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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

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CONTENTS

UNIDO's *Emerging Technology Series: Genetic Engineering and Biotechnology* 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.

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Compiled and edited: Diana Rhind
Editorial Board: Y. Maruno, V. Podshibyakin; G. Tzotzos;G. Ramsey; B. Sugavanam; Z. Cziser

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Tel.: (43-1)21131-3736; Fax: (43-1)21131-6843
e-mail: drhind@unido.org

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TO OUR READERS

At present, there is an increasing awareness of the economical potential of genetic resources. The emergence of so-called "third generation" biotechnology has opened the doors of a new era for research and development that has revitalised the economic value of biodiversity. This has taken place parallel to the alarming disappearance of flora and fauna. Legislation, however, still lacks adequate property rights protection and the power to determine uses for this new "green gold".

The widely publicized agreement between Merck & Co. and the Costa Rican National Institute for Biodiversity (INBio) for the payment of fees and royalties for germplasm collected in Costa Rican preserves has received considerable attention in the literature under the name of "germplasm prospecting" and precipitated discussions on payments for germplasm, and how potentially lucrative biodiversity prospecting may be. It is argued that great potential exists for discoveries of new medicines because many important pharmaceuticals on the market today have been derived either directly or indirectly from plants, fungi, microorganisms and marine life, and because only a small fraction of the world's biodiversity has been screened for chemical activity of pharmaceutical interest. However, biodiversity prospecting is not like gold mining, where the commodity is concentrated in a given area and, when extracted, is almost immediately worth a considerable amount of money. While biodiversity is everywhere, finding out if it has pharmaceutical value requires considerable investment in time, money, technology and scientific expertise (between at least 10 to 20 years and US$ 200 to 300 million). To accurately assess the value of successes and potential successes of natural products drug discovery, one must also consider the significant costs involved over time and whether these are paid by governments (taxpayers) or by the private sector. For instance, once an active compound is found, it is sometimes quite difficult to get enough of it to do proper testing. Because these compounds are often found in minute amounts in the natural products, huge quantities may have to be gathered in order to produce the small measures that advanced testing requires – and such large-scale gathering could actually endanger a species in the wild. Chemical synthesis or cultivation to avert species extinction would most likely have to be undertaken, involving additional time and money.

Biodiversity prospecting is certainly useful in providing experience in innovation, not only in science but also in the management of innovation and the development and marketing of innovative products. The lack of experience with innovation has been quite a limiting factor for developing countries. Beyond uses in human health, biodiversity prospecting for chemicals of agricultural, veterinary health or industrial importance could provide opportunities to develop innovative and commercially significant products. And it may turn out to be very useful indeed when combined with other efforts to produce scientifically validated and standardized herbal remedies to meet the primary health care needs in both the developing countries and those developed countries where there is a tradition for such products.

The first step in any bioprospecting programme is to inventory biological and genetic resources so that researchers may better know the materials and understand their potential. Inventories can be completely random, involving plants, insects, microbes or marine organisms, or they can be directed. Two types of directed bioprospecting inventories are ethnobotanical inventories and ecological inventories. The first makes use of the traditional knowledge of indigenous or other rural communities, while the second employs collectors trained to observe ecological interactions among species. Since scientists are far from recording all plant, insect, etc. uses, those with economically important close relatives are probably more likely to possess economic potential than those with no known economically imporatant relatives.

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A. SPECIAL ARTICLE

ISSUES AND STRATEGIES FOR BIOPROSPECTING

by
Ana Sittenfeld, Director, Centre for Research in Cell and Molecular Biology, University of Costa Rica and Scientific Advisor, National Biodiversity Institute (INBio), Costa Rica

Historically, pharmaceutical and agricultural industries have benefited from biodiversity through developing drugs from natural compounds that earn up to US$ 1 billion per product, and through improving crops by breeding them with undomesticated predecessors. Even today, the returns from potential new drugs found and developed in tropical forests is estimated to exceed US$ 100 billion in value to society as a whole. Gene technology promises an even brighter future for biodiversity prospecting. New pharmaceutically-active peptides and proteins from wildlife are already on the market or undergoing preclinical and clinical trials. Natural attack and defence mechanisms of micro-organisms, plants and animals are used in agricultural biotechnology to create pest resistance, and include the expression of insectacidal proteins and peptides from bacteria and spider venom in genetically engineered plants. Engineering of metabolic pathways, such as the transfer of the thioesterase gene of an undomesticated bay into *Brassica*, will also have a fundamental impact on agriculture, just as the production of waxes for lubricants and poly-hydroxybutyrate for plastics in rape seed may turn the farm field into a chemical factory.

However, many of these advances were originally developed in the North, in close proximity to growing biotechnology companies and therefore favour the agricultural practices of developed countries. This may pose a problem for the primarily agricultural economies of the South because these developments may displace or transfer the production of Southern commodities to the farm fields of the North, or even possibly to industrial bioreactors. The concept of modern biodiversity prospecting, already approved in drug research, addresses this threat through transferring biotechnology to Southern nations in exchange for access to their biological resources. This will enable developing countries to use their own biological riches while retaining a competitive edge with industrialized countries.

The Biodiversity Convention and other international agreements

The debate over biotechnology and its potential to increase the standard of living of countries and societies, together with its implications for the conservation and sustainable use of biodiversity, continue to be controversial and at the heart of many, if not most, of the discussions on economic development and sustainable use of biological resources. The relation between biodiversity and biotechnology offers two considerations: biotechnology is a tool or a technology, whereas biodiversity is an inherited property. Associated issues to the joining of both are intellectual property rights (IPR), technology transfer, ethics and environmental effects.

The last three years have seen a great deal of activity involving different issues on biodiversity and biotechnology in international fora, with the world-wide adoption of the UN Convention on Biological Diversity and the establishment of the World Trade Organization (WTO). Biological and genetic resources, as well as genetic technologies, are included in WTO regulations, which are intended to remove impediments to trade among member countries by reducing quotas and tariff rates. The transfer of services and technologies are incorporated as Trade Related Aspects of IPR or TRIPS in WTO. The imposition of any changes in IPR laws under TRIPs will have implications regarding biological-genetic resources, including product prices, research investments and structure of industry, among others.

The Convention on Biological Diversity marks an historic commitment by the 157 nations who signed the Treaty. The Convention entered into force in December 1993 calling for a framework to regulate access and control of biological resources, intellectual property rights, environmental protection, and commercial laws that must be harmonized with the goals of development, conservation and the fair and equitable sharing of benefits derived from the sustainable use of biological-genetic resources.

Putting the Biodiversity Convention into practice is not an easy task, for two reasons: first the Convention is a framework agreement, leaving individual countries to determine how most of its provisions are to be implemented; and second, the conservation of biological diversity and the sustainable use of biological resources are complicated and very limited experience is available. Controversial issues, such as IPR and technology transfer, are the ones that offer most conflict between different parties.

The Convention rejects the notion of genetic resources as the common heritage of mankind, as previously stated in the FAO International Undertaking on Plant Genetic Resources, and recognizes the sovereign rights of countries to exploit their own resources, with responsibility to ensure that activities do not cause damage to the environment of other States. (In 1993, FAO reviewed its International Code of Conduct for Plant Germplasm Collecting and Transfer in an effort to harmonize FAO activities with the Biodiversity Convention). Articles 8 and 9 set out major policies for "*in situ*" and "*ex situ*" conservation, respectively. Article 14 refers to environmental impact assessment, while Article 12 refers to research and training, and Article 13 refers to education and awareness.

Articles 15 and 16 on access to genetic resources and access to and transfer of technology, although complex and imprecise, also leave each party to decide how to implement the obligations on the control of genetic resources and benefit sharing. The Biodiversity Convention talks about equity and recognizes the right of developing countries to control access to biological resources. The movement of biological resources and local information is to be traded by expertise and the equipment for its use, through collaborative research efforts.

The controversy is felt when industry claims that the convention will restrict access to natural products, and tropical third world countries fear the loss of their rich chemical and genetic repertoire. The Convention highlighted the economic value of biodiversity, but has also spotlighted the practice of collecting genetic resources from developing countries. Nevertheless, and despite appearances, the Convention is not an attempt by conservationists to lock up the world's green house. On the contrary, it provides a framework to promote their use. The recognition of the sovereign rights of nations over their genetic resources is intended to encourage world trade in genetic resources, since it commits countries to facilitate access based on mutually agreed terms. According to Articles 15 and 16, the three mechanisms by which a country can benefit from the use of genetic resources are:

(1) By participation in research using the resource;
(2) By receiving technologies that utilize the resource;
(3) By sharing the financial benefits from the commercial exploitation of the resource.

Intellectual property rights can be applied to facilitate all these mechanisms. At the same time it should be noted that IPR would provide a possible mechanism for controlling the movement and use of genetic resources. It is clear that the Convention contains language that does not appear to compromise the value of IPR systems, as the access and transfer of technology shall be provided on terms consistent with effective protection of IPR and are subject to national legislation and international law.

Collaborative efforts between partners from developed and developing countries will design innovative ways to bring the intentions of the Convention to real grounds. The formation of strategic alliances with pharmaceutical, agrochemical or biotechnological companies from industrialized countries and institutions, and Governments from developing countries, are demonstrating that if these relationships are between professional research partners, they offer a convenient, cost effective solution to the problem of acquiring high quality natural resources and associated value adding services. At the same time, companies and developing countries are learning how Articles 15 and 16 from the Convention—in its vague wording—can be translated into relationships for mutual benefit.

The exploration and conservation of the world's biotic resources requires an approach involving bioindustries, research centres and developing countries, all collaborating towards a common goal, with each participant benefiting from the relationship. Learning how to be professsional partners represents a major challenge for countries rich in biological resources. Favourable legal and policy environments are required as a fundamental point of departure, followed by institutions capable of implementing coordinated schemes within the context of the Global Biodiversity Conservation strategy, based on the following three overlapping steps: saving, knowing and using biodiversity. Costa Rica's Instituto Nacional de Biodiversidad (INBio) represents a pilot project towards this end. INBio was created in 1989 as a private non-profit institution, following a governmental recommendation with instructions to participate in carrying out the second and third steps of the strategy. The first step produced the protection of 25 per cent of Costa Rica's territory. To achieve the second and third steps of the strategy, INBio is carrying out a biodiversity inventory, prospecting, and managing and disseminating information on Costa Rica's biological diversity. The concept of bioprospecting pioneered by INBio, integrates product discovery with financial and intellectual returns to nature, linking the understanding and non-damaging exploration of biodiversity to conservation activities and economic development of the countries where bioresources were first obtained. Previously, this activity generated benefits almost exclusively for industry, leaving biodiversity conservation and source countries to generate benefits and returns elsewhere.

In the light of the vast potential of biotic materials and the need to ensure their survival, in addition to measures taken to prevent and improve biodiversity conservation activities, it is imperative that industry move from the passive role of simple users to the more active exercise of reinvesting part of their revenues into conservation efforts. Companies should be aware that they are already among the first to lose in the face of species extinction, and indeed the awareness is growing.

The principle of this modern approach to bioprospecting may be simple, but the link between biodiversity conservation and its sustainable use requires a careful design and strategic planning. Its goals are to maximize those uses which generate information and reinvest part of the benefits obtained from bioproducts into acquiring knowledge and improving biological resource management. As a consequence, wildland biodiversity can be developed as part of the national economy at the same time as its preservation into perpetuity is guaranteed and the bioindustries are encouraged to initiate relationships with partners in biodiversity-rich countries. Following the guidelines of the Biodiversity Convention, such partnerships can facilitate sustainable and non-damaging biological and genetic resource use for research and development, while taking care to share economic and intellectual benefits with the owners of biological resources.

The diversity of nature itself is reflected in the manifold ways it can be made use of, and is therefore valuable to humankind, ranging from intellectual, ecological and spiritual uses to economic uses; from educational tools, watershed protection and aesthetic interests to the discovery of new food sources and medicines. The biological and chemical diversity of nature remains, however, a largely untapped source of information for pharmaceutical and agrochemical companies, fragrance and flavour manufacturers, biotechnology enterprises and crop breeders. In agreement with the Biodiversity Convention, modern biodiversity prospecting (or bioprospecting), involves a new concept where the systematic search for and development of new sources of chemical compounds, genes, micro- and macro-organisms and other economically valuable products, incorporates two fundamental goals:

1. The sustainable use of biological resources and their conservation; and
2. The socio-economic development for biodiversity rich countries.

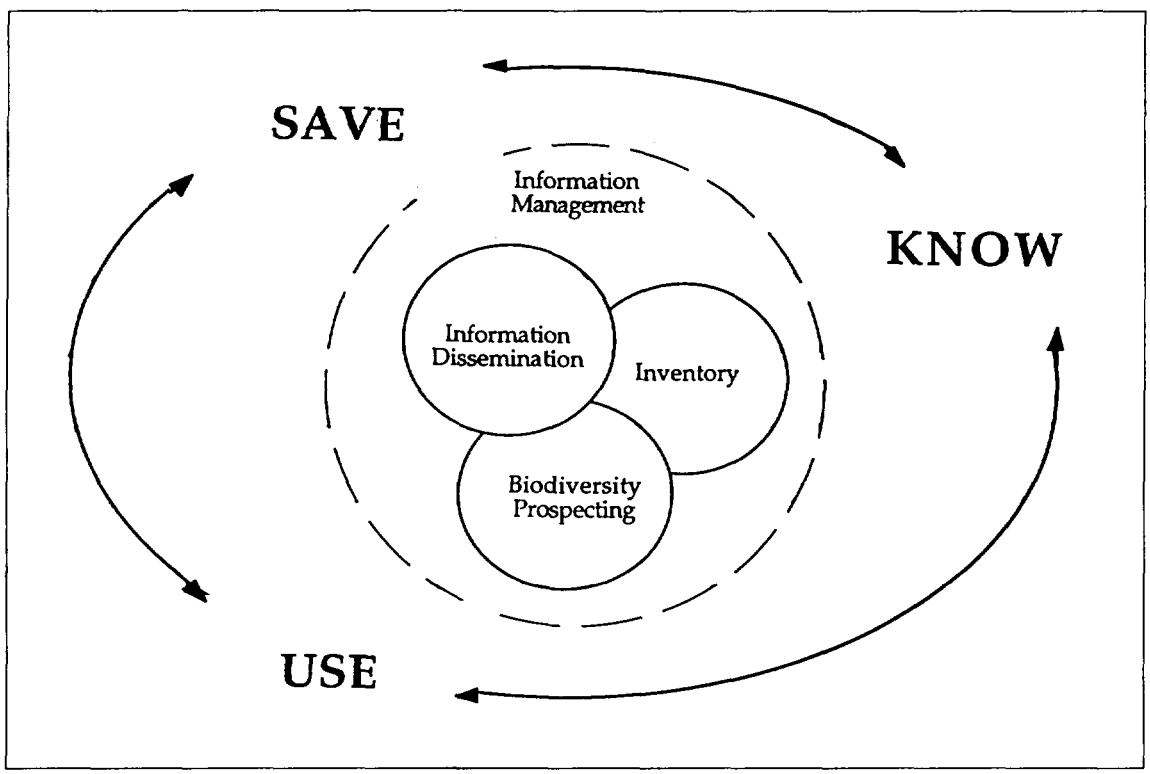
This modern concept of biodiversity prospecting offers developing nations a means to improve national capacities, to add values to natural resources, and to build the skills, infrastructure and technology to develop business activities. Benefits can be shared with industrialized countries to improve the quality of life and contribute towards the development of new products for global markets, while at the same time ensuring that the resource itself is protected and used sustainably. (Eisner, 1989; Joyce, 1991; Sittenfeld and Villers, 1993).

Needs and opportunities

Bioprospecting is notably complex and should incorporate benefits in terms of capacity building and techno-

logy transfer for the country as a whole. It should direct financial benefits for conservation, in addition to potential royalties; it should likewise involve a country's institutions and entities at the local, as well as national levels, creating industrial incentives, and attracting industrial activities in general. Supportive macro-policies, combined with an integrated set of biological research, business development and technology transfer options are needed to create a biodiversity prospecting programme that yields these long-term benefits for conservation and ultimately the developing countries in general. (Sittenfeld and Lovejoy, 1996).

Biodiversity conservation is essential to bioprospecting and, in addition to its application to sustainabililty, is one of the principal goals of bioprospecting. If capacity building and other returns are made to conservation and sustainable development, entire nations will benefit from the opening up of new avenues that increase the value of biodiversity. Presently, a global biodiversity conservation strategy—based on the following three overlapping steps—*saving, knowing* and *using* biodiversity is paving the way towards implementing biodiversity prospecting activities for the benefit of conservation efforts.



Bioprospecting frameworks

It is possible to manage biodiversity to meet conservation objectives while also using products of biodiversity to bring social and economic benefits. However, this can only be achieved if intricate systems, infrastructure and coordination of related activities are implemented. Adequate bioprospecting frameworks must be in place while the relationships between genetic resources, and the following four elements:

(1) Macro-policies;
(2) Biodiversity inventories and information management;
(3) Technology access; and
(4) Business development and strategic planning,

are understood and nurtured.

Macro-policies

The fundamental point of departure for a biodiversity prospecting framework leading to income generation is macro-policies, the set of governmental and international regulations, laws and economic incentives that determine land-usage patterns, access to and control of biological and genetic resources, intellectual property rights, technology promotion, and industrial development. Given a favourable policy environment, the framework should then focus on the following three components required for the rational use of biological resources:

- *Biodiversity inventories* and management of information regarding the taxonomy, distribution and ecology of organisms, as well as the biological interactions among organisms and their systems that adds value to the raw biological resources, including biological inventories and management information systems;
- *Business development*—definition of markets, market needs and major actors; identification of in-country capabilities, needs and institutional goals and strategies; and the formation of collaborative arrangements to achieve institutional and national strategic objectives;
- *Technology access*—access to technology through its development, transfer or other form of acquisition that converts the raw biological materials into higher value added products.

For bioprospecting, inventories and information management, technology access, and business development and strategic planning, biodiversity must be interrelated and interdependent. These elements revolve around biological resources, with biological resource conservation and

economic development being the ultimate aims. They are naturally mediated and controlled by international and national macro-policies, at the same time that these macro-policies regulate use and protection of biological resources. This relationship, which joins biological resources to new sustainable uses and introduces it to new national sectors, is termed a biodiversity prospecting framework.

Logically, the complexity of this framework depends upon, and demands, the cooperation of the international community, Governments, institutions, private enterprise, academia, scientists, lawyers, conservation managers, entrepreneurs and economists from developing and developed countries. These actors, working within the framework, will ensure that biodiversity prospecting meets its projected goals of elevating the value of biological resources, promoting sustainable resource use and improving resource conservation in the context of source country economic, scientific and technological development.

The international context

At the international level, agreements, conventions and other mechanisms establish the relationships and protocols for genetic resource sharing between countries. The more significant international conventions and agreements include the Biodiversity Convention, the General Agreement on Tariffs and Trade (GATT), with special attention to its Trade Related Intellectual Property Rights (TRIP), regional or subregional trade agreements such as the North American Free Trade Agreement (NAFTA), and fundamental agreements and conventions addressing issues of indigenous communities' rights. These mechanisms, in addition to many others, broadly define the international arena regarding resource access. Nevertheless, conventions, agreements and organizations have still left the responsibility of designing adequate legislature and regulations to each individual country, creating instances that are problematic for some and beneficial for others. The lack of laws and precedents to guide national policy makers has led to difficulties, largely because the language employed is often not specific enough to elaborate legislative details if there is no existing foundation upon which to build. At the same time, however, open interpretation has provided broad backing, while simultaneously allowing countries enough room to freely create new laws based on existing experiences.

The national context

At the national level, sovereign Governments determine the macro-policies, which deal with issues such as land and biodiversity ownership, land tenure rights, access to and control of biological resources, biosafety protocols, the creation of protected areas, intellectual property rights, the definition of public-domain resources, and the creation of market incentives or deterrents for undertaking research and industrial activities. Such policies create the national context in which bioprospecting can either develop favourably or be effectively stifled.

Incentives for bioprospecting

1. **Creation of protected areas**
   The creation of a favourable macro-policy environment began with the establishment of clearly defined, private and public protected areas. Knowing that biological resources will be preserved and protected within a given area makes it easier to justify the major investment required to undertake biological inventories, which provide important information on increasing biodiversity's intellectual and economic value. The protected status of conservation areas, coupled with effectively enforced laws that regulate the ownership of, access to, and use of biological resources, substantially reduces the risk for potential industrial partners interested in natural product development.
2. **Clear laws and regulations**
   Where they already exist, clear laws and regulations regarding land ownership and access to resources are conducive to collaborating on research activities.
   Such incentives promote in-country partner stability and manoeuverabililty attractive to private industry and academic and scientific research counterparts, on the one hand, while creating industry incentives by way of governmental mechanisms that advance the important objective of national economic development as a component of bioprospecting activities.
3. **Planning**
   A fundamental consideration in the implementation of macro-policies is planning. Planning will help the State organize and implement its strategy and national policies to determine access to genetic resources, while ensuring benefit-sharing. The need for new legislation and institutions, as well as designated focal points should reflect a consensus for action among the various actors and stockholders: governmental agencies, industry, the scientific community, *ex situ* conservation facilities, indigenous and local communities or their representative organizations and relevant non-governmental organizations, as well as private individuals (Glowka, 1996).
4. **Deterrents**
   National policy vacuums and outdated legislature existing in many countries create disadvantages:
   - Difficulties in elaborating legislature where no precedent exists;
   - Questions on how to enforce new legislature;
   - Obstacles in rewriting existing laws and regulations to accommodate changing global paradigms.

Regulations

Within the national context, regulations must be established in the following areas:

- *Land ownership and land tenure rights:*

Determine who owns the land and in turn, who owns biological resources. It also sets forth limitations to ownership. An instrument for determining property boundaries with a strong legal backing must exist in order to clearly establish ownership.

- *Definition of public domain resources and creation of protected areas:*

Determines which resources are considered to be within the public domain and set aside for protection. These resources, when assigned protected status or considered to be "public domain", will have their use limited by such definition. A particular concern will be defining the term "wildlife", and applying this term to the new law. The terms and application must be very clear.

- *Resource use:*

Access to resources, and the criteria on which access is based is not necessarily set forth through land ownership regulations, but governed by the two regulations above. Resource use is guided and controlled through permits, among other mechanisms.

- *Intellectual property rights:*

Establish what is defined as intellectual property, affecting when and how public and private domain resources may be

used, who will benefit from applied use, and who is the owner of innovations and their applied use. Promotion of the use of Certificates of Origin for Patent Applications, should improve the implementation of benefit sharing mechanisms for countries providing genetic resources.

- *Industrial capabilities:*

Industrial capabilities will affect the ability of countries to link natural resource use and conservation directly to socio-economic development. Numerous regulations control and regulate industrial development according to a nation's economic agenda. Advancing national economic development is a fundamental precept for biodiversity prospecting activities and their success is measured through national economic and governmental friendliness to these activities. Tax exemption, soft loans for biodiversity based industries, support for research, focus on biotechnology, import and export barriers, expanding or contracting intellectual property rights protection, and other measures arranged by Governments can create an environment that nurtures local industrial development.

