD, *International Transfer of GMOS: the need for a biosafety protocol*. It contains a table with examples of field tests carried out in Latin America.

To receive these papers, please write to GRAIN, Jonqueres 16-6-D, E-08003 Barcelona, Spain. Fax (34-3) 310 59 52.

Issues in Genetic Resources

The International Plant Genetic Resources Institute has launched a new "occasional papers" series entitled *Issues in Genetic Resources*. The first two issues were published last May. The first one examines the pros and cons of material transfer agreements (MTAs) in the exchange of genetic resources, and the implications for the International Agricultural Research Centres. The authors, who are the core legal consultants for the CGIAR at the World Bank, are strong advocates of using MTAs as a way of regulating the international flow of germplasm to the benefit of the original donors. The second issue makes a strong case for multilateral approach to genetic resources conservation and use. Both documents are well done to serve international

debates about how to manage genetic resources in a more equitable way.

John H. Barton and Wolfgang E. Siebeck, "Material transfer agreements in genetic resources exchange: the case of the International Agricultural Research Centres", *Issues in Genetic Resources*, No. 1, May 1994, 61 pp., ISBN 9043-239-x. David Cooper, Jan Engels and Emile Frison, "A multilateral system for plant genetic resources: imperatives, achievements and challenges, *Issues in Genetic Resources*, No. 2, May 1994, 42 pp., ISBN 92-9043-238-1. Both may be requested from IPGRI, Via delle Sette Chiese 142, I-00145 Rome, Italy.

Biotechnologia recursos fitogenéticos y agricultura en los Andes is a compilation of texts from NGO activists and researchers on critical issues related to plant genetic resources, biotechnology and the future of farming systems in Latin America. The chapters are based on papers prepared for a meeting on the subject in Piura (Peru), organized by the Comisión de Coordinación de Tecnologia Andina in 1992. After each presentation, the editors have summarized the discussions that took place.

T. Gianella and J. Aragón (eds.), *Biotecnologia recursos fitogenéticos y agricultura en los Andes*, Cuadernos de debate y reflexion, No. 4, CCTA, 1993, 230 pp. Available from: CCTA, Apartado postal 14-0426, Lima, Peru.

Two recent deliveries from new additions to UNEP's "Environment and Trade" series will interest *Seedling* readers. The first is by William Lesser and looks at "trade" in genetic resources under the new provisions of the Biodiversity Convention and the GATT TRIPs agreement. Lesser discusses intellectual property options and their implications, as well as wider trade-related matters. The second is by John Stonehouse and John Mumford looking at environmental risk analysis and policy-making.

William Lesser, "Institutional Mechanisms Supporting Trade in Genetic Materials: Issues under the Biodiversity Convention and GATT TRIPS", *Environment and Trade*, No. 4, UNEP, 1994, 72 pp. ISSN 1020-1610. John M. Stonehouse and John D. Mumford, "Science, Risk Analysis and Environmental Policy Decisions", *Environment and Trade*, No. 5, UNEP, 1994, 79 pp. ISSN 1020-1610. Both are available from: Environment and Trade, UNEP, 15 chemin des Anémones, CH-1219 Chatelaine, Geneva, Switzerland.

Redes and Grain launch Biodiversidad: Cultivos y Culturas: New Latin American agricultural biodiversity quarterly

A genetic resources, biotechnology and agricultural biodiversity seminar was held on 21-22 September 1994 by REDES-AT in Montevideo to launch a new quarterly publication. As announced in the last *Seedling*, *Biodiversidad: Cultivos y Culturas* aims at becoming a dynamic regional discussion forum, its pages open to all those involved in development and sustainable agricultural issues.

The first number of *Biodiversidad: Cultivos y Culturas* includes articles on alternative intellectual property regimes, biotechnology, medicinal plants in Argentina and maize genetic resources conservation and management by farmers in Brazil. The editorial invites to "share information, knowledge, experiences, worries, and actions to foster self-development of not only agricultural biodiversity, but also of those cultures which nurture it.

The seminar, during which a special public session was held to present *Biodiversidad*, brought together over 50 participants from several Latin American countries, including a large gathering of Uruguayan scientists, students, farmers and NGOs. Decentralization, farmer-led initiatives, alternative frameworks to current national and international legal structures, and socially responsive science were themes thrown out by the panelists and amply discussed during the two days. Among the consensus conclusions reached were the need to closely monitor the Human Genome Project, increase work and awareness on animal genetic resources, monitor changes in national legislation concerning genetic resources, improve links between universities and those involved in agro-ecology, and boost communication and information tools at a regional level.