Options for national politics and legislation to access genetic[1] resources

The Biodiversity Convention's provisions on access to genetic resources pave the way for national legislation governing access to resources. While every country is different, future legislation on access to genetic resources should consider the introduction of new legislation and policies clarifying which institutions in the country have the authority and responsibility to grant access to the nation's genetic resources and on what terms, thus setting the conditions for bioprospecting activities and the ability to monitor them (Glowka, 1996). An estimation of the volume of future request for access, past experience as a source of genetic resources, perceived value of the resources, land tenure and ownership, regulatory agencies, separation of land for conservation, capacity to add value to genetic resources and technical, administrative and financial capacity to create and oversee a regulatory programme (Glowka, 1996). The potential role of a national focal point is discussed below.

Practical considerations in the preparation of national access legislation and policies may include (Glowka, 1996):

- Sections on principles, objectives and definitions;
- The scope of application with reference to definitions on which genetic resources are covered (plants, animals or microbial, wild or domesticated life-forms);
- Considerations to organisms, either in whole or in part;
- Regulations for derivatives prepared from biological organisms (not modified or modified chemical compounds, associated materials, services derived, models, chromatographic traces, etc.);
- Considerations to the sources of genetic resources: *in situ* and *ex situ* sources, land ownership: public, privately or communally owned protected or unprotected areas;
- Considerations to the use and free exchange of genetic resources for the economic, religious and cultural well-being of indigenous and local communities;
- Designation of institutions to oversee access to resources;
- Export restrictions, sanctions and penalties;
- Consideration to the establishment of the necessary financial support to ensure and enforce the regulatory scheme, as well as the management of financial benefits from bioprospecting.

Designating a focal point

In designating institutions to process applications for access to biological genetic resources, considerations on the governmental level are important, especially in federated States and autonomous entities. Probably the simplest approach would be to create a centralized inter-ministerial or inter-agency governmental entity, with representatives of different sectoral ministries and institutions in areas related to biodiversity and benefit sharing the responsibilities, with provisions for advisory committees from expert groups and individuals (Glowka, 1996). It is more convenient to not have the same agency giving permits and performing bioprospecting activities.

The access determination process through collection permits, obliges the potential user to obtain the informed consent prior to access, and is the manifestation of the State's sovereign rights over genetic resources within the jurisdiction of the State. The permit could contain conditions of access, in particular conservation and sustainable use, and a material transfer agreement (MTA), with indications on rights and obligations of all parties and benefit sharing clauses on mutually agreed terms. Variations on the basic procedures and administrative appeals process could be included, as well as expedited procedures and special considerations for indigenous and local communities.

Material transfer agreements

A material transfer agreement can be used for any material or intellectual property that is only truly useful when there is physical possession of the material (Gollin, 1994 and 1995; Putterman, 1996). For example, this can include not only biological material, but information on sources for bio-active molecules or genes. The key elements of a material transfer agreement are as follows:

- A definition of the material being transferred and covered by the agreement. It may or may not include derivatives made by the receiving party which incorporate material provided by the donor.
- A statement that the material belongs to the donor (and that the material does not pass through the act of giving the receiver physical possession).
- A statement that the receiver can use the material for research purposes only.
- A statement that the receiver cannot give the material to anyone else.
- A statement that the receiver will not commercialize anything based upon the material received, without the permission of the donor.
- A statement that the receiver obtains no licence expressed or implied by the agreement.

The agreement could be a simple one-page document or may run to many pages with a number of ancillary contract requirements, but the above are the key elements that must always be present. Another legal tool frequently used for more specific indications is the collaborative bioprospective agreements or contracts.

Authorized access permit system

Many developing countries are presently facing troublesome issues, such as who is really behind a research project, is the collector or observer going to use discoveries for commercial purposes, and if resupply is warranted, how can quantities be controlled to avoid damaging the ecosystem? Permits authorizing access can address the parti-

cular type of research being carried out (i.e., commercial, scientific and other), and the quantities for initial collections and resupplies. It falls to each sovereign Government to make the ultimate decisions regarding what kind of research is allowed and how it will be carried out, but resource owners must be the decision makers, and being the stockholders, must demand compensation.

Criteria to be addressed in permits for access include (Ten Kate, 1995):

- Strategic importance of the resource for national programmes;
- Collection and export restrictions, especially those related to conservation status or endangered species;
- Research participation and publication;
- Duplicates of samples deposited at national museums and herbariums;
- Technology transfer and adding value within the country;
- Royalties and or access fees, ownership of samples and derivatives, and intellectual property rights;
- Limits on third party transfer, reporting and tracking requirements, and terms of the agreement.

Are the regulations and tools of modern bioprospecting, as described above sufficient to face the challenge?

In a number of cases it is still nearly impossible to control the illegal transfer of genetic material. Microorganisms can be cultivated from much less than a handful of soil and genes can be cloned from minute amounts of DNA or RNA, and be isolated from biological material, easily fitting into an airmail envelope. Genes do not have tags designating their country of origin, and once they are cloned, they are no longer controlled by their source country. Authorized access permits and mechanisms to create and oversee a regulatory regimen are important tools, but not enough to warranty good bioprospecting practices. Promoting the use of Certificates of Origin from source countries as a requirement for patent applications, may contribute to tracking down sources of biological and genetic material. However, the real challenge for bioprospecting activities is to find ways to capture part of the financial revenues for the source country. Modern bioprospecting requires:

- That the source country create an infrastructure guaranteeing a supply of reliable natural products (including correct taxonomic identification, quality control, full support from Government and adherence to national or local regulations on access to resources);
- That a technology is acquired that adds value to natural products wherever possible (from extracts to partially purified or pure compounds or gene sequences);
- That advantage be taken of local capabilities, using all types of organisms as biological resources attractive to industry (from plants and microbial resources to marine or aquatic life forms, to arthropods);
- That a reputation be developed as a reliable business partner;
- That part of the revenues be reinvested in improving biodiversity management and conservation.

In exchange for access to biological resources, the industrial partner must agree to the fair and equitable sharing of benefits, both in intellectual and monetary terms; implementation of collection and production methods with minimum efforts on biodiversity; and the use of equitable bioprospecting practices for further research on tropical diseases and problems specifically associated with developing countries.

Supportive macropolicies in the social sector

At the social level, finally, investment in education and other social services creates a scientific environment of qualified institutions, researchers and educated personnel, which is a prerequisiste for research collaborations with private enterprise and essential for integrating biodiversity into economic development (Sittenfeld and Gámez, 1993).

Building on to macro-policies: biodiversity inventories, business development and technology access

Supported by a favourable international and national macropolicy, three basic elements guide the rational use of genetic resources in bioprospecting: biodiversity inventories and information management, business development and technology access. These elements also contribute to creating more attractive business partners and increasing bargaining leverage.

Biodiversity inventories and information management

Biodiversity inventories and information management become a crucial step in creating a biodiversity prospecting framework, creating a base of knowledge fundamental to prospecting activities. Biodiversity inventories, through the development and management of biological, ecological, taxonomic and related systematic information on living species and systems, increase the value and promote the sustainable use of raw biological resources (Raven and Wilson, 1992). The information-based system underlying a biodiversity prospecting programme is considered an asset by research collaborators because it:

- Creates catalogues of available resources and their location;
- Prevents damage to ecosystems, areas, species or populations by indicating what resources are available, and where they can be collected without damaging the ecosystems;
- Helps the in-country collaborator become a more attractive, knowledgable and reliable business partner;
- Reduces the risk of the researcher collecting more material than necessary.

Information shared between inventory and prospecting programmes results in an "information service" that increases the in-country collaborator's overall bargaining leverage by decreasing private, academic or scientific research investment risk and adding value to raw material. This information service can take care of many forms ranging from taxonomic data and research findings to traditional knowledge. Additionally, inventory activities can either be directly associated with prospecting programmes or operate as a separate activity whose information supports the prospecting programme activities.

Business development

Building an inventory-based knowledge of what natural resources are available and where, business development covers the entire process from identifying markets through strategic planning to negotiating collaborations and contractual agreements. Nevertheless, business development is essential to creating successful bioprospecting endeavours because it combines information obtained from biological inventories with an understanding of market opportunities, national scientific and technological capacities and institutional strategies and goals.

1. **Knowledge of one's assets and debilities,** and properly marketing them, is vital to negotiations. Logically, knowing what in-country skills and capacities are available is helpful when establishing institutional and national goals that include the acquisition or development of information, technology and products that increase the value of samples, augment existing capabilities, and advance national development (including economic development).
2. **Using market surveys** to identify potential economic users and elaborate research collaborations, complements in-country evaluations by pinpointing prospective collaborators capable of fulfilling predetermined institutional requirements. At the same time it increases the in-country partner's awareness of private enterprise, academic and scientific research collaborator needs and characteristics.
3. **Evaluating conservation requirements**: varying objectives may require research in many different areas. Principle goals now include the development of conservation efforts and initiatives, so researching in-country capabilities should also cover ways of increasing the value of natural resources and facilitate their conservation and sustainable utilization.

Some of the strategies for marketing value added materials or services are:

(a) To offer reliable natural products supply and add value to natural products wherever possible. Reliability includes correct taxonomic identification of samples and good quality control over research products. Reliability also takes the form of working with the full support of the Government, and adhering to national and local regulations on access to resources. When community land is involved, prior informed consent and the assurance of equity in benefit sharing is required.

(b) To develop a reputation over time as a reliable business partner and use equitable bioprospecting as a mechanism to further research in tropical diseases.

Technology access

Among the major components of successful biodiversity prospecting efforts, access to appropriate technologies, as emphasized by the Biodiversity Convention, deserves significant attention. The acquisition or development of technology and its transfer to industry provides developing countries with the means to convert the raw materials of biological diversity into products of greater value. Before negotiating technology transfer, technical assistance or training programmes that are to be included in a biodiversity prospecting research collaboration, those institutions representing the source country should develop a strategic plan for technology development and capacity building, tailored to the country's needs and capabilities and responsive to market opportunities.

Successful negotiation depends on complex factors, beginning with a solid foundation of knowledge and scientific expertise.

- *Strong scientific foundation of knowledge*: A pre-existing base of taxonomic and scientific expertise (such as a biodiversity inventory programme) together with traditional knowledge (when appropriate), creates the initial base for attracting research collaborators and is the point of departure for increasing in-country knowledge and technologies. Building up scientific expertise in the field of conservation management, is also expected to open avenues to increasing the value of biodiversity and providing incentives for biodiversity conservation.
- *Value-added*: Carrying out some level of in-country processing increases the value of simple raw materials by eliminating some steps of research counterpart processing. Traditional knowledge and preliminary screening also increase value, and have been argued to increase the ratio of "hits" per sample group, although debate on this is still going on.
- *Capacity building*: Some level of processing is highly desirable to the in-country partner and is fundamental to linking research to national and economic development. In-country processing improves national capabilities, creating a cycle in which continually advancing technological and scientific capacities attract more business partners and funding to be reinvested in building those capacities further, which in the source country can effectively foster incentives and reduce risks to prospecting efforts in the eyes of private enterprise. Once research collaborations have been formed, funding, equipment transfer and technical training provided by the industrial partner can be re-invested in building source country academic and industrial capacities to encourage innovative product development and strengthen the developing country economy.
- *Cost reduction*: Processing samples in the source country can be a cost effective advantage for private industry if in-country processing is less expensive than the research partner's processing cost.

Final touches for the framework: multi-sectoral collaborations and contract negotiations

Multi-sectoral collaborations

Beyond these elements of a biodiversity prospecting framework, bioprospecting activities must also seek to involve national and international entities. National collaborations will ensure that equitable returns make their way to support conservation efforts, academic, scientific and industrial development, and institutional objectives. International collaborations provide the needed scientific and technological expertise, as well as financial backing.

Principal actors include:

- The developing country Government, who acts as a gatekeeper, regulating access to biological and genetic resources and managing protected areas;
- The research collaborators (in academia or industry), who have the economic resources needed to finance the endeavour; and
- National and international academic and scientific communities whose expertise can contribute to increasing the relatively low market value of raw materials within the country.

Contract negotiation and legal issues

Contractual agreements should concentrate on promoting biodiversity conservation and increasing the value of biological materials by fostering knowledge of their ecology and taxonomy, and conducting some sample processing and research inside the country source. Agreements typically include a research budget covering costs for sample collection, and identification, processing and laboratory research, with a percentage of direct contribution to the maintenance of national parks and other protected areas. Royalty payments should support conservation efforts

and industry development if commercialization is successful. Payments shared between research institutions, shareholders and conservation areas promote better biodiversity management, while at the same time supporting the protected areas from where the materials were first obtained. Where research and processing are involved, collaborations frequently seek to incorporate academia and national and international university laboratories to assist in the research and development of technologies and new products derived from biodiversity.

Contract negotiation, an essential aspect of biodiversity prospecting frameworks, can be divided into three basic sets of issues:

(1) Scientific issues;
(2) Business issues;
(3) Legal issues and frameworks.

While the second and third are related, it is often helpful to outline scientific workplans carefully first, and then broadly define the business issues and later work at placing them in a legal framework. To negotiate business issues, an organization needs to have a good sense of its own fundamental needs and those of its potential collaborator. Some of the typical institutional needs that a developing country focuses on in research negotiations are:

- Generating income to support the conservation areas and conservation management activities;
- Limited sample supply, to ensure that ecosystems and species populations remain unaffected and undamaged;
- The transfer of biodiversity processing technologies (equipment and know-how);
- Creating opportunities for training local scientists;
- Limited sample exclusivity, to allow for broad sample-screening exposure;
- Guarantee of future potential, profit-sharing (typically through royalties and research fees) if commercial products are forthcoming.

The private-enterprise, academic and scientific research partner or collaborator needs and expectations include:

- Access to new and diverse sources of biological resources and related materials;
- A high level of assurance that interesting materials can be recollected;
- Limited resource exclusivity; limited sharing of intellectual property rights;
- Payment for resources commensurate with the estimated/perceived market prices; and assurance of legal, in-country practices for resource procurement, among others.

The deliberation of appropriate royalty rates and intellectual property rights for biological materials is one of the major business issues discussed during biodiversity prospecting contract negotiation. In practice, settlement generally comes down to arguing for the application of other industry precedents to the new situation of biodiversity prospecting (e.g. precedents from the biotechnology industry and market perception regarding resource supply and demand). Bargaining power in these negotiations is considerably enhanced by a firm knowledge of the user's industry (e.g. the pharmaceutical industry), the resource market (e.g. biological resources), knowledge of legal precedents in pharmaceutical and other industries, as well as understanding the needs of conservation activities.

The integrated strategy in action: Costa Rica's INBio

Established in 1989, Costa Rica's National Biodiversity Institute, INBio, represents a pilot project which has successfully integrated the strategy described above in its attempts to achieve modern bioprospecting's multiple goals. INBio, however, was not founded to specifically carry out biodiversity prospecting activities. Rather, INBio developed four divisions based on the institutional philosophy, which advocates adding economic and intellectual value to protected wildlands in order to encourage society's continued support for conservation.

INBio's four divisions: the National Biodiversity Inventory, the Biodiversity Prospecting, the Information Management and Information Dissemination Divisions, are discovering what biodiversity exists in Costa Rica, where it can be found, and how Costa Rica can find sustainable, non-damaging ways to use biodiversity (primarily using information extraction services) to help conserve it.

These divisions are interrelated and interdependent. However, activities remain separated from each other, with the flow of information loosely meshing the Inventory, Prospecting and Dissemination Division ideologies and activities together. For example, inventory specimens are not used for sample extraction, nor vice versa, although taxonomic information flows openly between the two divisions. In this way the specific goals of each division remain intact, while supporting the larger overreaching goal of biodiversity conservation.

While INBio was not created to be a bioprospecting mediating organization *per se*, its components have lent themselves to becoming such a facilitator. INBio's Inventory and Information Management Divisions described above, indicate how the institute was able to mould itself into an entity able to coordinate this new breed of bioprospecting as one part of its overall activities. Not only were a great part of the basic system requirements in place (i.e., favourable macropolicies, inventories and information management), but the organization's founding purpose and a philosophy, that of biodiversity conservation through distributing its benefits to society, coincided precisely with modern bioprospecting goals.

Additionally, a specific mechanism: the collaborative agreement established between INBio and the Ministry of Natural Resources, Energy and Mines, provided the groundwork upon which INBio carries out all its activities and was thus able to arrange, negotiate and succeed in its first bioprospecting agreement. This mechanism is also a principal tool for returning benefits to the Government, and specifically to the country's conservation activities.

Under the agreement INBio is permitted to collect samples for its Inventory and Biodiversity Prospecting Division. Access to biological resources is both clearly established and regulated, while returns to preserve these resources has been established through the return of 10 per cent of each bioprospecting research budget, and 50 per cent of potential royalties from each bioprospecting programme, to Costa Rica's conservation areas.

Further details regarding mechanisms for returning benefits to different sectors of Costa Rica are elaborated below and represent INBio's implementation of the integrated bioprospecting strategy.

Identifying, including and distributing benefits to different affected groups

In implementing the integrated strategy, INBio has targeted the following areas as recipients of benefits and returns, according to its institutional goals and the specific criteria of bioprospecting collaborations: conservation, science, industry, local communities and the Government.

Conservation

INBio provides important returns to conservation, channelling them through the INBio-MIRENEM agreement. This agreement permits INBio to access resources in order to add value to them and protect them indirectly, while direct benefits are returned in the form of upfront and royalty payments. INBio's other divisions also provide a multitude of benefits to conservation ranging from scientific publications, taxonomic and other scientific information distributed to the conservation areas, training courses and seminars in conservation management and educational services.

Science

The scientific community stands as the second largest benefactor of bioprospecting agreements. It is this community that provides the needed scientific support to bioprospecting activities without which bioprospecting could not succeed. This sector will receive training, equipment and know-how in exchange for their expertise.

Within the scope of INBio's bioprospecting activities, the MacArthur Foundation initiated a collaborative programme with Costa Rican universities and INBio to screen biological resources for their potential use in medicines and agriculture. Subsequently, INBio included the University of Costa Rica as the recipient of an extraction laboratory for the chemistry faculty and training opportunities under the INBio-Merck agreement. Other universities and research centres are providing valuable processing to INBio samples, for which they are also recipients of training and equipment, where possible.

As in all sectors, INBio distributes additional benefits to these sectors via other divisional activities. For example, science benefits tremendously from the wealth of information and knowledge generated by the National Inventory, in addition to access and participation in the inventory process. However the contribution that the scientific sector makes to INBio and *all* of the Institute's programmes should not be underestimated, for INBio would never succeed without this sector's continued support.

Industry

Targeting in-country industry is essential to contributing to the country's overall socio-economic development and has more recently become a focal point for INBio now that it has been able to negotiate collaborations to include industrial development. Under the INBio-British Technology Group (BTG), INBio Hacienda La Pacífica agreements, INBio is playing an instrumental role in opening up a new industry for Costa Rica to develop a non-toxic, biodegradable pesticide isolated from a tree native to the Guanacaste Province in the North Western area of Costa Rica. INBio has negotiated exclusive product development for the country.

Additionally, this pesticide has direct application in Costa Rica to its banana crop, one of the country's two largest export crops, and is therefore a doubly valuable private enterprise development.

Local communities

Analysing how local communities can be directly involved in bioprospecting activities fulfils the clauses of the Biodiversity Convention, demonstrating that biodiversity provides different kinds of benefits for society, and that special attention must be paid to those who live closest to natural resources and are the most influential custodians of those resources (Iwu, 1995). Community involvement in sustainable resource use and management will increase conservation awareness as well as the overall value of biodiversity.

INBio has concentrated on involving local communities both directly and indirectly. On the one hand, local communities directly participate in the inventory process, given that individuals from the areas surrounding protected wildlands are hired by INBio as parataxonomists to collect specimens for the National Biodiversity Inventory. On the other hand, bioprospecting agreements, such as the INBio-BTG, INBio-Hacienda La Pacífica agreements, are opening up new employment and development opportunities to provinces and their resident communities. In these agreements, the Guanacaste Province, and its communities will stand to benefit greatly from domesticating a tree from the Guanacaste Conservation Area being used to develop an important pesticide.

It should be noted here that the question of compensating indigenous knowledge is a complicated and important issue, but one in which INBio is not presently involved. INBio's biodiversity prospecting programmes focus on using taxonomic and ecological information for large-scale pharmaceutical research and development rather than indigenous knowledge for specialized markets.

Governments

Benefits returned to the developing country Government are actually quite general in scope and can be broadly considered the combination of all benefits provided to different sectors of society, as well as specific benefits to different governmental sectors. INBio has seen to it that these benefits be returned to Costa Rica under the INBio-MIRENEM collaborative agreement (and most specifically to the conservation sector), but that they also include indirect contributions to increasing the Costa Rican standard of living, and the on-going existence of biological resources.

Distributing benefits and contract negotiation

Recent experience in three biodiversity prospecting negotiations between INBio and Merck & Co. Inc., INBio and the British Technology Group/INBio and Hacienda La Pacífica, and INbio and the Bristol Myers Squibb Corporation, have succeeded in establishing favourable terms for technology-transfer, royalties, and direct payments, among others, for INBio and Costa Rica's Conservation Areas. These agreements provide living examples of different biodiversity prospecting frameworks.

The INBio-Merck agreement

In 1991, INBio signed its first biodiversity prospecting agreement with the pharmaceutical company Merck & Co. According to the terms of the two-year agreement, Merck compensated INBio US$ 1 million for a small, limited number of well-identified and documented biological environmental samples for micro-organism isolation and plant and insect extracts and fractions for use in its drug-discovery process. INBio has agreed not to provide these samples to any other organization for use in health or agricultural screening during this two-year period of initial evaluation in order to give Merck an opportunity to study them. All samples come from national parks or other kinds of conservation areas, in accordance with the INBio-MIRENEM partnership established in 1989.

The funds Merck has, and continues to provide to INBio, have been put towards research and certain start-up costs. Merck donated an additional US$ 180,000 in labora-

tory equipment and supplies and installed a "state-of-the-art" extraction laboratory, which was donated to the University of Costa Rica (Sittenfeld and Villers, 1993). The project also included the training of four Costa Rican chemists at Merck or other prestigious international research centres. In addition, the collaboration supported scientific exchange for INBio's curators and taxonomists (Sittenfeld and Villers, 1993). The conservation areas and the Ministry of Natural Resources received 10 per cent of the US$ 1 million supplied by Merck, which was invested in the Cocos Island National Park off the Pacific coast of Costa Rica. The funds went towards augmenting the Park's infrastructure and financing park rangers to establish ecotourism guidelines and enforce fishing regulations. Any royalties from products derived from the collaboration will be shared on a 50/50 basis between INBio and MIRENEM (Sittenfeld and Gámez, 1992).

The project's biodiversity prospecting framework was clearly understood by both parties, the end result of which demonstrates that companies can return part of the benefits of pharmaceutical development to the biodiversity-rich country where the chemical compounds originated. Both parties were conscious of the mechanisms needed to ensure that some of these benefits (i.e. part of the initial funding) would directly finance conservation, while the remainder would indirectly finance conservation through investment in biodiversity inventories, biodiversity information systems and biodiversity prospecting in association with the conservation areas and national parks.

The negotiation process centred on the complementary nature of the activities that INBio and Merck carry out, which once joined, would result in mutual benefits that could not arise solely from individual institutional efforts. INBio's experience and capability in biodiversity conservation and management, which rely heavily on the National Biodiversity Inventory, could only enhance Merck's drug discovery and development process, while Merck could support INBio's institutional mission and Costa Rica's conservation efforts. The collaboration even resulted in the additional benefits of scientific publications, which will be highly valuable not only for scientists, but also those interested in the advances of biochemical prospecting activities.[2]

In July 1994, INBio and Merck renewed the research project for another two years, maintaining almost precisely the same provisions as the first collaboration in terms of research budget, equipment and supplies, scientific training and donations to the conservation areas.

The INBio-British Technology Group, INBio-Hacienda La Pacífica agreements

In what could possibly result in the first commercial product from a Costa Rican conservation area since INBio's formation, INBio is collaborating with the British Technology Group (BTG, a major technology licensing company of the United Kingdom) and the Royal Botanical Gardens at Kew in the UK, to isolate and test a plant compound for non-toxic, nematocide properties. Following the lead of a ten-year ecological observation indicating that field mice would starve to death before eating the seed of a certain Costa Rican plant (Janzen et al. 1990), biochemical research on the seed financed by BTG was initiated. Research revealed that a naturally occurring sugar analogue demonstrated a range of activities against several plant-parasitic nematode species (Birch et al. 1993). This resulted in the filing of a patent (Patent No. GB 2 250 439 A in Great Britain) for the compound's use as a biodegradable, phloem mobile, non-toxic nematocide, that controls the growth of root nematodes through foliar, seed and soil application.

Once the patent was filed, BTG contacted INBio for assistance in obtaining the plant samples required for field testing, with the understanding that successful results would lead to large-scale plant domestication and production to promote sustainable resource use. Both INBio and BTG believe the product has major potential in eliminating the nematodes which plague banana and other crops. And as the world's second largest producer, Costa Rica could only stand to benefit from INBio's partnership with BTG.

In agreeing to provide BTG with the desired quantity of the isolated compound, INBio, upon the advice of Kew Gardens, first had to develop an effective protocol for isolating the compound from leaves (rather than seeds), which provide a more abundant and non-damaging sustainable supply source. In return, the BTG is funding INBio's initial research with 30 per cent of the budget proceeding to the Costa Rican National Park Fund. As part of the collaborative research agreement reached between INBio and BTG, INBio receives rights to the product's exclusive research and commercial development in Costa Rica—an activity that INBio is carrying out in partnership with local industry.

Support for field trials and other field research will come from the Costa Rican Association of Banana Growers (CORBANA), which has demonstrated a keen interest in the project. In addition, a major Costa Rican nematocide manufacturer has examined the feasibility of production at the industrial level. Further assistance comes from one of the country's better administered conservation areas, which is donating space in its experimental forestry station for research in plant domestication. Presently, in collaboration with Hacienda la Pacífica (Costa Rica) and Ecos Holding (Switzerland) studies are being carried out to determine the optimal conditions for creating large-scale plantation production of the tree within the country. Based on positive results, the nematocide, to be produced in Costa Rica, will be available on the market within three years with royalties awarded to the national parks and INBio. If all goes well, INBio, alongside national scientists and industry, will play a pivotal role in the development of the first environmentally friendly agro-chemical with the distinction of coming from a Costa Rican conservation area, and provides tangible benefits (jobs and improved exports, and direct financial returns from product development) for the country of origin.

INBio/Cornell/Bristol Myers Squibb

A partnership composed of INBio, Cornell University, the Guanacaste Conservation Area, the University of Costa Rica and the Bristol Myers Squibb Company, representing one of the five International Cooperative Biodiversity Groups (ICBG), is seeking to discover new chemicals from arthropods for drug development in an attempt to introduce insects and arthropods into the market-place as a new, potentially valuable source of pharmaceutical compounds. This five-year programme involves the extensive biochemical and ecological training of field experts, termed "biodiversity ecologists" who, in addition to their regular collection activities, are also trained to look for and record ecological indications of potentially powerful chemical compounds. An important component of the research effort focuses on developing expertise in chemical ecology, so that Costa Rican researchers will be better equipped to select, collect, extract, identify and characterize promising

chemical compounds proceeding from insects. INBio and Cornell expect that this consortium effort, and the knowledge resulting from it, will provide the impetus to formally introduce arthropods into the pharmaceutical market while generating valuable new ecological information that could increase the efficiency of drug screening in the long-run.

The grant also supports an INBio/University of Costa Rica tropical drug discovery effort to test and identify chemical compounds developed from insect extracts for treating malaria. As part of the overall consortium agreement, Bristol Myers Squibb directly contributes 10 per cent of the research budget to the conservation areas to support biodiversity conservation efforts and provides limited research funding to INBio, in addition to laboratory equipment and training for two Costa Rican scientists at its laboratories. If valuable drug compounds are identified and developed by Bristol Myers Squibb as a result of this collaboration, an intellectual-property-rights agreement signed among the consortium members guarantees INBio, Cornell and the University of Costa Rica a share of potential future profits. Half of INBio's share of potential future royalties will be directly awarded to Costa Rica's National Park Fund through the parallel bilateral agreement signed between INBio and the Government of Costa Rica through MIRENEM.

From theory to practice: pilot prospecting development projects involving collaborative research efforts within the hemisphere

Based on the integrated strategy and living examples, developing countries must take an important step and initiate biodiversity prospecting pilot projects following guidelines, where available. Such projects will test the feasibility and capability of biodiversity prospecting ventures, and will provide the opportunity for "learning by doing". This process is intended to facilitate larger initiatives and will depend first and foremost on inventory generated information (development and management of biological, ecological, taxonomic and related systematic information on living species and systems). Information derived from reviewing in-country capacities and technological capabilities, in addition to market needs and realities, will form the criteria for developing the pilot projects. Ultimately selecting and designing them will need to consider current national and international macropolicies regarding biological resource access and utilization.

Designing and implementing a pilot project will allow developing countries to compare alternative scenarios and approaches to bioprospecting according to national realities. This will help establish effective long-term management policies and practices for all sectors involved in the bioprospecting process. Pilot projects should carefully consider the three general areas following, including each alternative presented, in order to design a project suiting the needs of a particular country.

Access to biological resources

- Access to resources in private lands *vs.* access to resources in public lands.
- Distant and inhospitable access *vs.* close easy and well-defined access.
- Access to resources in protected areas with management plans, strong administration and good facilities *vs.* access to areas with non-existent or rudimentary management.
- Access to resources close or related to indigenous communities *vs.* access in lands with no links to existing communities.
- Access to resources in areas under local or State management.

Management issues

- Areas of activity and types of products. For example, food and drink additives, cosmetics, medicinals, pesticides, enzymes for chemical transformation industry, fuel alternatives and new materials.
- Definition of institutions and individuals and their roles and commitments in terms of responsibility, contractual agreements and intellectual property rights.
- Multidisciplinary and multisectoral participation.
- Diverse market approaches with multiple products and different levels of value-added processing.
- Financial requirements and sustainability.
- Mechanisms for returning benefits (economic or intellectual) to conservation and local communities by sharing at different stages of research and product development and commercialization.

Experimental considerations

- Market driven inventory by taxa selection *vs.* all taxa inventory.
- Science and technology intensive efforts *vs.* less intensive efforts that provide more rapid access to market and short-term benefits to local communities.
- Projects based on existing information or research near to final product development *vs.* newly generated information.
- Industrial relationships established very early in the process *vs.* providing products to industry in the late phases of research.
- Products for the local market *vs.* products for national and international markets.

Pilot projects for the hemisphere

Eventual hemispheric collaborations will be an important addition to pilot bioprospecting projects. Although each nation is different, overlapping scientific, industrial and biological resources, governmental and environmental agendas and paradigms lend themselves to regional cooperation and assistance. These similarities and mutual understandings can be the key to building up the regional as a whole, interdependent unit. Such partnerships could involve a consortium of four or five countries, each of which would carry out a different step of the bioprospecting process. For example, one nation might collect samples, one or two others carry out the different stages of processing, another take responsibility for product development. This will require a high level of trust and intricate coordination.

Such elements, including the South-South technology transfer involved, are not likely to be possible at present.[3] Currently, technologies are owned and controlled by the North and technology transfers are largely North-North and North-South (Lesser and Krattinger, 1993). Therefore, gaining experience in this field through launching pilot bioprospecting projects which involve access or acquiring technologies will lay an important foundation for future hemispheric collaborations. At the same time, developing countries can use these projects to familiarize themselves with all stages of the process. Well-informed and experi-

enced partners will enable future hemispheric collaborations to succeed for all parties.

Conclusion

Research collaboration in bioprospecting is notably complex and should incorporate benefits in terms of capacity building and technology transfer for the country as a whole, direct financial benefits for conservation in addition to potential royalties, the involvement of a country's institutions and entities, on the local as well as the national level, the creation of industrial incentives, and the attraction of industrial activities in general. Supportive macropolicies, combined with an integrated set of biological research, business development and technology transfer options are needed to create a biodiversity prospecting programme that yields these long-term benefits for conservation and for developing countries as a whole.

In general, biodiversity prospecting programmes that aspire to succeed in future, face the challenge of expanding into different markets and developing macropolicies that attract industrial investments beyond the prospecting activities themselves, thus guaranteeing a solid industrial base for national economic development. In the meantime, by continuing to integrate human and material resources in colaboration with highly capable industries, new products will hopefully be produced simultaneously with the development of new mechanisms for biodiversity conservation.

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Notes

[1] For practical reasons, in this paper genetic resources include biological resources, although biological resources might not contain units of nucleic acids.

[2] Two examples of publications resulting from the INBio-Merck collaboration are: Bills, Gerald F., Amy Rossman & Jon D. Polishook; 1994. Rediscovery of *Albosynnema elegans and Sleimia costapora. Sydowia*—Band 46(1):1-11, and Bills, Gerald F. and Jon D. Polishook; 1994. Abundance and diversity of microfungi in leaf litter of a lowland rain forest in Costa Rica. *Mycologia* (by the New York Botanical Garden) 86(2):187-198.

[3] Currently, South-South technology exists on the level of sharing experiences and mechanisms employed in developing countries for biodiversity prospecting and does provide for valuable exchange in as far as those experiences apply to modern bioprospecting.

Viewpoints

Costa Rica's INBio: A special case and a word of caution

In spite of the high visibility of INBio as a biodiversity prospecting institution, caution is also urged before trying to replicate it. Firstly, it should be understood that INBio is not primarily a biodiversity prospecting institution, but rather an institution dedicated to the inventory, conservation and sustainable use of biodiversity. Biodiversity prospecting is a means of financing inventory, conservation and sustainable use of Costa Rican biodiversity. Pharmaceutical companies do not need a complete and accurate inventory to do "high throughput" screening, but they do need accurate identification of samples and the assurance of being able to get more of the same sample should the need arise. An inventory such as INBio's may be useful, but it is not the only means of guaranteeing this. Therefore, it is strongly recommended that cost-benefit analyses be undertaken before embarking on an inventory. Secondly, although some published information exists, INBio's total capital costs, past and current operating costs, and total revenue flows are not available. Much of these costs have been covered by foreign capital in the form of non-repayable grants by Governments, foundations, aid agencies, non-governmental organizations, and pro-bono services of foreign professionals in various fields. Such funding is not sustainable for INBio, nor is it likely to be available to other countries and institutions in the same magnitude that INBio received. Non-grant revenues appear to be quite small by comparison, thus a detailed financial analysis of INBio would be most instructive.

Thirdly, INBio developed in the particular and unique cultural environment and historical context of Costa Rica, a country with strong Government support for conservation (and now for sustainable development); existing conservation institutions (including the Organization for Tropical Studies); considerable long-term biological research on local biodiversity; over 20 years of established national parks and conservation areas; scientific capacity in cellular and molecular biology and in chemistry; and significant foreign technical and financial assistance. Moreover, INBio was founded during the period of preparatory commissions preceding the 1992 Earth Summit. All of these factors coalesced to make the moment propitious and funding and assistance more readily available than they might have been at another time or to another country.

(Source: *Diversity*, Vol.12, No.2, 1996)

B. NEWS AND EVENTS

UNIDO news

Within the framework of the **Alliance for Africa's Industrialization**, UNIDO's Studies and Research Branch is organizing informal consultations on agro-related industrial development in Africa with a small group of selected experts from Africa and developed countries. These consultations are undertaken in cooperation with the relevant units within UNIDO, in particular the Agro-based Industries Branch, the Engineering and Metallurgical Industries Branch and the Chemical Industries Branch.

These consultations take place within the context of preliminary research being undertaken by UNIDO on agro-related industrial development in Africa. The issue of agro-related industrial development has assumed increased importance in the light of globalization, and of Africa's potential comparative advantages in these industries, which cover both forward and backward linkages. This was fully recognized at the launching of the **Alliance for Africa's Industrialization**, which encompasses—as one of its main pillars—strengthening of agro-industrial development in line with UNIDO's thematic priority on Africa and the least developed countries, specifically linking industry and agriculture.

UNIDO has an extensive programme of assistance to agro-related industrial development in Africa. There is strong justification for further strengthening and supporting these programmes through additional resources, with a focus on both food security and industrial competitiveness.

Agro-related industries account for over half of Africa's manufacturing value added, manufactured exports and employment. Stimulating their growth can make a key contribution towards poverty alleviation, the achievement and maintenance of food security, enhancement of agricultural productivity and the expansion of foreign resource inflows to Africa.

Agro-related industrial development has stalled during the past decade. Investment has fallen. The privatization programme has failed to take off in several countries, and export and foreign financing opportunities remain limited. UNIDO is concerned to make a contribution towards relieving these constraints on socio-economic development in Africa.

The consultations being undertaken will seek to examine the practicability of ideas presented in the research papers and to identify a viable strategy for accelerating the development of agro-related industries in Africa. It will review the existing evidence on performance and constraints on the development of specific branches, focusing on strategic issues of relevance to their development, with a view to identifying viable approaches for structuring UNIDO's contribution towards the further development of key branches of agro-related industry. UNIDO's programme is concerned with developing the type of strategies that can restructure agro-related industries in such a way that it boosts their contribution towards achieving better food security, poverty alleviation and increased agricultural productivity while at the same time increasing foreign resource inflows to the African continent. UNIDO's programme is also expected to facilitate on-going private, public and multilateral programmes in these areas and serve as a catalyst for their expansion.

Following these consultations, field missions will be undertaken to selected countries to elaborate the approach and scope for assistance, and on the basis of these missions, a major UNIDO-wide initiative covering technical assistance, financing, negotiations, investment and economic research will be developed within the framework of integrated teamwork with all relevant units of the Organization, in view of the overarching nature of agro-industrial development that permeates many of UNIDO's activities—for example, policy issues, small and medium enterprise development, investment and technology, industrial information, the role of women in industrialization and human resource development.

In addition, the Industrial Sectors and Environment Division implements several biotechnology technical cooperation projects in several countries, including the manufacture of pharmaceuticals and vaccines. One activity of particular relevance to the present paper is an international convention on *Food Ingredients: New Technologies, Fruits and Vegetables* that will take place in Cuneo (Italy) from 15-17 September 1997. The event will consist of the presentation of research papers from industry and from public and private R&D centres in developing and industrialized countries selected by a committee composed of representatives from six Italian and foreign universities, and UNIDO. The convention is being organized and co-sponsored with Allione S.p.A. (Italy), a private company which has also agreed to set up small pilot plants to demonstrate the new technologies being proposed. More than 500 participants from all over the world are expected to attend the convention, coming from industry including multinationals, industrial associations and R&D centres, and from the academic community. The areas of cooperation with the Allione group of companies encompass training and study tours for experts; technical visits for representatives of R&D centres from temperate climate countries with a view to eventual transfer of technology and investment projects—for instance in the production of baby-food in Africa and Asia and the production of non-conventional fruits and vegetables from temperate climates, and tropical products for export; projects for the development of new processed products, particularly from tropical areas; and for the utilization of databanks. A compendium of the innovative technologies selected from developing country R&D centres will also be published.

UN and other organizations news

UN biodiversity advisers warned: stick to science

The chairman of a panel of scientific advisers to the United Nations (UN) biodiversity convention, signed at the Earth Summit in Rio de Janeiro in 1992 to provide a framework for protecting global biodiversity, has urged its members to restrict their advice to scientific issues, amid signs that some are using the body as a political forum.

Peter Schei, chairman of the convention's Subsidiary Body on Scientific, Technical and Technological Advice (SBSTTA), repeatedly urged members during a meeting in Montreal, Canada, in September, to avoid digressing into discussions on the politics of biodiversity.

Among other topics, the meeting considered the monitoring and assessment of biodiversity, practical

approaches to taxonomy, and the economic valuation of biodiversity. But sharp disagreement emerged during discussions on agricultural biodiversity, involving the need to balance the preservation of forests and other natural ecosystems against pressures to clear the land for farming. There was also disagreement on the issue of indigenous knowledge and biodiversity conservation.

The biodiversity convention came into force in December 1993 and now counts more than 150 countries as "parties"—those that have signed the convention and ratified it in their national parliaments. A spokesman for the International Institute for Sustainable Development, an environmentalist group based in Canada that closely follows all UN environmental agreements, said that SBSTTA has an additional handicap: the fact that some of its members are not scientists at all, which is putting the body's scientific authority under strain.

According to some participants, delegates often arrive with national priorities in mind and are the same people who attend the annual meeting of countries that have signed the biodiversity convention, known as the Conference of the Parties.

Schei agrees that scientists advising the biodiversity convention face similar difficulties to those advising the climate convention: having to advise Governments on issues whose scientific underpinnings may be relatively weak. But he says he would not want to discourage the practice of Governments sending the same group of delegates to both the scientific and political segments of the convention. (Source: *Nature*, Vol. 383, 19 September 1996)

World Bank in forefront of linking biodiversity conservation to agricultural development

The crucial linkages that entwine biodiversity and agriculture are sometimes poorly understood, often to the detriment of both sustainable agricultural development and the effective conservation of the world's irreplaceable biological resources. This predicament and possible options for dealing with it are the subject of a recently released World Bank report* that recommends a new perspective be applied to the Bank's considerable global interest in and support of both.

The relevance of biodiversity to agriculture is frequently overlooked, according to the report, because biodiversity concerns typically focus on attempts to save endangered species or particular habitats, thereby "eclipsing another, critically important dimension to biodiversity: the connection between raising the productivity of crops and livestock and safeguarding the biological riches of the environment".

The report underscores "the dynamic nature of the relationship between agriculture and biodiversity as new technologies emerge, conservation strategies shift, and new trade agreements and conventions on biodiversity surface" and suggests that "a conceptual framework" analysing the interface between them "will sensitize policy makers to the relevance of biodiversity for agricultural improvement".

While the Bank's environmental lending has increased considerably since the early 1980s and biodiversity has been singled out as one of that programmes's priority concerns, the report notes that little of that spending has focused on the agricultural dimensions of the issue. Conversely, biodiversity issues have not been addressed sufficiently in the Bank's agricultural development projects.

Recognizing that the issue of biodiversity cross-cuts not only with agriculture, but also with other sectors and themes of concern to the World Bank such as environment, industry, health, and poverty alleviation, the authors state their belief that the Bank is in the unique position—through its policy advice, developmental aid, and lending portfolios—to play "a major role in assisting national Governments to develop policies and practices that capture the benefits of managing biodiversity for rural development".

The report also looks at "the piecemeal fashion" in which many international biodiversity agreements have evolved, notes that "many have been forged too late to have much impact", and is emphatic that "agriculture should be featured prominently in future conventions". Not only can the World Bank play an important role through policy dialogue with numerous countries that contain centres of biodiversity to promote the wiser use of this important resource, contends the report, but it can also play a "catalytic role" among the other players working to promote the conservation and management of biodiversity. These would include such organizations as other development agencies, non-governmental agencies, farmers' organizations and indigenous groups.

The World Bank analysts also urge greater support for documenting species and understanding their systematic relationships. Noting their sophisticated use of computer technology and ability to synthesize ecological information, the report says those scientists working in herbaria and zoological museums, as well as field biologists, are critical for the conservation and management of biodiversity.

The report calls for "a new paradigm for agricultural research" that incorporates the experience and aspirations of indigenous knowledge, acknowledging that intellectual property rights (IPR) and biodiversity "are tightly interwoven in complex ways". Some of the issues that need to be explored in this vein are:

- The impact of various international trade agreements on biodiversity both on- and off-farm;
- The impact of various forms of IPR (patents, plant breeders' rights, trade secrets, trademarks) on biodiversity;
- The seed trade and biodiversity; and
- The interplay of the Convention on Biological Diversity, IPR legislation, and trade agreements on biodiversity, particularly from the agricultural perspective.

The challenge, according to this initial study, is to develop the incentives and instruments that would encourage broad-based participation to achieve the goal of harmonizing agricultural development and biodiversity conservation. Such a framework—the ultimate goal of initial efforts such as this assessment—should be based on a set of performance indicators that would be "robust, discriminating, easily understood, and linkable to various policy levers".

Medicinal plants impact, health care, conservation and sustainable development

In another related technical paper, World Bank scientists and economists grapple with the expanding role of medicinal plants in their role as biological resources for development. While various agencies, such as the World Health Organization are involved with the efficacy, safety

* World Bank Paper No. 321: *Biodiversity and Agriculture: Implications for Conservation and Development* by Jitendra Srivastava, Nigel G.H. Smith and Douglas Forno.

and general health merits of healing plants, the World Bank's Agriculture and Natural Resources Department is concerned with its responsibility to achieve and/or maintain sustainable production of plant species already accepted for health care purposes.

The paper** views medicinal plants "as a possible bridge between sustainable economic development, affordable health care, and the conservation of vital biodiversity" and questions "why little or nothing is spent on supporting the world's medicinal plant resource base."

For further information on the reports, contact: Jitendra Srivastava, Agricultural Technology & Services Division, Agricultural & Natural Resources Department, The World Bank, 1818 H St. NW, Washington, DC 20433, USA. Tel.: +1-202-473-8975. Fax: +1-202-334-0473. For copies of the reports, contact: Distribution Unit, Office of the Publisher, The World Bank, 1818 H St. NW, Washington, DC 20433, USA, or Publications, The World Bank, 66 Avenue d'Iena, 75116 Paris, France. (Source: *Diversity*, Vol. 2, No. 2, 1996)

Biodiversity/biotechnology programme

Pursuant to the short-term goals set at the beginning of the year, the Biodiversity/Biotechnology Programme of the International Academy of the Environment (Switzerland), carried out the following main activities during the first half of 1996.