For further information please contact: *Biodiversidad: Cultivos y Culturas*, REDES-AT, Avda. Millan 4113, 12900 Montevideo, Uruguay. Tel.: (598-2) 35.62.65. Fax: (598-2) 39.16.40. E-mail: redesur@chasque.apc.org. Subscriptions are free for POs and NGOs in Latin America, US$ 20 for others in Latin America, and US$ 25 for the rest of the world.

The Internet

The information superhighway is here, for those that know how to get on it, and the highway is the Internet. More importantly, the internet is becoming a competitive advantage for companies knowing how to use it as such. In the current era of cost-cutting, partnerships, tight money and hyper-regulation in the pharmaceutical and biotechnology industries, the Internet can serve a real communication need, and despite several watch-outs, it has the potential to go beyond research-collaboration monitoring and clinical-trial monitoring to be a useful business tool - a way to reach customers and a better way to partner with suppliers and regulators.

For two decades, the Internet was almost exclusively the domain of research, government and educational applications. The growth of commercial Internet applications over the past three years has changed all that. Thousands of businesses, including more than half of the Fortune 500 corporations, are connected to the Internet today, together with millions of other users around the world. Standard communication protocols allow all types of computers to exchange e-mail, information, graphics and enormous data files over the 40,000-plus interconnected networks that make up the global Internet. This level of international connectivity has enormous potential for business, particularly for the pharmaceutical and biotechnology industries, where up-to-the-minute information is essential for success.

The Internet is faster, and more efficient, than faxing, calling, mailing or flying. It simplifies the collection of data and accelerates the transfer of creative ideas. In addition to speed, it gives the researcher a larger palette to work from. On the Internet, you have a wonderful, immediately accessible array of protein-sequence databases, genomic sequences, electrophoretic gels and virus databases, all available to all. On one particularly rich bioserver, at Johns Hopkins University (Baltimore, MD), there are over 9,000 people a day accessing the server and its databases, people from all over the world. From the Johns Hopkins server, you can leap to the European Molecular Biology Network (Basel) and the National

Cancer Center Japan (Tokyo) and, though a series of hyperlinks, thousands of other research institutes, government agencies, universities and corporations.

High-technology companies were among the first businesses to adopt the Internet as a new communications channel for interacting with customers and development partners. Each has a well-designed, multi-functional on-line presence that includes network-based technical support for customers, product descriptions, user discussion groups, and on-line ordering. The Internet channel has translated into millions of dollars in new sales and substantial savings over traditional methods of customer support for these companies.

One of the major factors driving the development of a true Internet "marketspace" is the widespread adoption of the Mosaic software. Mosaic was developed by the National Center for Supercomputer Applications (NCSA) at the University of Illinois (Urbana, IL) as an intuitive, point-and-click interface to the Internet. In addition to the high-quality graphic images, Mosaic incorporates audio and video into an easy-to-script, hypertext format that sits on top of standard Internet navigational tools, such as World Wide Web and Gopher. Over 2 million copies of the public domain versions of Mosaic were downloaded from the NCSA Internet server during the past year. Commercial development of Mosaic the software has been licensed to a number of companies will include expanded capability for information management and new features for end users, such as printing and downloading data.

Using Mosaic, companies design a "home page", or introductory-information screen, that integrates a variety of Internet applications and information resources for easy customer access. A customer connecting to a typical home page will be able to choose from new product announcements, detailed catalogues of products and services, and whatever other resources and services the company wishes to highlight. Hypertext links connect the graphics and information on the home page to more extensive files or to direct contact with sales and support divisions.

Taking full advantage of Internet capabilities offers special value for the knowledge-intensive pharmaceutical and biotechnology industry. There are five areas where the Internet would be immediately useful to pharmaceutical and biotechnology companies:

- Regulatory activities;
- International presence;
- Supplier partnerships;
- Customer support;
- Discovery watch.

There is a sea of information available on the Internet in the life-science and bio-science area. With all major universities on the Internet, with foundations, agencies and databases, it is important for competitive reasons to have an intelligent, systematic watch for issues and discoveries. (Extracted from *bio Technology*, Vol. 12, November 1994)

Smithsonian Internet Service

The Department of Botany of the US National Museum of Natural History at the Smithsonian Institution has launched the "Internet Gopher", a service that will allow Internet access to its numerous documents and databases. Most notable is the Type Specimen Register of the US National Herbarium, which is the world's largest electronic database of plant types with more than 88,000 records. The Index of Historical Collections, another valuable service, is the most comprehensive listing of the collectors represented in the US National Herbarium. The museum hopes for a favourable public response so that it can make more information available in the future. Users can reach the Department of Botany on-line through University of Minnesota Gopher Client software. Contact your Internet provider for more information about this service.