"Management of Biological Diversity for Sustainable Development at the Local Community Level"—a project proposal in the area of national biodiversity planning.

This integrated project proposal, submitted to the Swiss National Science Foundation, proposes a number of activities to be carried out in Switzerland, Costa Rica and the Ivory Coast by the International Academy of the Environment, the United Nations Research Institute for Social Development, the "Institut für Volkswirtschaft" in Basel, together with the "Institut für Wirtschaft und Ökologie" of the University of St. Gallen, the "Forschungs-Institut für biologischen Landbau" in Oberwil, and the International Bureau of Education in Geneva, working jointly with the "Institut suisse de pedagogie pour la formation professionelle" in Lausanne and the "Laboratoire didactique et d'épistémologie des sciences", Geneva.

The project analyses on-going initiatives at the national, regional and international levels which further the conservation and sustainable use of biological diversity and its components. As most of the agreements and recommendations from these initiatives have not been sufficiently translated into concrete programmes for the conservation and sustainable use of biological resources, the project will:

- Analyse, in specific situations, the prevailing obstacles to the implementation of the agreements and recommendations—not only scientific and technical obstacles, but also socio-economic, political and cultural;
- Formulate, through a participatory approach, options for the appropriate management of biological resources;
- Test and select the most appropriate options with the use of socio-economic and biological indicators; and
- Facilitate the application of selected options through the development of incentives and capacity building.

(Source: *International Academy of the Environment Newsletter*, 6 August 1996)

ICARDA to step up collaboration with Palestine

ICARDA, the International Center for Agricultural Research in the Dry Areas, is to strengthen its collaboration with the Palestinian Authority in agricultural research, with the possiblity of joint projects in integrated crop/livestock development and proper land management and conservation.

ICARDA is also to expand its support to agricultural research by the Authority in a number of areas. Improved crop germplasm for testing will be supplied at once, and other cooperation will include training in germplasm conservation and documentation, rehabilitation of marginal land and rangeland, and water-harvesting.

ICARDA expressed its willingness to support the Palestinian Authority in its efforts to rehabilitate its research programme. Direct and immediate support will include the supply of improved germplasm of legumes and cereals, which the Authority wants to field-test under local conditions. There will also be large quantities of seed of the most promising cultivars of wheat, barley, lentils, chickpea and vetches released elsewhere in the region for ecological conditions similar to those in Palestine.

Other support to be provided by ICARDA in the near future will be in the area of human resources development. ICARDA will accord high priority to Palestinian researchers for general training in crop-improvement research, plus individual training in germplasm conservation and documentation, conservation of marginal land and rangeland, and water-harvesting. Other activities planned in the short term include in-country training in Palestine and Jordan in management and conduct of field trials and data collection, improved seed production and other matters.

In the long term, project proposals for collaborative activities will be jointly developed and submitted to donors; for example, for integrated crop/livestock development and proper land management and conservation.

For further information, contact: Mike Robbins, Communication, Documentation and Information Services, ICARDA, P.O. Box 5466, Aleppo, Syria. E-mail: M.ROBBINS@CGNET.COM. or ICARDA@CGNET.COM. Fax: +963-21 213490, 225105, 551860. Tel.: +963-21 213477, 225012, 225112. Telex: (492) 331206, 331208, 331263 ICARDA SY. Cable: ICARDA Aleppo. (Source: *News Release*, 21 August 1996)

New UN body to support Africa's community-based efforts to battle HIV

Africa is a "forerunner" in proving one of the main lessons of the past decade's fight against AIDS (acquired immune deficiency syndrome)—that "prevention can work". And it is also at the forefront of positive responses to the epidemic, with a network of community-based and non-governmental organizations which have actively "taken on this disease", says Dr. Peter Piot, Executive Director of the recently created Joint United Nations Programme on AIDS (UNAIDS), which is based in Geneva.

Striking men and women primarily in their most productive years, AIDS effects critical sectors of the workforce, both urban and rural, and ultimately impacts on overall economic performance. The epidemic's indirect costs—the value of lost economic output through morbidity and early death—are difficult to measure, but nonetheless

** World Bank Technical Paper No. 320: *Medicinal Plants—An Expanding Role in Development* by Jitendra Srivastava, John Lambert and Noel Vietmeyer.

substantial. Dr. Piot cited case studies of countries which may lose 10-15 per cent of their teachers to AIDS.

There are direct costs as well, which are mainly health-related. By the year 2000, the World Bank estimates that costs of care for people living with HIV and AIDS in Africa will double, rising to $347 million per year. But the heaviest socio-economic impact fall "on individuals and households which are on the verge of poverty", because the disease attacks the breadwinners—those responsible for the care and support of children, the elderly and other members of the extended family.

While virtually every African country now has a national AIDS programme, there is still a "heavy stigma" attached to the disease at the official level. This is manifested in a continued denial of the severity of the epidemic's impact and a lack of commitment to address it by some Government leaders.

Even those who have acknowledged the gravity of the public health threat may ignore the epidemic's wider socio-economic impact, focusing only on the clinical aspect of the disease and its treatment.

Central to any effective response to the epidemic, said Dr. Piot, are two core elements. One is a legal and ethical environment which protects and supports the rights of people living with HIV and AIDS. The second is a commitment to involving people living with HIV and AIDS in raising awareness, in policy discussions, and in lobbying for their rights. Africa has made progress in these areas by launching continent-wide networks (see box).

UNAIDS actively seeks to involve such indidivuals and organizations in its work, and has at least two HIV-positive persons on its governing board. Superseding the World Health Organization's Global Programme on AIDS, UNAIDS became operational in January 1996 and also encompasses the AIDS programmes of the UN Development Programme, the UN Children's Fund, the UN Population Fund, the UN Educational, Scientific and Cultural Organization, and the World Bank. It was devised to facilitate "joint planning for the UN response to the AIDS epidemic so that we speak with one voice and we can increase our support to the countries", said Dr. Piot.

Donors and some of the most affected countries, such as Uganda and Thailand, which had been critical of perceived overlap in AIDS programmes in the past, are now looking at UNAIDS as "a more efficient and effective response of the UN system, an experiment in coordination" Dr. Piot said.

Africa will be a focal point for UNAIDS programmes "because of the stage of its epidemic, because of the experience that is there—we will make it clear to the world that a lot of what we can do about AIDS was developed in Africa—and because of a greater need for external assistance in many African countries", Dr. Piot said. "That is a commitment we have".

Africa's AIDS networks provide support and advocacy

Along with the recognition that AIDS must be tackled within a broader socio-economic context has come an awareness of the importance of creating a protecting and supportive legal, ethical and human rights environment in Africa and other regions hard-hit by the epidemic.

The UN Development Programme (UNDP) sponsored exploratory missions in 1992 and 1993 to various African countries for discussions on forming a network on ethics and the law with lawyers, ethicists, people living with HIV and AIDS, and representatives of national AIDS programmes, government ministries, non-governmental and community-based organizations and human rights and women's groups.

The African Network on Ethics, Law and HIV was officially set up during and inter-country consultation held in Dakar, Senegal, in 1994, which also drafted and signed the Declaration of Dakar, a 10-point statement of principle for formulating ethical responses to the HIV epidemic. The declaration addresses issues of non-discrimination, empowerment, confidentiality and privacy, ethics in research, and prohibition of mandatory HIV testing.

Since the Dakar meeting, members of national networks have been involved in stimulating debate in their countries, providing support to relevant HIV and AIDS service organizations, and ensuring that issues of ethics, law and human rights are integrated in national responses to the epidemic.

Another important element in formulating effective responses to the HIV epidemic is involving people affected by HIV and AIDS in advocacy and programme planning. The Network for African People Living with HIV and AIDS (NAP+) was born out of the meeting of two young HIV-positive men, Michael Angaga of Kenya and David Chipanta of Zambia, at a UNDP-sponsored HIV and development capacity-building workshop in Senegal in 1993. Together, they drew up a proposal which received seed funds from UNDP to help prepare the network through coordination offices in Nairobi and Lusaka.

A regional conference of Africans with HIV and AIDS was then held in Mombasa, Kenya, in May 1994, bringing together 50 participants from 13 African countries, who then agreed to form the network. Additional national chapters are being established and added to the continent-wide network. NAP+ was able to participate in the March 1995 meeting of the Global Network of People with HIV and AIDS in Cape Town, South Africa, and the International Conference on AIDS and STDs in Africa, held in Kampala, Uganda, in December.

The objectives of NAP+ include: to strengthen the quality of care for people with HIV and AIDS, to empower people with the virus to influence policies on issues that affect them, to help set up support groups and coordinate their activities, to push for the availability of therapeutic drugs, to do advocacy work on legal and ethical issues, and to lobby decision makers for increased support to people with HIV and AIDS.

(Extracted from *Africa Recovery*, May 1996)

Ethical issues

European Bioethics Convention nears final stage

After a final vote on the draft European Bioethics Convention, including the first legally binding international rules on genetics, parliamentary representatives of the Council of Europe's 39 member States have demanded that the Convention should be opened for signature by the end of 1996.

The Convention will lay down ethical guidelines and restrictions in a wide range of issues raised by medical practice, research and genetics. More detailed rules will be set out in future protocols to the main accord. Specific questions in genetics are covered by the Convention's Chapter IV on the Human Genome.

"Any form of discrimination against a person on the grounds of his or her genetic heritage" will be prohibited by Article 11, in response, says the Convention's explanatory report, to widespread concern that "genetic testing... may become a means of selection and discrimination".

This restriction would in theory outlaw genetic tests as a condition of recruitment—and the weighting of insurance premiums for policies sought by applicants with a known history of genetically inherited disease, or the refusal of cover on those grounds.

Self-imposed moratoria on the use of genetic data have been agreed by national insurance federations dating back to a Dutch initiative in 1990. Other countries have made at least initial moves towards legislation.

Members were not only concerned about pressure from insurers or employers for disclosure of unfavourable test results, but also the longer-term possibility that candidates with an impeccable genetic profile might present themselves as superior candidates for employment or insurance cover—or even mortgages and other forms of credit.

As drafted, the Convention's Article 13 on Interventions on the Human Genome echoes voluntary agreements in the international science community by specifying that "an intervention seeking to modify the human genome may be undertaken for preventive, diagnostic or therapeutic purposes and only if its aim is not to introduce any modification in the genome of any descendants".

Of the Council of Europe's 39 member States, only Germany has indicated reluctance to sign the Convention, at least for the time being. However, Germany is expected to sign in due course, once other States have confirmed that parties to the Convention are free to maintain higher national standards. (Extracted from *Biotechnology Business News*, 9 October 1996)

Tribal groups attack ethics of genome diversity project

Citizens' groups in the United States and representatives of tribal peoples in poor countries attacked proposals for the Human Genome Diversity Project, which plans to systematically collect and make available for research genetic information about people from different ethnic groups.

The critics told a panel of the National Research Council (NRC), chaired by William Schull of the University of Texas at Houston, that the proposal should be suspended on ethical grounds.

The Arhuaco people of Columbia who came to Washington to testify before the panel, alleged that scientists had already taken thousands of samples from tribal people in Columbia without meaningful informed consent, and without consulting with tribal leaders.

According to Abadio Green Stocel, president of the National Indigenous Peoples' Organization of Columbia, the samples had been given on the basis that they would be used "to analyse the health of the communities". They ended up, however, in gene banks at the Centre for Disease Control and the National Institutes of Health (NIH) in the United States.

The NRC panel had been asked by the National Science Foundation (NSF) and the NIH to look at various proposals that exist to bring together research in this field under a Human Genome Diversity Project.

Proposals under consideration include a summary prepared by the Human Genome Organization, the international genome group, and output from scientific workshops held at Stanford University in California in 1992 and in Sardinia, Italy, in 1993. (Extracted from *Nature*, Vol. 383, 19 September 1996)

NABC committee proposals on ethics

The Executive Committee of the US National Agricultural Biotechnolgy Council's (NABC) subcommittee on ethics has issued a number of recommendations. The recommendations involve measures that NABC and its member institutions could and should undertake to ensure that ethical issues receive an appropriate level of consideration as one component of the non-profit sector's programme of research and development of food and agricultural biotechnologies.

The committee recommended that:

- Each NABC member institution should ensure that subject matter on ethical issues associated with food and agricultural biotechnology is systematically integrated into the curriculum of their institutions.
- Each institution should develop an institutional mechanism for supporting faculty interest and research on ethical issues.
- Each institution should include information on ethical issues in its public education programmes on biotechnology.
- NABC should support these efforts by sponsoring regular workshops or conferences on ethical issues, aiding in the development of modules and teaching materials, and aiding in the dissemination of materials in both printed and electronic form.

(Source: *AgBiotech Bulletin*, August 1996)

Regulatory issues

Proposed Canadian biotech amendments published

Documents containing proposed amendments to various federal regulations affecting the agricultural biotechnology sector were published in the *Canada Gazette*, Part I, on 17 August 1996. These documents include:

- Regulations for Environmental Safety Assessments of Releases of Plants with Novel Traits Under the Seeds Act;
- Regulations for Environmental Safety Assessments of Veterinary Biologics Under the Health of Animals Act;
- Regulations for Environmental Safety Assesssments of Releases of Novel Fees Under the Feeds Act; and

- Regulations for Environmental Safety Assessments of Releases of Supplements Under the Fertilizers Act.

All of these documents can be accessed on the Internet at http://aceis.agr.ca/fpi/agbiotec/english.html.

Interested parties are invited to review and comment on these regulatory amendments and to distribute them to colleagues or to any others who they believe may have an interest in this area. Recommendations and comments would be appreciated, particularly on the appropriate level of detail of information requirements in this proposed regulatory amendment compared to the level of detail in existing guidelines on plants with novel traits.

Further information from bsco@em.agr.ca or to the Associate Director, Biotechnology Strategies and Co-ordination Office, Food Production and Inspection Branch, Agriculture and Agri-Food Canada, 59 Camelot Drive, Nepean, Ontario K1A 0Y9.

Contact: Biotechnology Strategies and Coordination Office, Agriculture and Agri-Food Canada, Nepean, Ontario K1A 0Y9. Tel.: 613-952-8000; Fax: 613-941-9421. (Source: *The Agbiotech Bulletin*, October 1996)

Biosafety

Towards a biosafety protocol

The first meeting of the Open-ended Ad hoc Working Group on Biosafety held in Aarhus, Denmark, in July 1996 succeeded in establishing a firm foundation for negotiating a future biosafety protocol under the Convention on Biological Diversity.

An important step forward was taken in determining the range of issues that the protocol might address for the safe transfer, handling and use of living modified organisms which may have adverse effects on the conservation and sustainable use of biodiversity. Some of the elements proposed for inclusion in the protocol include objectives, jurisdictional scope, focal points, risk assessment and risk management, advance informed agreement and notification, monitoring of and compliance with protocol obligations, emergency procedures, public awareness, socio-economic considerations, liability and compensation. One of the main concerns underlying the discussions was to provide developing countries with the necessary technical, financial and institutional capacities for addressing biosafety issues.

The Working Group elected a ten-member Bureau which will be chaired by Mr. Veit Koester from the National Forest and Nature Agency of Denmark. (Source: *Our Planet*, Vol. 8, No. 4, 1996)

Biosafety protocol stalled over liability issue

Agreement on a draft protocol covering the use of genetically modified organisms (GMOs) under the United Nations Biodiversity Convention has stalled on the question of liability. Several representatives of developing nations attending meetings in Aarhus, Denmark, are attempting to widen the scope of a protocol covering transborder movement of GMOs to include, among other things, a clause that provides compensation in the event that a GMO release damages human health and the environment or has a negative impact on traditional agriculture.

Representatives of several European countries are resisting the introduction of such a clause on the grounds that stronger regulations will inhibit the development of the biotechnology industry. The meeting is also at odds over definitions of GMOs, whether these include only Living Modified Organism (LMOs) or also products arising from processes involving genetic engineering. However, all the delegates agree that an exporter of a GMO should obtain prior agreement from the importing country and comply with local biosafety regulations.

A draft text of the protocol is expected to be completed by 1998. (Source: *The AgBiotech Bulletin*, September 1996)

"Safety in Biotechnology" workshop for West and Central Africa, Abidjan, Côte d'Ivoire, 10-14 June 1996.

The workshop was held under the auspices of H.E. Mr. Ezan Akele, Ivorian Minister of Economic Infrastructures and H.E. Mr. Pierre de Graffenried, Ambassador of Switzerland in Côte d'Ivoire, in partnership with the Swiss Federal Office of Environment, Forests and Landscapes (FOEFL), the West Africa Rice Development Association (WARDA, Bouak, Côte d'Ivoire), and the United Nations Environment Programme (UNEP).

The objectives of the workshop were to:

- Catalyse the development and implementation of national biosafety regulations in the region; and
- Enable Government representatives, designated as members of the Open-ended Ad Hoc Working Group on Biosafety established by the Conference of the Parties to the Convention on Biological Diversity, to prepare for their meeting (22-26 July 1996) in Aarhus, Denmark.

The workshop gathered at least two Government-nominated participants, including a biotechnologist and a lawyer, from Cameroon, Côte d'Ivoire, Ethiopia, Gabon, Ghana, Senegal and Zaire. Resource-persons were invited from France, South Africa, Switzerland, Zimbabwe and USA, as well as a representative of bioindustry.

After an assessment of the needs for biosafety regulations in each of the participating countries, elements usually included in national and international biosafety regulations were considered and discussed. These included the procedures for risk assessment and management through case studies, as well as the structures to be set in place for the development and implementation of biosafety measures. Participants discussed in particular how the UNEP International Technical Guidelines and biosafety guidelines being drafted in other African countries could be used as a starting point for the development of national biosafety regulations. In addition, participants proposed an outline for national biosafety regulations that could guide them upon return in their respective countries. Finally, some recommendations were formulated on follow-up activities and WARDA was designated as the interim regional focal point for the coordination of biosafety matters in West and Central Africa for a two-year term.

The Biodiversity/Biotechnology Programme is preparing the proceedings of the workshop and will continue interacting with the participants to identify and implement ways in which their task could be facilitated. An ex ante assessment of the workshop was presented at a meeting on "Capacity Building in Biosafety for Developing Countries: Evaluation Criteria Development", organized by the Biotechnology Advisory Commission of the Stockholm Environment Institute on 22-23 May 1996 in Stockholm, Sweden.

Contact person: Jo Mulongoy -<Kalemani.Mulongoy @iae.unige.ch> (Source:*International Academy of the Environment, Newsletter 6*, August 1996)

General

Biotech financing window closing fast

Recent figures show that comparing June to July, there was a greater than 50 per cent reduction in funding. As a result, a number of companies withdrew their public offerings due to "deteriorating" market conditions. Overall, biotechnology stock deals in July counted for nearly 4 per cent of the total $9.8 billion that traded hands during the month. On the brighter side, over $2.5 billion was raised for biotechnology companies during the second quarter of 1996—more than twice the amount raised a year earlier. Facing the possibility of another funding drought, what should the "haves" and the "have nots" from this financial round do to ensure success? According to one expert, find a strategic alliance. With many cash-rich, mid-sized European pharmaceutical companies struggling to find a niche in the new mega-merger pharmaceutical landscape, they are looking for new products that will replenish their failing pipelines. (Source: *Nature Biotechnology*, Vol. 14, September 1996)

COST Agriculture and Biotechnology Programme

Researchers from 27 countries are involved in 14 networks that have been established by the COST Agriculture and Biotechnolgy Programme of the European Union. Seven new COST proposals involve biotechnology of soil; estimating the agricultural contribution to eutrophication; microbial inoculants in agriculture and environment; the role of organic waste in sustaining agriculture; a multidisciplinary approach to salinity; and lentiviruses of sheep and goats.

For contacts and information contact Dr. Owen Doyle, NAVBC, Biotechnology Building. University College, Belfield, Dublin 4, Ireland. Tel.: 353-1-706-2801; Fax: 353-1-269-2016. (Source: *The AgBiotech Bulletin*, September 1996)

Gene-altered crops may accelerate pest resistance

A high-level conference held recently by the United States Department of Agriculture called attention to the potential loss of one of US agriculture's most valuable natural pesticides—*Bacillus thuringiensis* (Bt)—as a result of widespread adoption of crops engineered with Bt. Over 150 people participated in the forum, including organic and conventional farmers, extension specialists, industry representatives, environmentalists, scientists and policy makers. Scientists at the conference agreed that widespread resistance to Bt could develop in less than five years unless adequate resistance management plans are developed. Resistance to Bt would be a major blow to organic and sustainable farmers, many of whom use the insecticide in spray form to control insect pests. Many participants emphasized that current measures to control Bt resistance are unproven and are unlikely to be adopted by farmers. Some participants urged the Government to withhold further approvals of Bt crops pending development of science-based resistance management plans. In the next few months, USDA will produce a report on the conference proceedings and recommendations. (Source: *Biotech Bulletin*, 15 May 1996)

Global biotechnology financing

One of the largest European biotechnology initial public offerings (IPO) was completed by Genset (Paris) at the beginning of June. The French genomics company raised $86.4 million in a dual listing on the Nouveau Marché (Paris)—the new French exchange—and NASDAQ. Genset's market capitalization is now over $400 million.

Genset's IPO not only demonstrates that European biotechnology companies with a strong story can attract investors, but also that companies, wherever they are based, now have a real choice of public financial markets. Four years ago, for companies like Cantab Pharmaceuticals (Cambridge, UK) and the French company Sangstat (registered now in Menlo Park, CA), NASDAQ was the only real option for raising capital. But biotechnology companies have now raised money in financial markets in London, Paris, Copenhagen and Vienna. And the European NASDAQ clone, EASDAQ (European Association of Securities Dealers Automated Quotation), has attracted its first biotechnology IPO—the diagnostics company, Innogenetics (Ghent, Belgium). Several US companies are now looking to raise money in Europe. (Extracted from *Nature Biotechnology*, Vol. 14, July 1996)

Borer-resistant corn get EPA approval for marketing

Monsanto has received EPA registration for its genetically engineered corn. Sandoz Seeds subsidiary Northrup King, which is Monsanto's marketing partner, will begin offering the corn seed for the 1997 planting season. The corn seed produces an insecticidal protein to protect the plant against the European corn borer. The corn borer is estimated to be in 75 per cent of US corn fields, costing growers as much as $1 billion annually in lost yield. However, the majority of growers do not treat for the pest, says Monsanto, because it is difficult to obtain effective control throughout the season. Monsanto has also developed and received approvals in 1995 for insect-protected potatoes, herbicide-resistant soybeans, and insect-protected cotton. In the first growing season for its cotton, extremely high infestations of cotton bollworm are severely testing the cotton's ability to perform. Only a "small percentage" of the genetically engineered cotton crop has been affected, says Monsanto, and growers using the cotton have been able to eliminate the need for applying insecticide until recently. With the dramatic increase in bollworms since mid-July, the company suggests that farmers may need to spray. The cotton, normally expected to provide about 95 per cent protection against bollworm, is even more effective against tobacco budworm and pink bollworm, which appear later in the growing season, says Monsanto. The real test of the cotton's effectiveness will best be determined at the end of the growing season. (Source: *Chemical and Engineering News*, 19 August 1996, page 20)

ACS projects boost chemistry education in developing countries

Even in a time of pinched budgets for research and instrumentation, access to high-technology analytical tools used to educate new generations of chemistry professionals are items that nations of the developed world take almost for granted, says John Malin, head of the American Chemical Society's Office of International Activities. In developing countries, on the other hand, scarce resources often mean a desperate scramble for research instruments, textbooks and journals.

To help meet some of the demand for research instruments at needy institutions in the US and in impoverished countries, the International Activities Office has launched

Project Instrumentshare, a programme in which chemical companies can donate used research instruments to educational and non-profit institutions. Already, several companies have stepped forward with offers of research instruments.

Malin's office identifies appropriate recipients at educational and non-profit institutions around the world—including some in the US—where the needs are particularly acute. The programme generally focuses on those nations listed as most impoverished by the International Monetary Fund.

The International Activities Office coordinates shipping of donated equipment from donor's laboratories or offices.

Training chemists and other scientists is an essential part of building a regional economy that will support developing nations, but the costs—high even in the US and other developed countries—are next to impossible in places such as Paraguay, the former Soviet Bloc nations of Eastern Europe, and many of the poverty-stricken nations of Africa. A single instrument such as an infrared spectrometer or a nuclear magnetic resonance (NMR) instrument, Malin points out, can range in price from $50,000 to $500,000 when new.

Project Instrumentshare was inspired by the success of another ACS programme, Project Bookshare. Since 1984, Project Bookshare, coordinated by ACS staffer Joyce C. Torio has collected chemistry textbooks and back issues of journals from donors and made the publications available to libraries at selected small US colleges, including tribal colleges, and to university libraries in developing countries.

As just one recent example, Project Bookshare recently coordinated the donation of 12 tons of books and journals to the National University of Paraguay.

Another related project, managed by Jeffery Osborn of the International Activities staff, helps reroute expired but still usable chemical reagents from Fisher Scientific and other companies to needy institutions abroad. Late this summer, for example, ACS and Fisher will arrange to ship approximately 15 tons of research-grade reagents to Estonia. Fisher has also donated $5,500 to the ACS World Reach Fund, which helps support projects of the ACS International Activities Office. (Extracted from *Chemical & Engineering News*, 5 August 1996)

What's coming to market?

An update on commercialization

☐ Approved for sale ☐ Awaiting approval

The chart below summarizes agency actions on commercialization of genetically engineered agricultural products as of May 1996

Product	Company	Altered trait	Purpose	Sources of new genes	Agency action[1]	Approved for sale/name
Canola (oilseed rape)	Calgene	Altered oil composition—high lauric acid	Expand use in soap and food products	California bay, turnip rape, bacteria, virus	USDA/Approved FDA/Approved[2] EPA/Not required	1995 Laurical
Corn	Ciba-Geigy	Resistance to corn borer (Bt toxin)	Control insect pests	Corn, bacteria, virus	USDA/Approved FDA/Approved EPA/Approved	1995 Maximizer
Corn	Mycogen	Resistance to corn borer (Bt toxin)	Control insect pests	Corn, bacteria, virus	USDA/Approved FDA/Approved EPA/Approved	1995 NatureGard
Cotton	Calgene/Rhone Poulenc	Resistance to herbicide bromoxynil	Control weeds	Bacteria, virus	USDA/Approved FDA/Aproved EPA/Approved	1995 BXN Cotton
Cotton	Monsanto	Resistance to bollworms and budworm (Bt toxin)	Control insect pests	Bacteria	USDA/Approved FDA/Approved EPA/Approved	1995 Bollgard
Cotton	Monsanto	Resistance to herbicide glyphosate	Control weeds	Arabidopsis, bacteria, virus	USDA/Approved FDA/Approved EPA/Approved	1996 Roundup Ready
Potato	Monsanto	Resistance to Colorado potato beetle (Bt toxin)	Control insect pests	Bacteria	USDA/Approved FDA/Approved EPA/Approved	1995 NewLeaf
Soybean	Monsanto	Resistance to herbicide glyphosate	Control weeds	Petunia, soybean, bacteria, viruses	USDA/Approved FDA/Approved EPA/Approved	1995 Roundup Ready
Squash	Asgrow	Resistance to two viruses	Control two virus diseases	Viruses	USDA/Approved FDA/Approved EPA/Not required	1995 Freedom II

Product	Company	Altered trait	Purpose	Sources of new genes	Agency action[1]	Approved for sale/name
Tomato (cherry)	Agritope	Altered ripening	Enhance fresh market value	Bacteria	USDA/Approved FDA/Approved EPA/Not required	1996 Unknown
Tomato	Calgene	Delayed ripening	Enhance fresh market value	Tomato, bacteria, virus	USDA/Approved FDA/Approved EPA/Not required	1995 Flavr Savr
Tomato	DNA Plant Technology	Delayed ripening	Enhance fresh market value	Tomato, bacteria, virus	USDA/Approved FDA/Approved EPA/Not required	1995 Endless Summer
Tomato	Monsanto	Delayed ripening	Enhance fresh market value	Bacteria	USDA/Approved FDA/Approved EPA/Not required	1995 Unkonwn
Tomato	Zeneca/Petoseed	Thicker skin, altered pectin	Enhance processing value	Tomato, bacteria, virus	USDA/Approved FDA/Approved EPA/Not required	1995 Unknown
Bacillus thuringiensis	Ecogen	Toxicity to Lepidopteran insects (Bt toxin)	Control insect pests	Bacteria	USDA/Not required FDA/Not required EPA/Approved	1995 Crymax
Bacillus thuringiensis	Ecogen	Toxicity to Colorado potato beetle (Bt toxin)	Control insect pests	Bacteria	USDA/Not required FDA/Not required EPA/Approved	1995 Raven
Pseudomonas fluroescens[3]	Mycogen	Toxicity to insects (Bt toxin)	Control insect pests	Bacteria	USDA/Not required FDA/Not required EPA/Approved	Yes M-Peril M-Trak MVP
Vaccinia virus vaccine	Rhone Merieux	Immunity to rabies	Control raccoon rabies epidemics	Rabies virus	USDA/Approved FDA/Not required EPA/Not required	1995 Raboral
Canola	Hoechst/AgrEvo	Resistance to herbicide glufosinate	Control weeds	Bacteria	USDA[5] FDA/Approved EPA[5]	No
Canola	Monsanto	Resistance to herbicide glyphosate	Control weeds	NA[4]	USDA[5] FDA/Approved EPA[5]	No
Canola	Plant Genetic Systems	Male sterility/Fertililty restorer	Facilitate plant breeding	NA[4]	USDA[5] FDA/Approved EPA[5]	No
Corn	DeKalb	Resistance to herbicide glufosinate	Control weeds	Bacteria, virus	USDA/Approved FDA/Approved EPA[5]	No
Corn	Hoechst/AgrEvo	Resistance to herbicide glufosinate	Control weeds	Bacteria, virus	USDA/Approved FDA/Approved EPA/Pending	No Liberty Link
Corn	Monsanto	Resistance to corn borer (Bt toxin)	Control insect pests	Bacteria	USDA/Approved FDA[5] EPA[5]	No YieldGard
Corn	Plant Genetic Systems	Male sterility	Facilitate plant breeding	Bacteria, virus	USDA/Approved FDA[5] EPA[5]	No
Corn	Sandoz/Northrup King	Resistance to corn borer (Bt toxin)	Control insect pests	Bacteria	USDA/Approved FDA[5] EPA/Pending	No
Cotton	DuPont	Resistance to herbicide sulfonylurea	Control weeds	Tobacco, bacteria	USDA/Pending FDA[5] EPA[5]	No
Papaya	Cornell University/ University Hawaii	Resistance to virus	Control virus disease	Bacteria, virus	USDA/Pending FDA[5] EPA/Not required	No

Product	Company	Altered trait	Purpose	Sources of new genes	Agency action[1]	Approved for sale/name
Soybean	Hoechst AgrEvo	Resistance to herbicide glufosinate	Control weeds	Bacteria	USDA/Pending FDA[5] EPA/Pending	No
Squash	Asgrow	Resistance to three viruses	Control three virus diseases	Bacteria, viruses	USDA/Pending FDA[5] EPA/Not required	No
Bacillus thuringiensis	Ecogen	Toxicity to Lepidopteran insects (Bt toxin)	Control insect pests	Bacteria	USDA/Not required FDA/Not required EPA/Pending	No Crystar
Rhizobium meliloti	Research seeds	Enhance nitrogen fixation	Increase yield in alfalfa	Bacteria	USDA/Not required FDA/Not required EPA/Pending	No

[1] Action may respond to either voluntary or required submissions from companies.

[2] FDA Approval means that FDA has completed consultations with the company and will allow the product to enter the market once regulatory requirements are met at other agencies. Except for the Calgene tomato approved in 1994, FDA consultations are abbreviated reviews of company safety assessments.

[3] The organism is killed before it is applied in the environment.

[4] Information is not available.

[5] Status of consultations, if any, is unknown.
(Source: *The Gene Exchange*, June 1996)

Public/private technology transfer in developing countries

The USAID Agricultural Biotechnology for Sustainable Productivity (ABSP) Project is managed by Michigan State University to assist developing countries in the application and management of plant agricultural biotechnologies. The project takes an integrated approach to technology generation and transfer. Part of this integrated approach involves the safe and legal transfer of technologies among public and private sector institutions in developed and developing countries. Successful transfer of technology has many requisites, one of the most important being the resolution of intellectual property issues for the benefit of all parties. One goal of ABSP activities is to assist its partner countries in developing a policy environment for biosafety and intellectual property which is conducive to the successful transfer of ABSP-generated and other related technologies.

As a part of its networking programme, ABSP has helped to develop linkages between the public and private sectors in and between the USA and ASBP partner countries. Many of the technologies arising from these partnerships are proprietary in nature, involving intellectual properties that must be managed in a manner different from the traditional sharing of knowledge and technologies in the public sector. In most developing countries, public sector research has been predominantly supported by Government and the mandate of public institutions has been to freely serve society. The technologies generated by the public sector were freely exchanged for research and development purposes without entering into any kind of commercial agreement. As the global community moves towards privatization of the agricultural sector, many governmental policies around the world are shifting towards the commercialization of agricultural research. Policy makers and senior administrators are now rethinking the manner in which technologies from the public sector are to be managed. Adapting to and leading this change clearly requires strengthening the technology transfer framework, especially in public sector institutions.

Michigan State University (MSU) is committed to meeting the needs of the global community. That commitment led to the development of an internship programme in intellectual property rights and technology transfer, a cooperative effort between the MSU Office of Intellectual Property, the University's Institute of International Agriculture, and the ABSP Project. The two-week programme attracted eleven international participants from eight different countries in Africa, Asia and Latin America. The programme provided hands-on experience in the day-to-day management of intellectual properties and technology transfer among public and private sector institutions. Ecompassed were various aspects of intellectual property rights, and technology transfer, application, and management within the context of recent changes in the Uruguay Round of the General Agreement on Tariffs and Trades (GATT).

A broader exposure to the rapidly growing area of technology management and transfer was afforded through the annual meeting of the Association of University Technology Managers (AUTM). AUTM is a non-profit organization dedicated to facilitating technology transfer and comprises more than 1,400 members representing licensing, research and development, patent law and business development.

The programme participants took advantage of immense networking opportunities with technology managers from universities, private companies and private

law firms from across the USA and Canada, and freely attended sessions, including two special workshops organized by the internship programme designers. (Extracted from *BioLink*, Vol. 2, No. 4, 1996)

Conference on affinity chromatography

A conference entitled "Recent Developments in Affinity Chromatography, Affinity Bioprocessing and Molecular Imprints" is to be held at Queen's College, Cambridge, UK, on 1-3 July 1997, organized by the Chromatographic Society and sponsored by Novo Nordisk, Denmark.

The conference highlight is the disclosure of the complete process for the design and large-scale application of a customized synthetic affinity medium to separate a major recombinant-manufactured pharmaceutical protein through a collection of papers including: the development of the R&D contract with a design agency; the stages in developing a suitable affinity media; the use and comparative virtues of designing via rational and combinatorial library methods; the development of the optimum ligand; pilot plant studies; development to process scale; and the economic advantages of the new affinity system compared to the traditional system.

The most recent developments occurring in molecular imprinting are also to be revealed. High profile speakers will represent industry, Government and academia, addressing the conference topics from both commercial and research points of view.

For further information contact: The Chromatographic Society, Suite 4, Clarendon Chambers, 22 Clarendon Street, Nottingham NG1 5JD, United Kingdom. (Source: *Press Release*, 6 December 1996)

Incubators for biotechnology research help to transfer technology to commercial markets

Biotechnology incubators provide a supportive environment that is tailored to creating new ventures. The National Business Incubation Association (NBIA, Athens, OH) estimates that there are more than 500 incubators in North America. An incubator's goal is to launch new businesses that are financially viable and able to stand on their own within two to three years. NIBA's statistics show that about 8,000 small firms currently reside within incubators and approximately 4,500 companies have already moved out into commercial space in the local community. Many of these successful "graduate" companies have a biomedical focus.

The incubator provides laboratory space and equipment as well as a variety of business services and technical support. Leased space is available in renovated university buildings and newly-built research parks. Personnel resources range from technical support to professional expertise. Business assistance in the form of telephone answering, bookkeeping, word-processing and secretarial services is provided for a fee. Incubator companies also offer legal (including patenting), accounting, marketing and business planning services as well as assistance with seed financing. *Growing New Ventures Creating New Jobs* is a "how to" book written by Mark Rice and Jana Matthews that describes the principles and practice of developing and managing an incubator.

Most incubators succeed if the client needs are served and if the incubator is run like a real estate operation with an economic development plan. It is necessary to become financially self-supporting. Taking equity may be important in the long term, but you also need to pay the bills in the short term. And it is important to provide the services small companies need without attaching strings. A small company that promises equity early on may have trouble raising money later.

Incubators were born in the 1970s when the idea of using old abandoned factories to house new companies was put into practice. Today, incubator sponsors are local Governments, economic development agencies, universities/colleges and the private sector.

The success of an incubated company is measured in terms of how it becomes independent. Companies leave the incubator when more space is needed to house a growing staff. NBIA calculations suggest that incubators have contributed to creating at least 82,000 jobs, which averages out to approximately 140 jobs per incubator. For a venture capital backed firm, an IPO or buy-out are realistic indicators of success.

Incubators provide a forum for technology transfer as well as serving as a proven tool for creating new jobs. An incubator must balance the needs for providing revenue to the university, economic development for a particular geographic area, and making the technology maximally available to the public. The incubator's goal is not necessarily royalty generation but technology utilization. Technology transfer is not synonymous with economic development, because transferring technology is not limited geographically, but involves a broader mandate of helping people. It is usual to license inventions locally because it is easier to make deals with companies that are close at hand. But, if there is no prospective licensee in the local environment, it is possible to create one by bringing the technology into an incubator company. (Extracted from *Genetic Engineering News*, 4 July 1996)

The Leipzig Conference and its backgrounds

In 1993 the FAO Commission on Plant Genetic Resources of the FAO decided that an "International Technical Conference" was needed to transform the relevant parts of the UNCED process, including Agenda 21 and the Convention on Biological Diversity, into a "costed *Global Plan of Action*" (GPA). A draft of the GPA was discussed during the Technical Conference in Leipzig, Germany, 17-23 June 1996.

GPA, declaration and the report

The GPA contains about 346 recommendations derived from data assembled into a large report entitled "*State of the World's Plant Genetic Resources*", which is the main background document for the GPA. To assemble data for the report, 154 countries, divided into 11 subregions worldwide, held preparatory meetings. In cooperation with FAO these countries also formulated policy standpoints to be expressed in the GPA.

While the report can be considered as the most recent state-of-the-art on ideas from various disciplines regarding optimal conservation and use of *plant genetic resources* (PGRs), the GPA formulates guidelines for future funding, conservation and use.

Another aim of the Conference was to formulate the "*Leipzig Declaration on Conservation and Sustainable Utilization of Plant Genetic Resources for Food and Agriculture*". The Leipzig Declaration explicitly formulates general rules and principles regarding access, conservation add use of PGRs and is of a less technical nature than the Global Plan. Minimal consensus was reached on the

Declaration due to "classic" issues such as national sovereignty, technology transfer, finance.

Global plan of action

The host of the discussions during the conference concentrated on the 346 recommendations of the Global Plan of Action. The negotiations on the Plan are not yet finalized but agreement has been reached on about 95 per cent of the items. The most significant elements were the following:

- The most preferable *conservation strategy* is a combination of *in situ* and *ex situ* storage. Local and indigenous knowledge should be recognized as important components of surveying and inventorying activities. Participatory, on-farm management of PGRs is recommended, although no consensus was reached on the question as to whether this should be supported by (financial revenues from) farmers' rights. Regarding *in situ* conservation, the GPA explicitly demands more attention for wild relatives which could be used for the improvement of food crops. Many of the world's nature parks, it states, contain wild relatives, but receive little concern.

  Regarding *ex situ* conservation, the GPA intends to give high priority to safeguarding as much diversity as possible in *ex situ* collections while countries have national sovereignty over, and responsibility for, their *own* PGRs. More finance is requested to support *ex situ* "core" collections (containing a selected and characterized amount of entries already available in *ex situ* collections).
- Regarding the *use of PGRs* the GPA supports a sustainable agriculture through diversification of crop production and a broader diversity in crops. Various strategies are opted for, starting with a further support for seed production and distribution in the public sector. A relatively new strategy to increase the demand for diverse PGRs was to develop new (niche) markets for local varieties and "diversity rich" products. The issue of the use of PGRs subject to property rights "*in accordance with applicable international agreements and national legislation*" was not resolved. Neither was the exchange of PGRs for technology. The final section of the GPA on "*Ensuring a Fair and Equitable Sharing of Benefits*" which demanded an effective implementation of farmers' rights was not agreed upon.

(Source: *Biotechnology and Development Monitor*, No. 28, September 1996)

Global Plan of Action for the Conservation and Sustainable Utilization of Plant Genetic Resources for Food and Agriculture. Selected major elements and recommendations

In the process of gathering information on national crop genetic resources and discussing the findings of regional meetings, the scientists who generated the *State of the World's Plant Genetic Resources* for food and agriculture (PGRFA) also compiled suggestions for saving, conserving and utilizing these precious resources. These appear in the *Global Plan of Action for the Conservation and Sustainable Utilization of PGRFA*.

The cost of implementing plans to save and develop crop germplasm is tentatively estimated between US$ 130.6-303.8 million, averaged over 10 years, depending on the determination of national and international responsibilities, the extent and duration of efforts undertaken, and each country's financial situation and genetic resource capabilities, among many other factors and considerations, all of which are under continuing deliberation.

***In Situ* Conservation and Development**

1. Surveying and Inventorying Plant Genetic Resoures for Food and Agriculture
2. Supporting On-Farm Management and Improvement of Plant Genetic Resources
3. Assisting Farmers in Disaster Situations to Restore Agricultural Systems
4. Promoting *In Situ* Conservation of Crop Wild Relatives and Wild Plants for Food and Agriculture

***Ex Situ* Conservation**

5. Securing Existing *Ex Situ* Collections
6. Regenerating Threatened *Ex Situ* Accessions
7. Supporting Planned and Targeted Collecting of Plant Genetic Resources for Food and Agriculture
8. Expanding *Ex Situ* Conservation through Botanic Gardens and Use of New Technologies

Utilization of Plant Genetic Resources

9. Expanding Evaluation and Increasing the Number of Core Collections to Facilitate Use
10. Increasing Genetic Enhancement and Base-Broadening Efforts
11. Promoting Higher Levels of Diversity in Crops to Reduce Genetic Vulnerability
12. Promoting Under-Utilized Crops and Species
13. Supporting Seed Production and Distribution
14. Developing New Markets for Local Varieties and "Diversity-Rich" Products

Institutions and Capacity Building

15. Building Strong National Programmes
16. Promoting Networks for Plant Genetic Resources
17. Constructing Comprehensive Information Systems for Plant Genetic Resources
18. Developing Monitoring and Early Warning Systems for Loss of Plant Genetic Resources
19. Expanding and Improving Education and Training
20. Promoting Public Awareness of the Value of Plant Genetic Resources Conservation and Use

Costing of the Global Plan of Action

Preliminary Cost Estimates Organized by Category and Tallied

Preliminary Cost Estimates Organized by Priority Activity

(Source: *Diversity*, Vol. 12, No. 2, 1996)

From chemical weapons to pharmaceuticals

What to do with a former Soviet Union biological and chemical weapons facility in Kazakstan now that the cold war is over? The Defense Nuclear Agency's (DNA) Cooperative Threat Reduction Board has provided $2.7 million to turn the former weapons facility into a pharmaceutical plant. Producing aspirin in a former anthrax plant is what the contract with Allen & Associates International (Sunnyvale, CA) specifies as part of a joint venture with ICN Pharmaceuticals (Costa Mesa, CA). Using this DNA seed money to get the plant up and running, ICN intends to manufacture everything from antivirals to vitamin A at the facility.

Milan Panic of ICN, says he estimates his company can capture 10 per cent of the estimated $600 million Kazakstan pharmaceutical market during the next three to five years through the manufacturing capability of this plant alone. ICN's track record in Eastern Europe seems to back up this raw capitalist ambition for a former communist State. The company privatized Yugoslavia's largest pharmaecutical company in 1991 and made it profitable. (Source: *Nature Biotechnology*, Vol. 14, July 1996)

African biology federation takes shape

Plans to launch a Federation of Biochemists and Molecular Biologists for Africa were due to be announced during the First Pan-African Conference on Biochemistry and Molecular Biology in Nairobi in September 1996.

According to Peter Campbell, professor of biochemistry and molecular biology at University College, London, the federation is intended to become a sister organization to the European, Pan-American, and Asian and Oceanic federations. Africa has until now been left out, largely because of travel restrictions that accompanied apartheid.

The concept of an African federation has the support of the United Nations Environmental Programme, which has provided facilities for the meeting. In addition, several non-African scientific societies and funding agencies have provided funds to enable biochemists from all over Africa to attend.

Wieland Gevers, deputy vice-chancellor at the University of Cape Town, and a former president of the Biochemical Society of South Africa, says there is a clear need for the continent's biochemical societies to work together. But he says that achieving this may not be easy in practice because of factors such as the large distances between countries and their serious lack of resources.