The Biomonitoring database now available on CD-ROM

The National Biological Impact Assessment Program (NBIAP) of the United States Department of Agriculture has developed a computer database that provides user-friendly access to information on field tests of genetically modified organisms used in agricultural research. Composed primarily of environmental assessments from field test permit applications prepared by the USDA Animal and Plant Health Inspection Service (APHIS), the first version of the database is now available free of charge on CD-ROM. The thoroughly searchable database contains 176 environmental assessments as well as several end-of-experiment reports. It is designed to inform the biotechnology research community, state and local governments, public interest groups and interested individuals by providing an accessible and user-friendly form of information.

The Biomonitoring Database is based on a Lotus software program called SmarText. SmarText runs in a Windows environment and costs between $50 and $100. Access to Windows, SmarText and a CD-ROM reader drive is required for operation of the database.

For more information about the Biomonitoring Database, or to order a free copy of the CD-ROM, please write to or fax: Dr. Ann Lichens Park, National Biological Impact Assessment Program (NBIAP), Ag. Box 2220, Washington, DC, 20250-2220, USA. Tel.: (202) 401-4892. Fax: (202) 401-4888. E-mail: Lichenspark *a* darth.esusda.gov.

Quebec Centre offers Bt DNA database

Researchers at the Horticulture Research and Development Centre in Saint-Jean-sur-Richelieu, Quebec, Canada, have amassed an extensive collection of DNA fingerprints from plants, insects, bacteria and fungi. The collection is used in conjunction with a novel technique that rapidly identifies plants and insects.

One of the bacteria, *bacillus thuringiensis* (Bt) is the only registered biological insecticide in Canada. One of its problems, that of variable effectiveness, could find a solution in the Quebec DNA library, this resource has already helped researchers develop Bt 10 times more effective against fly larvae.

The Centre welcomes collaboration with researchers interested in continuing these lines of research, as well as a company to market the new Bt.

New CD-ROMs

The Library at ICRISAT Asia Center has acquired two new CD-ROM products: SYB-CD and the Earth Summit.

The SYB-CD (*Statistical Yearbook*, 39th issue), published by the United Nations, is the most comprehensive standard international compilation of world statistics available. It provides hundreds of series on economic and social aspects of life in over 200 countries. It is identical to the print version (with data through 1990-1991) and is avail-

able on the CD-ROM both as a database and as images of text pages of the hard-copy publication. The CD-ROM facilitates the search of data by country, period, or specific series (e.g., population). Data retrieved can be printed or downloaded to text Lotus DBF formats.

The Earth Summit CD-ROM is a cooperative information project of UNCED, IDRC and the Canadian Centre for Occupational Health and Safety. It contains the full text of the documentation related to the Earth Summit and its preparatory stages, plus extensive background material. The documents are in their original language.

Using search and retrieval software, documents can be accessed either by title or topic, and can be printed or exported to a file. Images can be saved using the Microsoft Windows Paintbrush utility. The Library will be happy to provide search outputs from these two new products.

Directory of Biotechnology Information Resources

DBIR® is a multi-component database containing information on a wide range of resources related to biotechnology and molecular biology. These resources include on-line databases and networks, publications such as books and periodicals, organizations, and collections and repositories of cells and subcellular elements. DBIR also identifies groups and organizations working on issues of nomenclature in biotechnology or molecular biology. The database is available as a subset of the National Library of Medicine's DIRLINE® (Directory of Information Resources Online) database within NLM's MEDLARS® system.

Records in DBIR contain information such as the names of organizations, publications, or databases, relevant addresses and telephone numbers, and related DBIR records. Keywords drawn from NLM's Medical Subject Headings (MeSH®) and other special sources are assigned to each record to allow for ease in searching for particular concepts. Information specific to individual resources such as ISBN numbers for books, number of records for databases, etc., is also included.

DBIR is a component of DIRLINE, an NLM database that contains descriptions of a variety of information resources related to health and biomedicine. While searching DIRLINE, inclusion of the term DBIR (SI) in a search query will restrict postings to records from DBIR. DBIR can be searched by subject, the name of the entity, geographic locale, keywords and MeSH. NLM's GRATEFUL MED® software simplifies searching the database. On-line or off-line printing of entire or specific portions of records is available. A variety of print options allows additional customized formats.