The viability of an African federation is likely to depend on its receiving financial and organizational support from other bodies, without being dominated by them. (Source: *Nature*, Vol. 383, 5 September 1996)

Malaria research suffering relative neglect, study claims

Malaria research is drastically underfunded compared to other diseases, such as HIV and asthma, when its relative incidence and its global death toll are taken into account. That is the conclusion of a report published by the Unit for Policy Research in Science and Medicine (PRISM) of Britain's Wellcome Trust. The report* also suggests the results of research have not been sufficiently exploited.

Malaria kills between 1.5 million and 2.7 million people a year, particularly in sub-Saharan Africa; other regions with major problems include India, South America and the Far East. The prevalence and distribution of the disease is increasing. The *Anopheles* mosquito vector is gaining greater resistance to insecticides, and the principal infectious agents, *Plasmodium falciparum* and *P. vivax*, are becoming more resistant to antimalarial drugs.

The PRISM analysts looked at global expenditure on malaria research over the past decade, and associated international publishing activity. They asked 200 members of the malaria community—including researchers, clinicians, health service personnel, industrialists and administrators—about their views on current practice, and the most useful directions for research.

Total global expenditure on malaria research in 1993 was US$ 84 million—equivalent to $42 for every death. Calculations for HIV/AIDS gave $3,274 for each death, and $789 for asthma.

These figures confirm how research funding places a disproportionate priority on diseases with a high profile in the West. It has been received wisdom that tropical diseases get less attention than others. But PRISM has now produced "proper facts and figures that people can use to make policy decisions".

The situation appears to be getting worse. Global funding for malaria research declined significantly between 1985 and 1994, largely reflecting a drop in US investment as it reduces its military involvement overseas.

Nevertheless, more than half of all funding in 1993 still came from the United States, particularly the US Agency for International Development and the National Institute of Allergy and Infectious Diseases.

The report shows that international publishing activity reflects the relatively low funding. While Britain's global share of publications increased from 14 per cent in 1984 to 18 per cent in 1994, that of the United States fell from 42 to 34 per cent.

Obstacles to better exploitation, according to the survey, include poor orientation of research programmes to practical problems and public needs. Topics identified as having the best prospects for advancing understanding over the next five years were the genetics and biology of *Plasmodium* and disease epidemiology. (Source: *Nature*, Vol. 383, 26 September 1996)

Joining forces to beat HIV

The 11th Inernational Conference on AIDS, in Vancouver, Canada, opened with a mood of cautious optimism. Promising early results from a new breed of treatments have lifted the gloom that has characterized previous meetings.

The optimism follows newly-released clinical data from combination therapists—treatments that combine new protease inhibitor drugs, such as *Invirase* (Roche), *Crixivan* (Merck), *Norvir* (Abbott) and *Viracept* (Agouron), with one or more of the older drugs like AZT, ddc and 3TC.

The first generation of drugs aimed at HIV attacked the virus during its cycle of replication. However, HIV mutates very quickly during this process and can change into a drug-resistant form. The new protease inhibitors also attack HIV during replication, but at a different point. The idea behind combination therapy is to mount a two-pronged, or even three-pronged, attack on the virus and overwhelm it before it can mutate.

The results of the trials have been astonishing AIDS researchers. Data released at the conference showed that combination therapies involving *Viracept, Crixivan* and *Norvir* have led to near-undetectable levels of HIV in the bloodstream during periods of up to 60 weeks, and an increase in the number of CD4 immune system cells. A trial involving Roche's *Invirase* and ddc found that patients were 70 per cent less likely to die when treated with a combination than when treated by one of the drugs alone.

*Anderson, J., Maclean, M. & Davies, C., PRISM Report No. 7. *Malaria Research: An Audit of International Activity*. (Wellcome Trust, London, 1996. £10.)

However, researchers are urging caution. No-one yet knows whether the effects of these drugs are permanent, or how toxic they are over the long term.

The reality of the pandemic is daunting. The United Nations estimates that nearly 22 million people are living with the virus, which has led to about six million deaths since the early 1980s. Around 90 per cent of the 8,500 new people infected with HIV every day are in the developing world and, with new drug therapies costing around $15,000/a, these new treatments are out of their reach. (Source: *Chemistry & Industry*, 15 July 1996)

TB returns

Tuberculosis (TB) killed more people in 1995 than in any other year in history. And it is on the rise, according to a recent report (*TB: Groups: Groups at Risk*) issued by the World Health Organization (WHO, Geneva). Nearly three million people died from the disease in 1995, over 30 per cent more than in any of the worst epidemic years at the turn of the century.

Three years ago, WHO declared TB "a global health emergency", but today the disease is more threatening than ever, having outpaced the modest efforts of the past few years that followed years of neglect in the 1970s and 1980s. TB is now the leading infectious killer of both children and adults and the main cause of death in those who are HIV-positive. It is epidemic across a third of the globe and according, to the WHO report, if it continues unabated, it will affect up to half a billion people over the next 50 years. An article (*New Engl. J. Med* 334:933-938, 11 April 1996) last spring described the transmission of multidrug resistant TB (MDR-TB) during a long flight and confirms that TB is a world-wide threat. "There is nowhere to hide," warns Arata Kochi, director of the WHO global TB programme.

Not only is there nowhere to hide, there is nothing new to hide behind. The most recent drug for TB—rifampicin—was approved nearly a quarter of a century ago and the vaccine for TB, BCG (Bacillus-Calmette-Guérin) has changed little in 75 years.

A dearth of genetic approaches—such as an easy way to knock out genes in the causative organism, *Mycobacterium tuberculosis*—has slowed down TB research. But now such approaches are emerging, and the prospects for TB patients—in the long term, at least—seem considerably brighter. It was only in January 1996, for instance, that the first DNA vector for TB was developed. The first good animal model for the chronic form of the disease—the Philippine cynomolgus monkey, *Macaca fasicularis*—was also only recently described (*Nature Medicine* 2:430-436, 1996).

The sequence of the *M. tuberculosis* genome is expected to be completed shortly by Genome Therapeutics (Boston, MA) and the Sanger Centre (Cambridge, UK)—work funded by the Wellcome Trust (London) and the UK Medical Research Council (London).

One of the most advanced vaccine projects involves the London-based biotechnology company, Stanford Rook, and the TB Prevention and Control Research Unit at Case Western Reserve Medical School (Cleveland, OH), which is NIAID-funded. Stanford Rook is testing a vaccine based on *Mycobacterium vaccae*, a soil-based saprophyte related to *M. tuberculosis*. The vaccine, SRL-172, which is inexpensive to manufacture, is being tested in a 370-patient phase III trial in Durban (South Africa) and in a parallel study in London. This is the first major study of a new TB treatment in the United Kingdom in 30 years. The US National Institutes of Health (Bethesda, MD)-sponsored phase II trials of the heat-killed vaccine are under way in Uganda, and at Albert Einstein with HIV-positive patients, including children, to demonstrate that the vaccine can prevent MAC, which kills at least 30 per cent of those infected in the United States. These, and a third trial in Victoria (Brazil), are being coordinated by Jerrold Ellner of Case Western.

Stanford Rook believes that investing in TB treatment can and will pay off. Although US interest in the vaccine is still limited, Stanford sees a great interest in, and market for, the vaccine in Europe, Africa, the former Soviet Union and India. A product license application has been filed by Stanford Rook for the vaccine, and the company is currently seeking marketing partners. (Extracted from *Nature Biotechnology*, Vol. 14, September 1996)

Research confirms risks of transgenic crops

Two recent research papers from Nature and the New England Journal of Medicine confirm the reality of risks of genetically engineered crops in two areas—weediness and allergenicity.

Genes from a transgenic crop move quickly into weedy populations

Danish scientists have shown that herbicide-tolerance genes from engineered oilseed rape (canola) became established in weedy populations after just two generations of interbreeding. The results reported in the 7 March 1996 *Nature* showed for the first time that genes from transgenic crops could become established *quickly* in weedy populations.

In the study, canola plants, which had been engineered with a herbicide-tolerance gene to make it resist a herbicide, were allowed to interbreed naturally in field experiments with weedy relatives. Many of the hybrids produced by the crop/weed interbreeding turned out to be herbicide tolerant, that is, they carried the herbicide-tolerance gene from the engineered crop. The scientists then bred some of the transgenic herbicide-tolerant hybrids with weedy relatives in what is called a backcross. The backcross produced many herbicide-tolerant plants that closely resembled the wild, weedy parents. In other words, just two generations of interbreeding produced herbicide-tolerant weeds that could resist the same herbicide to which the crop was tolerant—obviously creating a weed control problem for farmers growing the herbicide-tolerant crop.

Scientists have disagreed on the seriousness of the risk of moving genes into wild, weedy relatives. Ecologists have long predicted that transgenes could become established in wild populations and that some of the new genes in wild populations may have ecological impacts, just as the Danish study showed. But some scientists have suggested that the risk would be minimal because crosses between genetically engineered crops and weeds would produce hybrids too weak and infertile for further interbreeding. Unable to get over the barrier presented by the weak hybrids, the new genes would have trouble moving into wild populations. This study shows that at least in one case the hybrids were no barrier at all. (Source: T. Mikkelsen et al., "The risk of crop transgene spread", *Nature* 380:31, 1996; *The Gene Exchange*, June 1996)

Genetically engineered soybeans are allergenic

The *New England Journal of Medicine* of 14 March 1996 reported that an allergen transferred from Brazil nut to soybean by genetic engineering retained its allergenic

properties and caused a reaction to the serum of people sensitive to Brazil nut. This result confirms another predicted risk of genetic engineering: that foods previously safe to eat may become dangerous as a result of the transfer of allergenic proteins. Allergic reactions are immune system responses to substances that most other people tolerate. Food allergies cause reactions ranging from mild, such as erratic heart beats, to serious, such as seizures and even death.

The NEJM study was undertaken after Pioneer Hi-Bred, a seed company, began developing a transgenic soybean containing a new protein from Brazil nut. The protein was being added to the soybean to improve its nutritional makeup. The Brazil nut protein is rich in methionine, an amino acid essential in human and animal nutrition. When the blood serum from persons allergic to Brazil nut was tested against engineered soybeans and Brazil nut, the reactions were the same, indicating that the engineered soybean contained the Brazil nut allergen. Non-engineered soybeans did not react with the blood serum. On skin-prick testing, three people allergic to nuts reacted positively to engineered soybean extracts containing the Brazil nut protein but negatively with non-engineered soybeans. (The experimenters decided not to do feeding tests with the transgenic soybean because the allergic persons reacted to Brazil nuts with life-threatening responses.) Once Pioneer Hi-Bred learned of the allergenicity of the transgenic soybean, the company decided not to market the product. (Source: J. Nordlee et al., "Identification of a Brazil-nut allergen in transgenic soybeans", *The New England Journal of Medicine*, 334: 688-92, 1996; *The Gene Exchange*, June 1996)

Global biotechnology conference

Over two years ago the Agricultural Biotechnology for Sustainable Productivity (ABSP), began the process of planning a global conference on agricultural biotechnology for 1997. The Agricultural Biotechnology for a Better World conference, in keeping with the ABSP philosophy, will take a highly integrated approach in its examination of the application of agricultural biotechnology in developing country settings. The conference will focus on the opportunities and obstacles involved in the development and transfer of biotechnology products.

The global conference will be held from 28-30 April 1997, in Pacific Grove, California, on the Monterey Peninsula. The three-day conference will focus on pathways to commercialize agbiotechnology products, that is, the process whereby a crop product is researched and developed, tested in the field, provided to growers in the form of more resistant sustainable alternatives to varieties currently in use, and finally, marketed to consumers. The conference programme will be arranged in a commodity-oriented fashion. Presentations and panel discussion will examine pathways to commercialization of biotechnology products for major commodity groups such as cereals, roots and tubers, legumes, horticultural crops and high-value tropical crops. Conferees will examine the course of product development through matters of science, policy and law. Biosafety guidelines, intellectual property considerations, and the particulars of technology transfer are all issues that will be discussed.

Concurrent with the presentation session will be an open, interactive poster session where conference participants will have the opportunity to present information on their own projects and programmes.

For additional information: Mr. Dean Norton, Conference Coordinator, Michigan State University, ABSP Project Global Conference Secretariat, 414 Plant & Soil Sciences Building, East Lansing, MI 48824-1235, USA. Tel.: 517-353-2290; Fax: 517-432-1982. E-mail: global97@pilot.msu.edu (Source: *BioLink*, Vol. 2, No. 4, 1996)

C. COUNTRY NEWS

Canada

Ag Canada approves 113 field trials

Approvals for 113 field trials of plants with novel traits have been granted by the Food and Inspection Branch of Agriculture and Agri-Food Canada as of 18 June 1996. The trials, which are taking place over 747 sites, are being carried out for 14 genetically modified crops by 20 companies and organizations.

Canola is the most widely tested crop, with 483 trial sites, followed by corn (107), potato (93), and alfalfa (30). The largest number of trials are taking place in Saskatchewan (224), followed by Alberta (186), Ontario (152), and Manitoba (95). A number of new species are being tested for the first time this year, including Ethiopian mustard, cherry, and grape vine.

The majority of trials are evaluating herbicide resistance in crops (569), although these trials involve multiple testing sites for just 52 submissions. Other trials are evaluating insect and viral resistance, stress tolerance and nutritional changes. The trials involve plants altered through three different biotech processes, although *Agrobacterium* transformation is the most commonly used method. A number of trials involve backcrossing to transgenics, which reflects decisions to advance modified lines into varietal development.

Contact: Simon Barber, Agriculture and Agri-Food Canada, Plant Protection Division, Nepean, Ontario K1A 0Y9. Tel: 613:952-8000, ext. 4390. (Source: *The AgBiotech Bulletin*, September 1996).

Programme for agricultural cooperative education

The College of Agriculture at the University of Saskatchewan has introduced a programme for agricultural cooperative education (PACE). PACE is a three-way partnership between students, employers, and the college involving alternating semesters of academic education with planned and supervised related work experience in business, industry, or government. While providing students with opportunities for experiential learning, the programme also gives employers access to well-motivated employees for short-term projects, or for evaluation for later longer-term employment.

Contact: PACE, College of Agriculture, University of Saskatchewan, 51 Campus Drive, Saskatoon, Saskatchewan S7N 5A8. Tel: 306/966-7766; Fax: 306/966-7788; e-mail: PAGE@usak.ca; home page at http: //www.ag.usask.ca/cofa /PACE. (Source: *The AgBiotech Bulletin*, September 1996)

Test for survival of transgenic micro-organisms studied

As interest in the ability to genetically modify micro-organisms for use in agriculture, forestry and environmental applications has increased in Canada, say federal authorities, there have been a number of requests to government regulators for approval to release these micro-organisms to the open environment. Regulators are responsible to assess the risks posed by such releases, including the long-term persistence or survival of the micro-organism.

Environment Canada and Agriculture and Agri-Food Canada are sponsoring a project involving a field test of a genetically engineered micro-organism called *Pseudomonas aureofaciens*. The purpose of the field test is to study the ability of a simple laboratory procedure, originally developed at the University of Maryland, to accurately predict the survival of the micro-organism in the field before actually releasing it.

The test involves the first multi-site release of a genetically modified micro-organism in Canada. The soil-borne micro-organism being tested was isolated from the rhizo-sphere of wheat. Two genes have been introduced to the bacteria. The genes do not add agricultural or environmentally significant traits; their only function is to facilitate detection for counting purposes.

The Microcosm Validation Project addresses a need for reliable and easily comparable risk assessment data. The generation of empirical data under controlled conditions can be used by regulators to predict the environmental behaviour of micro-organisms with a higher degree of certainty prior to their release.

The University of Saskatchewan is one of four co-operators in the study across Canada. The micro-organism will be released in 8 one metre plots in five locations across the country, including the Saskatchewan Wheat Pool Research Farm in Saskatchewan.

Contact: Dr. Terry McIntyre, Environment Canada. Tel.: 819/994-1105 or Hans H. Yu, Agriculture and Agri-Food Canada. Tel: 613/952-8000. (Source: *The AgBiotech Bulletin*, August 1996)

European Union

Two thousand projects in Europe

Two thousand projects related to the development of transgenic crops are under way in countries of the European Union, according to the report *European Crop Biotechnology*. Cereals, potatoes, and oilseed rape are the chief targets for genetic transformation. Twenty-five per cent of the projects are aimed at disease control or prevention and 9 per cent at alterations of crop quality, while 40 per cent involve basic plant science relevant to the improvement of specific crops. Only 4 per cent of projects have herbicide resistance as a goal. The investigation of new plant breeding techniques is another important area of research.

Despite this research activity, the tighter regulatory environment in Europe means that less research is making its way from the laboratory to field trials than is the case in North America. There were just 500 field releases in Europe between 1991 and 1995; by comparison, some 500 releases occurred in Canada in 1995 alone. The regulatory environment in the EU varies considerably from country to country; France, for example is considerably more liberal in issuing permits for field trials than is Britain or Germany. Subsequently, 30 per cent of field trials occurred in France, 17 per cent in Britain, and just 9 per cent in Germany.

Contact: L.P. Meredith Lloyd-Evans at Biobridge, Cambridge, UK. Fax: 44-1223-566851. (Source: *AgBiotech Bulletin*, September 1996)

EU moves on orphan drugs

Orphan drugs may in future benefit from the same sort of protection within the European Community which is already available in the US and Japan. It will be an either/or choice: if a medicinal product already has orphan drug status in one of those countries, then it will not be eligible for market exclusivity in the EU.

It will take some time to set up the machinery, but a European Commission paper is a significant first step. Moreover, the principle of the EU introducing orphan drug status is already supported in principle by EU member States and the European Parliament, even if there is room for discussions on details. (Extracted from *Biotechnology Business News*, 25 September 1996)

France

French science takes stock

Officials reporting to the French Research Minister, plan to change rules that have so far prevented scientists employed by government bodies such as the Centre National de la Recherche Scientifique (CNRS) and the Institut Nacional de la Recherche Medicale (INSERM), from owning shares in companies they may be working with.

Although the French officials clearly want to encourage scientists to be involved in the entrepreneurial biotechnology sector by amending the restrictions on share ownership, they also want to establish ground rules to ensure that scientists are not seen to personally enrich themselves at the French taxpayer's expense.

Nevertheless, it is precisely this same experience that has underpinned much of the growth of new companies in the UK and US.

French private enterprise is also trying to tempt government-backed scientists into the private sector. Although France clearly has the potential to be a major force in European biotechnology—currently it is home to 79 entrepreneurial bioscience firms, the second highest number in Europe after the UK—many observers believe that the country's high-quality science base is currently underutilized. A new forum, dubbed Biotech France (Paris), has now been established by French biotechnology chief executives and venture capitalists to provide a starting point for scientists looking to establish new businesses as well as a lobbying focus for French biotechnology. (Extracted from *Nature Biotechnology*, Volume 14, September 1996)

India

Scientists back Indian patent bill

India's scientists are lending support to a new bill on patents, which the Government proposes to introduce in the parliament session. Among other things, the legislation will allow patenting of plant varieties, man-made micro-organisms, and gene sequences yielding new products.

A group of leading biologists, meeting recently under the umbrella of the Indian National Science Academy has voiced concern over the delay in amending the 1970 Act, as India has promised to do to qualify for membership of the World Trade Organization. (Source: *Nature*, Vol. 383, 12 September 1996)

Israel

Israeli biotech companies

Israel possesses a strong concentration of biotech businesses for a small country for a number of reasons. First and foremost, it is home to a large percentage of scientists, 30 per cent of whom specialize in life sciences. Additionally, the Israeli Government has traditionally provided significant incentives to new businesses, especially those with an immigrant work-force or management. While Israel's newly elected prime minister, Benjamin Netanyahu, has vowed to trim government, he has also stated that he is committed to building a free-market economy and will encourage domestic business growth and trade abroad. Despite recent financial upheavals in Israel, prospects for business are generally seen to be positive.

Some statistics indicate that Israeli biotech companies are able to bring products to market more rapidly and at lower cost than elsewhere. For example, the average time to market in Israel is 3 to 5.3 years, compared to 7 to 15 years in the US, Japan and Europe.

Biotech in Israel began in 1978 with three biotech companies. Today there are over 150, including those that focus on pharmaceutical and medical products; human diagnostics; cell and gene therapy; veterinary products (including vaccines, drugs and diagnostics); agricultural products; marine and aquaculture; research products; environmental; plant diagnostics; and health care and cosmetics.

Most Israeli biotech companies are small, private concerns and are located not only in the four major cities but also in the suburbs, collectives and development towns. All of Israel's universities have biotech R&D arms and they feed technology to outside companies as well as maintaining growing biotech businesses of their own.

Hebrew University's (HU) company, Yissum (Jerusalem), files for 30-40 patents per year. Yissum signed 120 contracts in 1995, 44 of which were with US concerns and 21 with European companies and universities.

Areas of ongoing research include Alzheimer's and other CNS diseases, wound healing, infectious diseases, cancer and osteoporosis. Human therapeutics and diagnostics account for approximately 50 per cent of all HU biotech activity and 70 to 90 per cent of all US biotech investments and sales.

A recently developed HU Mab test measures the way patients produce RNA coating for IL-2 and gamma interferon. The test can determine the likelihood of recurrence of bladder cancer, as well as predict the outcome of acute lymphocytic leukaemia and systemic lupus erythematosus. Scientists at HU's agriculture school in Rehovot have developed transgenic plants that are drought-tolerant and virus-resistant, and, in a joint venture with the US, are focusing on producing protective Trichoderma fungi super-strains that can prevent damping-off disease in young seedlings.

Other university-affiliated biotech companies are located at Ben Gurion University of the Negev, Haifa's Technion, Tel Aviv University (Ramot) and Rehovot's graduate science institution, the Weizmann Institute (Yeda), as well as at a nearby science part in Rehovot that houses other biotech companies. In addition, Hadassah Hospital,

which is affiliated with HU, has its own biotech arm, Hadasit Medical Research Services and Development, which specializes in gene therapies, oncology, neurology and diabetes. It also conducts clinical trials for a number of US and European companies. (Extracted from: *Genetic Engineering News*, 15 September 1996)

Japan

Japan to boost science and technology

The Japanese cabinet has approved a plan to boost government spending on science and technology research. Under the plan, proposed by an advisory panel to prime minister Ryutaro Hashimoto, public spending on science and technology would total ¥17 trillion over the five years to 2000, a 50 per cent rise from the previous five years.

The plan does not specify just how much will be spent in each of the five fiscal years, but a Science and Technology Agency official said government spending would most probably be about ¥ 4.3 trillion in 2000, double the level in 1992.

The panel's report also urged introducing more competition to public research institutes, improving links among the private and public sectors and increasing the number of foreign researchers. (Source: *Biotechnology Business News*, 5 July 1996)

Biotechnology R&D projects in FY 1996 industrial and scientific R&D programme

The 1996 Industrial and Scientific R&D Programme implemented by the Agency of Industrial Science and Technology includes four R&D projects relating to biotechnology: technology to manufacture high-functional chemical products (utilization of marine and tropical organisms), technology to apply functional protein molecular assemblies, technology to manufacture and utilize complex carbohydrates, and technology to create accelerated biological functions (time-machine biotechnology).

Complex carbohydrates, fundamental components of organisms, have vital functions such as substance recognition which cannot be achieved only by nucleic acids, proteins or lipids. Complex carbohydrates adhere to enzymes which immobilize carbon dioxide and stimulate reaction promoting functions, so the application of these complex carbohydrates has great potential in the industrial sector. The aim of the project is to establish technologies to manufacture and utilize these complex carbohydrates.

Technology for the high-sensitivity detection of carbohydrate chains, the efficient isolation of carbohydrate chains, and basic technology using various carbohydrate chain recognition substances to identify the base sequences of residual carbohydrate radicals from non-reduced terminals will be established.

An artificial mutation selection system (Experimental evolution system) is to be established, based on knowledge on the molecular level of the mechanism of biological evolution, to establish new fundamental biotechnologies for creating excellent biological functions for target proteins.

Research is to be advanced in connection with the experimental evolution system of proteins to develop a method to investigate the fitness landscapes. Investigations are to be conducted, and an efficient adaptive walking system based on fitness landscape is to be developed. (Source: *JETRO*, October 1996)

The Netherlands

IntroGene signs gene therapy deal

A collaborative agreement between Dutch biotechnology company IntroGene and the University of Leiden will potentially ensure that the university's basic gene therapy research can move more speedily to preclinical and clinical evaluation by the IntroGene gene therapy development team.

The University of Leiden gene therapy research team is associated with a total of 14 working groups in the university developing programmes identifying genetic involvements in oncologic and cardiovascular diseases, immunological disorders as well as overtly genetically inherited diseases like haemophilia and muscular dystrophy.

IntroGene will, under the agreement, have exclusive commercial rights to products developed as a result of this collaboration. The university will share with IntroGene both the risks of early-stage development as well as the rewards of commercial success.

Among the techniques under development at IntroGene are gene therapies for a number of congenital and acquired diseases including Gaucher Disease, Aids and cancer using a range of different viral vector systems. (Extracted from *Biotechnology Business News*, 11 September 1996)

Singapore

New biotechnology institute

A new Institute of Molecular Agrobiology (IMA), affiliated with the National University of Singapore (NAS), will work with colleagues in the Chinese mainland to develop, among other things, genetically altered pest-resistant cotton.

IMA is one of several new institutes set up by the Singapore Government to develop a research and development infrastructure. Others include the Institute of Molecular and Cell Biology, which has already established its name in the world of science, and the Institute of Microelectronics, which is headed by Bill Chen, a returnee from Bell Laboratories.

IMA has recruited several young Chinese mainland scientists from Europe, where they had encountered a "glass ceiling" with no job opportunities beyond the postdoctoral level.

China is the world's leading producer of cotton, but production has fallen drastically from 28 million bales in the mid-1980s to 18 million bales. Under a joint venture between Delta and Pine Land Company and Monsanto of the United States with Imagen Holdings, an investment arm of IMA, Monsanto technology will be used to introduce a bacterial gene into cotton that produces a toxin to kill the pest. Some adaptation of the US technique is required because Chinese cotton differs slightly from the US variety. The "Singapore-China" connection between Chinese scientists will help the US company license its technology with the Chinese Government, says IMA acting director Hong-Woo Khoo.

There are several other projects on agricultural products in progress under a Singapore-China Biotechnology Programme established between IMA and the Chinese Academy of Sciences. (Extracted from *Nature*, Vol. 383, 5 September 1996)

United Kingdom

Watchdog on human genetics

The UK Government is to set up a Human Genetics Advisory Commission to oversee developments in human genetics and foster public confidence in the new science.

The advisory commission will comprise a group of eminent independent people who will report their findings periodically to government ministers. The Government will be able to seek the commission's advice on particular issues and reports will be published. It will be supported by a joint secretariat from the Office of Science and Technology and the Department of Health.

The watchdog body will monitor gene patenting, genetic medicines and the use of genetic information by insurance companies and employers. In addition, it will also consider ethical issues such as the potential to create a "genetic underclass" and "designer babies". (Extracted from: *Biotechnology Business News*, 25 June 1996)

Crusading from the biosciences industry

The UK Department of Trade and Industry has put forward new measures to steer UK biotechnology research into commercial application. The "Crusade for Biotechnology" aroused cautious optimism in the biotech industry.

An earlier report on European biotechnology showed that Germany was rapidly closing the gap on the UK's lead in Europe.

The Medical Research Council plans to raise £25 million over five years from private sources to plough into an MRC Seed Investment Fund, "UK Medical Adventures". The scheme is hoped to encourage university scientists to set up biotech firms and commercialize their research.

The Scottish Office is to play a similar rote by establishing the "Scottish Equity Partnership". This aims to raise around £25 million from private sources for lump sum investments of up to £500,000 in Scottish businesses.

Another part of the scheme is to expand the Biotechnology Means Business (BMB) initiative launched last year. (Extracted from *Chemistry and Industry*, 1 July 1996)

United States of America

Register to fight bio-terrorists

A US biological institute has proposed a new regulation to restrict the transport of infectious agents. The proposal follows concern over threats of biological terrorism.

The regulation, which is likely to come into force in September, covers 40 pathogens and toxins which "have the potential for causing mass destruction or widespread disease in humans". The list includes the Ebola virus and the bacteria that cause bubonic plague, botulism and anthrax. It would require all shippers and recipients of the agents to register with the federal government so that all transfers of such material would be recorded.

The Centers for Disease Control and Prevention (part of the Public Health Service) based in Atlanta, Georgia, proposed the regulation, after being disturbed by two cases of potential bioterrorism. (Extracted from *Chemistry & Industry*, 1 July 1996)

Biotechnology therapeutic medicines and vaccines under development

Two-fifths of the 284 biotechnology medicines in development are for different forms of cancer, including cancer of the brain, colon and breast, according to a new survey by the Pharmaceutical Research and Manufacturers of America (Washington, D.C.).

PhRMA's 1996 "Biotechnology Medicines in Development" survey, the number of biotechnology drugs has increased 21 per cent—from 234 in development in 1995 to 284 this year. The number of companies involved in the research has increased 11 per cent to 113 firms.

The fastest-growing category of biotechnology medicines is human gene therapy, with 28 products listed in development this year, compared to 17 in the last survey. Gene therapies are being developed for cystic fibrosis, cancer, AIDS and Gaucher's disease.

The number of biotechnology-derived vaccines in development has increased 44 per cent to 62 products for cancer, AIDS, rheumatoid arthritis, sickle cell anaemia, osteoporosis, whooping cough, multiple sclerosis, genital herpes, hepatitis B and other ailments.

The new survey shows that biotechnology drugs are being tested for the first time against the common cold, Parkinson's disease, Huntington's disease, sickle cell anaemia and osteoporosis. (Extracted from *Genetic Engineering News*, 15 September 1996)

New National Rice Germplasm Center

The US Department of Agriculture's Agricultural Research Service (ARS) rice scientists will, for the first time, be able to conduct collaborative, multidisciplinary research involving molecular biology, genetics, plant physiology and pathology, cytogenetics, and chemistry, all housed under a new National Rice Germplasm, Evaluation, and Research Center scheduled to open at Stuttgart, Arkansas by October 1997.

The facility will be located on 5.8 acres of land near the University of Arkansas Rice Research and Extension Center. Scientists at the Center will evaluate potentially valuable characteristics of rice varieties from the 16,476 accessions now held in the USDA/ARS Rice Germplasm Collection at Aberdeen, Idaho. Studies at Stuttgart already have revealed that up to 500 rice varieties from the collection may have some natural ability to repel weeds. One of the first goals of the Center's staff will be accelerated efforts to transfer feed blight resistance using molecular techniques.

For further information, contact: Robert H. Dilday, National Rice Germplasm Evaluation and Enhancement Center, Highway 130 East, Agricultural Research Service, USDA, Stuttgart, Arkansas 72160, USA. Tel: +1-501-673-2661. Fax: +1-501-673-4315. E-mail: A03CSTUTTGA @ATTMAIL.COM. (Extracted from *Diversity*, Vol. 12, No. 2, 1996)

D. RESEARCH

Research on human genes

Specialists close in on DNA behind cancer's destruction of skeletons

Scientists are closing in on some of the genes and gene products that cause tumours to spread like wildfire when they metastasize from organs into bones, resulting in the agonizing destruction of a patient's skeleton.

Bone metastasis, one of the most painful complications of the disease, occurs in virtually all cases of breast and prostate cancer and about 75 per cent of all lung cancers.

Bone is loaded with growth factors that are released when it breaks down, either through injury or disease. Tumours have mechanisms that bore bone lesions. This activates the skeleton's repair mechanism, a flood of growth hormones designed to help bone cells knit, but when a tumour is present, the growth hormones stimulate the cancer cells.

Studies in which human cancer cells were injected into the hearts of nude mice showed that tumours with a molecule called src tyrosine kinase (src) appear to be more aggressive, able to stimulate production of a bone degrading substance called parathyroid hormone related peptide (PTH-rP).

Bones react to the breakdown by secreting several growth factors to repair the damage. The result is that the tumours are bathed in growth factors, such as TGF-beta, that either accelerate their growth or enhance their destructive power.

In his experiment, Gregory Mundy, Professor at the University of Texas Health Science Center in San Antonio, Texas, injected breast tumour cells that had been altered genetically to produce a high level of the src tyrosine kinase receptor. Mice who received these cells had more bone lesions than those receiving malignant cells that produced low levels of the molecule. Cells with the most tyrosine kinase activity were also able to grow faster in the test tube.

Mundy has also injected mice with tumour cells that were unresponsive to TGF-beta or treated the test animals with antibodies to block production of PTH-rP. Both strategies reduced bone damage and the size of tumours and extended the lives of the mice.

Based on these findings, Mundy believes that the src gene will be a good target for the development of drugs or antibodies designed to prevent bone metastasis.

Mundy hopes to develop a drug, like tamoxifen, that can be used to inhibit cancer spread after surgery. (Extracted from *McGraw Hill's Biotechnology Newswatch,* 16 September 1996)

Hybrid DNA-RNA efficiently repairs gene

Cancer researchers have designed a hybrid DNA-RNA molecule that can zero in on a mutation in a human chromosome and correct it with what is being deemed astounding efficiency. They demonstrated the technique by correcting the point mutation that causes sickle-cell anaemia in cells from the blood of patients with this genetically acquired disease.

The team includes research associate Allyson Cole-Strauss and associate professor of pharmacology Eric B. Kmiec at Thomas Jefferson University in Philadelphia; colleagues there and at Cooper Hospital University Medical Center in Camden, N.J.; and researchers at Cornell University School of Medicine in New York City.

Sickle-cell disease is caused by a single mutation in the gene for the β-strand of haemoglobin. The mutated gene contains a thymidine (T) instead of an adenosine (A). The researchers designed a short (68-unit) oligonucleotide segment containing both DNA and RNA residues that loops around to form a double-stranded segment.

The chimera contains a sequence of bases—both DNA and RNA—that contain the normal sequence of the gene. These align as closely as they can to the corresponding bases in the gene to form a triple helix.

The two make a perfect match except at the mutation where their mismatch "causes a pucker or distortion in the helix that is recognized by the normal DNA repair system of the cell, which excises the T on the gene and replaces it with an A", Kmiec says. The chimera is designed to be very stable, particularly to degradation by nucleases. A number of scientists suggest that this chimera works so well simply because it stays in the cell long enough to find its target.

The researchers have not "cured" anyone with sickle-cell disease. The cells they have treated—lymphoblastoid cells—do not make haemoglobin. But all cells in the body contain the same chromosomes, and these are convenient for experimental purposes. The team has preliminary data that the procedure also works in a type of stem cell called $CD34^+$, which does develop into a haemoglobin-producing blood cell. (Extracted from: *Chemical and Engineering News*, 9 September 1996, p. 11, by Rebecca Rawls)

Test demonstrates for first time cell damage from cigarette smoke

A new in vivo assay that is both non-invasive and highly specific has shown for the first time that cigarette smoke promotes free-radical attacks on a molecule that helps support cell membranes.

The technique also demonstrates that vitamins C and E can bate that attack, thus opening the door for a means to test and to titrate doses of drugs and other therapeutics believed to quench free radicals.

The destructive action of free radicals, called oxidative or oxidant stress, has been implicated for years in cancer as well as in cardiovascular, neurological and immunological diseases—even aging. In the past few years, geneticists have found that carcinogens in cigarette smoke can kink the DNA in lung cells with multi-ringed, aromatic additions to the double helix.

Free radicals—highly unstable forms of oxygen molecules—are the likely vehicle. It is still unclear precisely what role an unsaturated fatty acid called arachidonic acid plays in the architecture of cellular membranes.

What is known is that oxidative stress can convert the acid to isoprostanes (enantiomers, or mirror-image isomers, of prostiglandins). These metabolites, researchers discovered, remain stable and are excreted in urine.

Garret FitzGerald, head of pharmacology at the University of Pennsylvania Medical Center, and colleagues used techniques in gas chromatography and mass spectrometry to quantify levels of 8-epi-prostiglandin F2-alpha in

healthy smokers, non-smokers, and former smokers who used nicotine patches.

The control group of age- and sex-matched non-smokers averaged 64 +/-5 picomoles of 8-epi-PGF2-alpha per millimole of creatinine (a waste product of protein metabolism). Chronic smokers averaged twice as much, with their range linked to how much they smoked.

A group of five heavy smokers who ingested two grams of vitamin C a day, however, saw their levels of the isoprostane drop from 195 to 134 pmol/mmol (+/-about 38) in five days. Vitamin E had little effect over the same period, though FitzGerald added that subsequent, longer studies indicate a similar decrease. Six heavy smokers who traded cigarettes for nicotine patches regained normal levels of the isoprostane in two weeks—thus, as the researchers suspected, nicotine itself does not spawn free radicals. (Extracted from: *McGraw Hill's Biotechnology Newswatch*, 5 August 1996)

Damage to childhood eye tumour gene can predict course of lung cancer

Measuring damage to one gene may help doctors predict if a person has early stage lung cancer, how virulent the cancer is or if the person is predisposed to the disease.

Professor Antonio Giordano at Jefferson Medical College of Thomas Jefferson University, Philadelphia, said injury to a gene related to retinoblastoma—an eye tumour usually seen in babies—has been linked to lung cancer.

The more damage to the gene, the more ominous is the prognosis for the patient, Giordano said. "In very aggressive lung cancer, we see almost none of the Rb-2/p130 gene", he said.

The Rb-2/p130 gene normally suppresses the growth of cancer by interfering in the way abnormal cells divide, Giordano said. The gene is found throughout the body and when it works well cancer does not develop, he said.

However, scientists believe that environmental insults—cigarette smoking or industrial pollutants—can damage the gene, permitting cancers, especially lung cancer, to develop.

Giordano said Rb-2/p130 is related to the gene which is known to be involved in the development of retinoblastoma—which when untreated can cause blindness and death in children. Giordano and his colleagues found that when they looked at 77 human lung cancer samples they were able to correlate the aggressiveness of the tumour to the amount of Rb-2/p130 gene in the tissue. That finding will lead to development of a test which can determine how treatable a cancer is, Giordano said, allowing doctors to treat the tumours accordingly.

Giordano also predicted a test will be developed to screen people who are subjected to pollutants or cigarette smoke to determine if they have early cancer—at a stage where it is treatable and curable. Another test could determine the susceptibility of a person to lung cancer, especially if there is cancer in his or her family, Giordano said. (Extracted from *McGraw Hill's Biotechnology Newswatch*, 15 July 1996)

p53 gene therapy for lung cancer shows promise

The published results of a clinical trial in which gene therapy was used to treat lung cancer suggest that the technique could have a real future in the more widespread treatment of specific types of human cancers.

Most of the known genetic lesions associated with cancers cause either a grain of transforming function or loss of tumour suppressor function by the gene's product, explains Jack Roth and colleagues from the Anderson Cancer Center (USA).

Tumour suppressor genes themselves are among those which can undergo loss of function through genetic mutation or deletions, causing carcinogenesis. Theoretically, at least, replacing a non-functional copy of the tumour suppressor gene with a functional copy could restore the cells' normal growth, halting proliferation of the cancer.

One such candidate for replacement through gene therapy is the tumour suppressor gene, *p53*, that is frequently found to be non-functional in human cancers. About half the one million or so new cases of cancer diagnosed every year in the USA carry a mutation in one copy of the *p53* tumour suppressor gene and exhibit loss of the other wild-type allele. More specifically, among the 170,000 new cases of lung cancer, the frequency of *p53* mutations is estimated to be 56 per cent (90 per cent in small-cell lung cancer, and about 55 per cent in non-small cell lung cancer).

Previous studies have shown that correction of a single genetic abnormality in human cancers with multiple genetic lesions is sufficient to cause regression of the tumours. This fact was "critical" to the development of the approach taken in the reported gene therapy trial.

Roth et al. used a retroviral carrier to deliver the normal (wild-type) *p53* gene into tumours in nine patients with recurrent non-small cell lung cancers, by direct injection of the gene into accessible tumours. In all the patients these tumours were associated with *p53* mutations.

Following treatment, seven of the nine patients were suitable for evaluating the effects of the *p53* DNA injections on tumour growth. Three of these showed evidence of tumour regression in their treated lesions, while in another three there was evidence that tumour growth had stabilized. Each of the patients also had untreated tumours which continued to progress through the course of gene therapy, providing an obvious contrast to the stabilization or regression seen in the treated tumours.

No toxic effects attributable to the vector were seen, and none of the non-tumour tissues analysed by polymerase chain reaction (PCR) showed retroviral sequences. Further analysis did show that the efficiency of retrovirus transduction into tumour cells was low, compared with adenovirus carriers, but Roth et al. say their study shows it is sufficient to bring about a therapeutic effect. In some parts of the injected tumour more than 20 per cent of tumour cells were shown to have taken up the virus. (Source: *Biotechnology Business News*, 28 August 1996)

Gene imprinting may lead to new approach in anti-cancer drugs

Imprinting, a phenomenon in which the same DNA appears to behave differently in an individual, may help scientists design new weapons against cancer.

Imprinting is a normal condition in which genes inherited from one parent behave differently from those inherited from the other, even though they are alleles.

When the imprinting process goes awry, the result may be cancer, said Professor Andrew Feinberg of the Johns Hopkins University School of Medicine.

Scientists estimate that imprinting abnormalities may play a role in up to 70 per cent of cancers, said Feinberg.

Feinberg's work has focused on a childhood kidney cancer called Wilms' tumour. Other research groups have identified imprinting abnormalities in adult and other childhood cancers, such as Beckwith-Wiedmann syndrome, which causes prenatal overgrowth and embryonal tumours.

Since this is a relatively new area of investigation, the scientists do not know how many genes are normally imprinted in the human body. So far, they have found about 10, and many of these genes appear to cluster in one chromosomal region and work in concert. (Extracted from *McGraw Hill's Biotechnology Newswatch*, 19 August 1996)

Skin cancer-associated gene identified

Fair skinned individuals, who worry about UV radiation triggering sporadic basal cell carcinoma—the most common form of skin cancer—may take hope. Researchers at Stanford University (Palo Alto, CA) and the University of California, San Francisco have identified mutations in the *patched* gene as a causative factor in this type of skin cancer. The gene product appears to inhibit the Hedgehog family of cell-differentiation signalling proteins, which are active in cell fates, embryonic development, and tissue growth. Because over 750,000 new cases of this type of skin cancer are reported every year in the USA alone, development of a therapeutic based on this pathway, rather than depending on surgery to eradicate the disease, would be in strong demand. Both the *patched* and *hedgehog* genes are licensed to Ontogeny (Cambridge, MA). (Source: *Nature Biotechnology*, Volume 14, July 1996)

Research team finds first direct evidence of genes for stroke

A team of scientists has found the first direct evidence for the existence of genes linked to stroke, one of the deadliest and most complex afflictions of modern life.

The team, led by Klaus Lindpaintner of Brigham and Women's Hospital in Boston, identified three loci in a genome-wide screen of specially bred rats that point to genes that protect against and raise the risk of stroke.

While it has long been known that hypertension is a major risk factor for stroke, some people with hypertension never suffer a stroke. On the other hand, studies have indicated that there are genetic susceptibilities for stroke, including evidence that men whose mother suffered a stroke were twice as likely to have a stroke compared to men whose mothers never had a stroke.

The researchers studied the second generation offspring of two different strains of equally hypertensive rats. One strain developed stroke if given a high sodium, low potassium diet while the other was stroke-resistant despite being hypertensive and on the special diet. The researchers then performed a genome-wide screen of over 1,000 genetic markers and found a locus on chromosome 1 that showed "a highly significant linkage to the occurrence of stroke", because these rats had early strokes. The group also identified loci on chromosomes 2 and 5 that offered some protective effect against stroke. (Extracted from: *McGraw Hill's Biotechnology Newswatch*, 2 September 1996)

Growth factors may hurt response rates of AML patients

European researchers have found that use of haematopoietic growth factors fails to provide any clinical benefit for patients suffering from acute myelogenous leukaemia.

In fact, researchers administering granulocyte-macrophage colony-stimulating factor (GM-CSF) found significant decreases in the complete response rates of patients receiving the growth factors.

Robert Zittoun of Hotel-Dieu, Paris, said the study attempted to prove two theories for use of GM-CSF in fighting leukaemia: The supposition that growth factors could recruit leukaemia cells into cycle and enhance sensitivity to chemotherapy, and when administered after cytotoxic therapy could stimulate haematopoietic recovery and decrease morbidity and mortality from infection. (Extracted from *McGraw Hill's Biotechnology Newswatch*, 19 August 1996)

Receptor cloned for unknown growth-related hormone

The existence of a second hormone that stimulates the release of pituitary growth hormone has been suspected since 1984, when a hexapeptide was synthesized that synergistically promotes the release of growth hormone. Now researchers at Merck have cloned the receptor for this as-yet-unidentified hormone. Their work paves the way for the design of oral drugs to treat growth-hormone-deficient children and age-related muscle degeneration caused by declining growth hormone levels. To express the receptor and simultaneously provide a sensitive way to detect it, the 32-member team injected into frog eggs mRNA from pig pituitary, mRNA for a G protein believed to be associated with the receptor, and mRNA for aequorin, a protein that illuminates when cellular Ca^{2+} concentration rises. A few days later, they added a spiroindane compound (MK-0677) that mimics the hexapeptide and detected bioluminescence in all of the eggs. This showed the receptor was being synthesized, because binding of MK-0677 causes Ca^{2+} concentration to rise. The group eventually homed in on the receptor. The new receptor, although distinct, "fits into a broad category of G-protein-coupled receptors", says Merck team member Roy G. Smith. (Source: *Chemical and Engineering News*, p. 34, 19 August 1996)

Scientists take DNA to hearts to prevent cellular suicide

In about 20 years, doctors could treat a heart attack by injecting genes into damaged heart muscle that will stop cells from committing "suicide" and by inserting other genes to trick mature heart cells into thinking they are young enough to grow new cells.