DBIR can be used to answer such questions as:

- What databases characterize cloning vectors and where can these vectors be obtained?
- Are there any nearby university-affiliated biotechnology centres in New York State?
- What software is available to analyse molecular sequences?
- Are there any publications which focus on the legal aspects of biotechnology?
- Is there a source for obtaining pathogenic fungi in England?
- Is the Genbank® Genetic Sequence Data Bank available on magnetic tape?

DBIR is available 24 hours/day, seven days/week through the DIRLINE database.

Registered users of NLM's on-line services can access DIRLINE and thus DBIR by direct dial or through INTERNET, TYMNET, SPRINTNET and COMPUSERVE telecommunication networks searching either directly or using GRATEFUL MED.

For information about DBIR contact: DBIR Representative, Specialized Information Services, National Library of Medicine, 8600 Rockville Pike, Bethesda, MD 20894. Tel.: (301) 496-3147; Fax: (301) 480-3537; E-mail: arnesen@nlm.nih.gov.

Directory of Information Resources On-line

DIRLINE is the National Library of Medicine's on-line database containing location and descriptive information about a wide variety of information resources including organizations, research resources, projects, databases and electronic bulletin boards concerned with health and biomedicine. This information may not be readily available in bibliographic databases. Each record may contain information on the publications, holdings and services provided.

DIRLINE focuses primarily on health and biomedicine, although it also provides limited coverage of some other special interests. These information resources fall into many categories including federal, state and local government agencies; information and referral centres; professional societies; self-help groups and voluntary associations; academic and research institutions and their programmes; information systems and research facilities.

DIRLINE contains over 15,000 records merged from the following sources:

- **National Library of Medicine (NLM)**
  General biomedical resources compiled by the National Library of Medicine.
- **ODPHP National Health Information Center Database (HR)**
  Supplied by the Office of Disease Prevention and Health Promotion.
- **Poison Control Centers List (PCC)**
  Accredited centres compiled in collaboration with representatives of the American Association of Poison Control Centers.
- **Regional Alcohol and Drug Awareness Resource Network (RADAR)**
  Information provided by the Office of Substance Abuse Prevention's National Clearinghouse for Alcohol and Drug Information.
- **History of Medicine (HMD)**
  Produced by the History of Medicine Division, National Library of Medicine.
- **Maternal and Child Health (MCH)**
  Produced by the National Center for Education in Maternal and Child Health.
- **AIDS**
  Produced by the Centers for Disease Control's National AIDS Clearinghouse.
- **Directory of Biotechnology Information Resources (DBIR)®**
  Produced by the American Type Culture Collection under contract to NLM.
- **Self-Help Clearinghouses (SHC)**
  Produced in response to the Surgeon General's initiative in Self-Help and Public Health.

- **NIH Research Resources (NIHRES)**
  Information on NIH-funded research resources provided by the National Institutes of Health.
- **Health Services Research Information (HSRI)**
  Produced by ECRI under contract to the National Library of Medicine.

DIRLINE can be accessed via direct telephone line, the TELENET SprintNet, TYMNET or CompuServe nationwide telecommunications networks, or by the Internet. DIRLINE is also available using GRATEFUL MED® software.

DIRLINE can be searched in a variety of ways. Geographic searching by country, or US Postal Service abbreviation for state names, and zip or other postal codes, allows the retrieval of resources within a specified region. Users interested in locating resources by name or subject-matter can specify either words appearing in the name field, the text of the record, or keywords, or enter Medical Subject Headings (MeSH).

The following represents portions of a DIRLINE record:

Secondary source id: HR 2389
Name: National Women's Health Resource Center
Address: 2440 M Street, NW, Suite 325; Washington, DC 20037
Institution contacts: Program Director,(202)23906045
Abstract: The National Women's Health Resource Center is a national organization devoted solely to the health of women. Its services include a complete range of clinical, education, research, psychological support and information programs. HOLDINGS: Publications include the National Women's Health Report (quarterly newsletter), a five-year index and NWHR Series Packets. There are charges for subscriptions and back issue orders.
MeSH heading: *Gynaecology; *Women's Health Services.

DIRLINE is available on the NLM computer facility 24 hours a day, seven days a week.

For information about DIRLINE access, or MEDLARS® services contact: MEDLARS Management Section, National Library of Medicine, 8600 Rockville Pike, Bethesda, MD 20894. Tel.: (800) 638-8480.

For information about DIRLINE content and search strategies contact: Specialized Information Services, National Library of Medicine, 8600 Rockville Pike, Bethesda, MD 20894. Tel.: (301) 496-1131 or (301) 496-3147.