Michael Schneider of the Baylor College of Medicine in Houston said that researchers already have the key to one of two locks to developing the genes and are making progress in opening the other.

Geneticists have been looking at the mechanisms of cell division and believe they can develop tools which will allow scientists to make these cells produce new cells to replace damaged and destroyed tissue.

Schneider said that two cell phases are critical to the effort: the "S phase" when the cell synthesizes new DNA and the "M phase" when the cell undergoes mitosis or divides.

Laboratories have resolved the problem of making the cell undergo the "S phase", he said. The M phase, forcing a division of the cell, and in essence creating a new cell is still a challenge.

Aside from this aspect of treating an evolving heart attack, Schneider said scientists are also trying to find the mechanism to stop apoptosis—the condition in which cells undergo what is known as programmed cell death or suicide.

In a heart attack, cells starved of nutrients or cells that receive conflicting message due to the heart attack, die.

The role of gene therapy, Schneider said, would be to express a substance that will prevent this cell death process, thereby limiting heart damage. Schneider has been successful in infecting animal cardiac muscle with cells

containing the new genes using an adenovirus vector. (Extracted from *McGraw Hill's Biotechnology Newswatch*, 5 August 1996)

Research on animal genes

Technique to effectively isolate microsatellite DNA

Japan's National Institute of Agrobiological Resources of the Ministry of Agriculture, Forestry & Fisheries has established a technique to rapidly isolate genes (microsatellite DNA) which enable discrimination of the species of animals.

The base sequence that serves as the marker for discriminating the deoxyribonucleic acid (DNA) in genes is extracted efficiently by utilizing multiple enzymes. In chickens, for example, the DNA is extracted at an efficiency that is about 30 times better than conventional techniques. In addition, the technique is applicable to DNA extraction from cows, pigs and horses whose species cannot be specified simply by visual observation.

The microsatellite DNA consists of a repeated sequence of several base sequences, and the DNA used for discrimination are CA repeat base sequences consisting of repeated sequences of cytosine and adenine. Investigating the lengths of these repeated sequences enables the discrimination of species. However, only one of these repeated sequences exists in as many as 1,000-10,000 base sequences, so extraction is quite difficult.

The National Institute severed a gene extracted from the sperm of an animal into several fragments with a restriction enzyme, then removed the phosphatic acid that links DNA together by using a dephosphatization enzyme. By mixing the vector that induces the gene into *E. coli* and processing the DNA fragments processed with multiple enzymes, the institute induced the DNA into a vector while preventing the mutual bonding of the fragments and succeeded in mass reproduction of the DNA. The experiments used a gene that recognizes the configuration of cytosine and adenine, and a synthesizing enzyme, by which DNA was synthesized successfully that consists of the repeated configuration of cytosine and adenine.

Further details from The National Institute of Agrobiological Resources of the Ministry of Agriculture, Forestry & Fisheries, 2-1-2, Kannondai, Tsukuba City, Ibaraki Pref. 305; Tel: +81-298-38-7002; Fax: +81-298-38-7044. (Source: *JETRO*, October 1996)

Fluorescent jellyfish protein seen as perfect marker for gene tracking

A fluorescent protein that *Aequorea victoria* manufactures appears almost tailor-made as a marker to track genes and proteins in living cells. Delineating the protein's three-dimensional structure is expected to lead to more sensitive markers and additional colours as well to more information on how this highly unusual molecule works in the first place.

Unlike the firefly's luciferase, for example, Green Fluorescent Protein (GFP) requires no co-factors to fluoresce. Such simplicity means that nearly any organism—bacteria, yeast, plant, animal—or cultured cell can express the tag: the protein spontaneously rearranges and glows when exposed to blue light.

George Phillips of Rice University, together with his colleagues, solved the protein's crystal structure. GFP was first expressed in a heterologous system—*E.coli* bacteria—in 1994. The protein is now a tool in nearly 3,000 research laboratories to study genetic processes in such disparate life forms as potato plants, zebra fish and human kidney cells.

Unravelling the structure of GFP has been particularly critical because of its apparently unique shape: 11 strands that form a near-perfect cylinder around a coil of 15 amino acids. Nestled within that alpha-helix is the three-amino-acid chromophore. (Extracted from *McGraw Hill's Biotechnology Newswatch*, 16 September 1996)

Research on plant genes

Waging war on fungi with natural chemicals

For many years, agriculturists have waged war on a particular family of fungus which afflicts a wide variety of plants. Relatively harmless themselves, *Aspergillus* fungi produce a group of substances that can kill plants and cause cancer in animals. Now Japanese researchers think they may have found a way to protect plants more effectively than chemical fungicides.

Aspergillus fungi are found on most grain crops and nuts, and are especially common in Africa and Asia. They produce a group of poisonous compounds called aflatoxins.

Although there are fungicides available that can kill *Aspergillus* fungi, these can be toxic to mammals and can easily produce resistant strains of the fungi, according to the Japanese team. Shohei Sakuda and his team at the University of Tokyo working with scientists from Morinaga and Company in Yokohama, and the Nara Institute of Science and Technology, have discovered a novel natural chemical that they claim may be more effective.

The researchers fermented *Aspergillus parasiticus* with *Streptomyces* bacteria, which are known to be sensitive to aflatoxins. Then, they screened the mixture for compounds that the bacteria might have produced as a defence against the aflatoxins.

The team found one very potent compound, a poly-hydroxylated long chain hydro-carbon compound with a nitrogen-containing ring at one end and two fused sugar-like rings at the other. They have called it aflastatin.

Only small amounts—0.5μg/l—of aflastatin are needed to stop *A. parasiticus* producing aflatoxins. At these concentrations, the fungus still continues to grow. At high concentrations, aflastatin acts like a fungicide and kills the fungus.

However, while scientists think they may be on the way to winning this particular battle, the war is not nearly over. Other fungi produce many compounds apart from aflatoxins. Some of these substances are also toxic and can enter the human food chain if not kept in check. (Source: *Chemistry & Industry*, 16 September 1996)

First plant genome sequencing planned

Four US federal agencies are about to announce an international effort to decode the genetic material of the fast-growing plant *Arabidopsis thaliana*—known as "laboratory cress"—in a move that represents the first complete sequencing of a plant genome.

The National Science Foundation (NSF) will lead the US contribution to the three-year sequencing effort, which will also involve the US Agriculture Department (USDA) and the National Institutes of Health (NIH). The project will be carried out in collaboration with Japan's Kazusa DNA Institute in Chiba Prefecture, east of Tokyo, and a consortium of 17 European laboratories funded through the European Commission.

Information from the sequencing is expected to be used to engineer plants to produce substances ranging from vaccines to chemicals and plastics. As well as boosting understanding of grain development, the project will lead to improvements in bioremediation.

The latter is an area of particular interest to DoE, in view of the huge clean-up tasks it faces around nuclear facilities. The energy department is also interested in the project's implications for the growing use of biomass for energy production. The project is expected to take six years to complete.

In addition to being a rapid grower, with a seed-to-seed cycle that can be as short as three weeks, *Arabidopsis* also has the smallest genome size of any plant, comprising only 100 million base pairs, or 100 megabases. By comparison, the human genome consists of 3 billion base pairs. (Source: *Nature*, Vol. 383, 19 September 1996)

Algae grow using one-step photosynthesis

Experiments with mutant algae are challenging some of the fundamental concepts of plant photosynthesis.

Two mutant strains of algae can carry out photosynthesis and grow even though they lack one of the two photo-systems generally held to be critical for photosynthesis to occur, according to work by Elias Greenbaum, a group leader in the biotechnology research division at Oak Ridge National Laboratory, Oak Ridge, TN, and colleagues there, and by Thomas G. Owens, a spectroscopist and plant biologist at Cornell University.

In work published a year ago the group demonstrated that the mutants could photoassimilate carbon dioxide from the atmosphere and simultaneously produce hydrogen and oxygen from water in a light-driven reaction—the two basic reactions of photosynthesis. The new work demonstrates, in addition, that the algae can use these reactions to divide and grow.

The mutants and Greenbaum's claims about them have caused quite a stir among photosynthesis researchers during the past year. Many questions need to be answered about what is going on in these organisms—including the quantum efficiency of the process and a detailed description of the reaction pathways involved—before the findings are likely to be widely accepted. (Extracted from *Chemical and Engineering News*, 22 July 1996, p. 12)

Photoswitchable "tweezers" for sugar molecules

Michinori Takeshita et al. at the Institute of Advanced Material Study, Kyushu University, Japan, have developed molecular "tweezers" that are essentially capable of picking up sugar molecules and then dropping them when irradiated with ultraviolet (UV) light.

The photoswitch is a diarylethene molecule with heteroaromatic rings. Such molecules are among a group of compounds that exhibit fatigue-resistant, thermally irreversible photoswitch properties. The compound described has boronic acid molecules attached, which are capable of binding to sugars.

In the presence of visible light, an open-ring form of the diarylethene molecule exists in two conformers, anti-parallel and parallel, which exchange rapidly at room temperature. The anti-parallel conformer undergoes photo-isomerisation to give a closed-ring form by irradiation with UV light. Meanwhile, in the parallel conformer, two saccharide-binding boronic acid sites face each other like tweezers, and these are capable of binding to the hydroxyl groups on a single saccharide (sugar) molecule and holding it. When irradiated with UV light, the whole molecule changes configuration to the closed ring form and drops its sugar molecule. (Source: *Biotechnology Business News*, 28 August 1996)

Research on viral genes

Tumours linked to viral infections

Up to 15 per cent of human cancers may be linked to viral infections, according to a new report from the UK charity Cancer Research Campaign (CRC).* This means that vaccines could prevent or treat some cancers.

It has been known for some time that certain cancers stem from viral infection, for example, cervical cancer is linked to the human papillomavirus. The report stresses that cancer is not infectious, but that "complex genetic accidents" triggered by viruses can lead to growth of tumours. Not all infected people will contract cancer, but all such cancers will contain evidence of a virus.

The CRC report analyses the extent and geographical distribution of certain cancers and identifies five viruses linked to tumour growth. They are hepatitis B; human papillomavirus; HTLV 1, which can cause leukaemia; Epstein-Barr virus, which causes glandular fever; and human herpes virus 8, which is implicated in Kaposi's sarcoma, a tumour found in old people and sometimes in AIDS patients.

Only some viruses have the potential to cause cancer, says Chris Bishoff of London's Institute of Cancer Research. They can disrupt the biochemistry of a cell, causing it to grow uncontrollably and become cancerous. This can occur if the viral DNA inserts itself into its host's genome and disrupts genes responsible for cell growth and division, or if the virus itself over-stimulates growth signals. However, in other cases, such as with cancers linked to hepatitis B, the mechanism is not well understood.

Geographically, virally induced cancers are widespread but the worst affected areas are Central and South America, Africa and the Far East. As many as 70 per cent of cancers in some African countries are viral in origin, according to the CRC. In some areas, HTLV1 infects up to a tenth of the population. Of these, up to 10 per cent will develop the cancer, says Bishoff.

Vaccination is an obvious way to combat the risk of viral cancer. In China, a new programme of hepatitis B vaccination aims to combat the country's high rate of liver cancer, as well as hepatitis infection, says Lesley Walker of the CRC. People infected with hepatitis B are 100 times more likely to develop liver cancer than those who are not infected. (Extracted from *Chemistry & Industry*, 19 August 1996)

Mechanism of HIV binding to cellular receptor described

The detailed molecular mechanism of how HIV uses its gp120 envelope glycoprotein to bind CD4 receptors on immune cells, permitting the AIDS virus to infect the cells, is not known. Frank A. Robey and colleagues at the US National Institutes of Health have demonstrated that C4, a peptide domain of gp120, plays a key role in binding CD4 receptor—but only when it is in a preferred conformation. Previously, the group found that the C4 peptide exists in gp120 as an amphipathic α-helix, with one hydrophobic

* "Viruses and cancer", £4, Education Dept., CRC, 10 Cambridge Terrace, London NW1 4JL, UK.

and one hydrophilic surface. Their new research shows that the hydrophobic surface of the helix occurs in nearly identical form in different strains of HIV, and they conclude that the binding of this hydrophobic surface to CD4 is the very first step in the HIV infection process. They also find that the α-helical C4 peptide binds the CD4 receptor with an affinity that is comparable to the affinity of the gp120 parent protein for CD4, suggesting that the interaction involves C4 and CD4 primarily or even exclusively. According to the researchers, "These findings will provide an understanding of the molecular mechanism used by gp120 to bind to CD4, and the information will be useful in designing therapeutics and vaccines to block HIV infection *in vivo*." (Source: *Chemical and Engineering News*, 5 August 1996)

HIV-1 targets CD8-positive T-lymphocytes

Despite the volume of research being carried out on the progress of HIV infection in people, new findings continue to surprise the research community. The most recent of these comes through a new study which shows that the virus infects cells of the immune system previously thought to remain intact in those infected with HIV-1.

Peter Simmonds, at the University of Edinburgh, and a team at the university and at Western General Hospital (Edinburgh, Scotland) have found "evidence for widespread infection" of CD8-positive lymphocytes and also dendritic cells.

It is well documented that the principal targets of HIV-1 are CD4-positive T-helper lymphocytes. However, the extent to which the virus infects other cell types within the immune system is unknown, the authors explain. To investigate this further, they isolated different immune cell types in peripheral blood, to determine which are infected with HIV, and also look at the relationship between the viral load in different subsets, and disease progression. Thirteen HIV-positive patients were included, eight of whom had clinical AIDS with CD4 counts of less than 200 per μL blood. The team detected proviral nucleic acid sequences in T-helper cells, cytotoxic T cells, dendritic cells and monocytes.

Infection of non-CD4 lymphocytes was more common in AIDS patients than in non-AIDS patients, so while CD4 T lymphocytes constituted the main reservoir of HIV in all symptom-free individuals (except one), for all individuals with CD4 counts of less than 200 per μL blood, most infected cells were CD8-positive lymphocytes and dendritic cells. Infection of CD8 cells accounted for 66-97 per cent of total proviral load in five of the eight patients with AIDS. These findings "tend to refute previous reports that CD8 cells were uninfected *in vivo*", the researchers point out.

Polymerase chain reaction analysis also detected HIV-1 provirus in peripheral blood dendritic cells of 10 of the 13 patients. Overall, there was a "remarkable variation" in the frequencies of infected cells within each subset (although the change in the CD4 T-helper target cells as disease progressed was consistent). (Source: *Biotechnology Business News*, 11 September 1996)

New findings on CMV serine protease structure

Three research groups have simultaneously reported on the three-dimensional structure of the human cytomegalovirus (hCMV) serine protease enzyme that is essential for viral replication. The protein represents a potential target for therapeutic intervention against hCMV, a member of the herpes virus family that includes herpes simplex viruses and varicella zoster virus (the cause of chicken pox).

The researchers report the crystal structure of hCMV serine protease along with similar, independent analyses described by teams at SmithKline Beecham Pharmaceuticals and Monsanto/Searle.

hCMV protease contains 256 amino acid residues and shares significant sequence homology with proteases of other herpes viruses, say the Boehringer Ingelheim team. However, as all three teams describe, the structure of the protein has revealed a fold not previously seen in other serine proteases. This fold can be described as a "seven-stranded β-barrel core with seven α-helices on three sides", the SmithKline beecham researchers say.

This core β-barrel is orthogonally packed, with the distinct features that it has two parallel strands (standard orthogonally packed β-barrel structures are always anti-parallel). Previous studies have shown that the hCMV protease exists in a monomer-dimer equilibrium in solution, and all three groups propose that dimerisation, which has been observed in the crystals, is probably necessary for activity. (The dimer interface between two hCMV protease monomers is "unusual", and most likely important to protease activity, the SmithKline Beecham researchers continue.)

The Monsanto/Searle group further suggests that the substrate binds to both subunits, and point out that targeted design of antiviral drugs may necessitate identification of the structural determinants that stabilize the quaternary structure of herpes virus proteases. (Source: *Biotechnology Business News*, 25 September 1996)

Researchers find 3-D structure of HIV protein

Scientists from the University of Maryland Baltimore County (UMBC) and University of Utah, have determined the three dimensional structure of a key section of the protein that forms the core of the HIV virus.

The research, led by Michael Summers, professor of biochemistry at UMBC, was supported by the National Institute of Allergy and Infectious Diseases (NIAID).

The protein, known as the p24 capsid protein, assembles with identical proteins to form the cone-shaped structure that encloses the genetic material of HIV in a mature virus particle. In addition to its structural function, scientists speculate that the p24 capsid protein plays other important roles in the HIV life cycle.

The UMBC researchers found the structure of the p24 capsid protein to be unlike any other protein previously described. The amino-terminal domain has seven corkscrew-shaped "alpha-helices", two regions called "beta-hairpins", and a single exposed loop.

The exposed loop may be of particular importance, noted Dr. Summers, Because it contains an amino acid—Pro90—that binds a protein known as cyclophilin A that HIV takes with it when it buds from a cell.

The binding of cyclophilin A by Pro90 appears necessary for viral particle to be infectious. If Pro90 is present in abnormal form, HIV particles are not infectious, even though they appear normal. (Source: *Biotechnology Business News*, 31 July 1996)

Safer viral vectors for gene therapy

A German team has developed a retrovirus vector for gene therapy which deletes itself after delivering its gene cargo into cells. Describing its construction, Harald von Melchner, at the University of Frankfurt Medical School, and a team based at the Medical School and the Institute

for Chemotherapy Research, Frankfurt, say this "new generation of retroviral vectors" could remove the potential problems associated with retroviral vectors currently available for gene therapy.

A wide range of gene dysfunctions could theoretically be corrected by delivering normal copies of the genes into body cells, and to get these genes into cells a range of viral and non-viral vectors are currently employed. The most widely used are based on the Moloney murine leukaemia retrovirus (MoMuLV), which normally infects mice. A crippled version of this retrovirus has been used in more than 75 per cent of human trials approved to date, the researchers say.

Retroviruses do, however, have inherent problems. Among these, one major concern is the potential for viral vector sequences to recombine with endogenous or exogenous helper viruses and generate new forms of infectious virus. Another is the concern that, as retroviruses integrate mostly randomly throughout the genome, the risk of cancer will be increased if activation sequences are inserted alongside cellular oncogenes.

The strategy taken by von Melchner et al. to develop a self-deleting retroviral vector exploited the natural life cycle of retroviruses. This includes duplication of the terminal control regions U5 and U3, to generate long terminal repeats (LTRs), and the ability of the P1 phage site-specific recombinase (Cre) to excise any sequences positioned between two *loxP* target sequences from the mammalian genome.

The constructed self-deleting retrovirus recombined consistently in recipient cells, offering a reasonable alternative to conventional vectors currently used in gene therapy. The authors conclude that such Cre-*loxP*-based self-deleting vectors should be "superior" to conventional retroviral vectors, by not only being safer, but also by increasing rates of transduction and gene expression. (Source: *Biotechnology Business News*, 28 August 1996)

Research on bacterial genes

Bacteria could cause heart disease

US researchers have reported new evidence of a direct link between hardening of the arteries and a particular family of bacteria. Previously this condition has been blamed on high cholesterol levels and fat in the diet.

The idea that bacteria could be linked to certain types of heart disease gained credence when scientists showed that the bacteria *Helicobacter pylori* caused some stomach ulcers, according to Joseph Muhlestein at the University of Utah Medical School. Now Muhlestein and his colleagues have reported high levels of bacterial infection in patients being treated for hardening of the arteries, or atherosclerosis, where fatty deposits build up on coronary artery walls.

After examining 90 tissue samples, the Utah researchers found that 79 per cent showed signs of infection by the bacteria *Chlamydia pneumoniae*. By contrast, only 4.2 per cent of the 24 samples taken from patients without artherosclerosis was infected.

Some scientists have suggested that the bacterium is an "innocent bystander" which thrives in diseased tissue. But the study found very low levels of *Chlamydia* infection in samples from patients who had other forms of heart disease which cause artery damage that could host bacterial growth. The researchers point out that this is the first study to show a difference in *Chlamydia* infection in the artery walls of patients with artherosclerosis and those with other forms of heart disease.

In artherosclerosis, cholesterol irritates the lining of an artery causing immune cells, called macrophages, to be dispatched to the site. They soak up the cholesterol, but can be drawn out of the blood and deposited in the vessel wall to form the characteristic fatty deposits. This worsens the inflammation which in turn increases the damage.

Supporters of the bacteria theory say that *Chlamydia* could worsen artherosclerosis or even initiate it. This family of bacteria cause chronic inflammation in other parts of the body when inhaled. Scientists suggest that once in the lungs, macrophages, which also attack pathogens, pick up the bacteria and carry them to the arteries. (Source: *Chemistry & Industry*, 17 June 1996)

Bacterial hydrogen evolution

The potential of hydrogen as a fuel has led to the development of its *in vitro* synthesis by Woodward and his colleagues at the Oak Ridge National Laboratory. By coupling glucose dehydrogenase (GDH) from *Thermoplasma acidophilum* with hydrogenase from *Pyroccocus furiosus*, sustained evolution of molecular hydrogen from glucose was achieved. GDH oxidizes glucose, which is subsequently hydrolyzed to gluconic acid; both enzymatic steps use the electron donor NADPH, which is continuously regenerated and recycled. Woodward et al. anticipate that this system could be used to derive hydrogen from abundant and renewable carbohydrate sources such as cellulose. (Source: *Nature Biotechnology*, Vol. 14, July 1996)

Metal scavengers

The specificity of bacteria used in bioremediation of waste waters contaminated with heavy metals could be increased by expressing peptides that form co-ordination spheres around metal ions on the surface of the cells. Sousa et al. from the Centro Nacional de Biotechnologia (Madrid) engineered histidine clusters on the LamB carrier protein of *Escherichia coli*, which allowed the bacteria to accumulate Cd^{2+} levels ten times greater than the wild-type, without affecting cell viability. The LamB-His chains were also sufficiently flexible to allow cells to adhere to a metal ion-coated solid support. (Source: *Nature Biotechnology*, Vol. 14, August 1996)

Novel inhibitor to beat antibiotic resistance in bacteria

In the race to keep one step ahead of the growing number of antibiotic-resistant bacteria, Canadian researchers have designed a new molecule that blocks the action of bacterial enzymes responsible for inactivating a wide range of antibiotics.

Many bacteria produce β-lactamase enzymes that cleave and therefore inactivate β-lactam-based antibiotics such as penicillins and cephalosporins. One representative member of the 2b (class-A) group β-lactamases, TEM-1, has achieved "clinical notoriety", says Natalie Strynadka, at the University of Alberta, and teams from the Alberta site and the University of Toronto.

This is because TEM-1's plasmid-encoded nature, coupled with an increasing number of site-specific mutations, have led to a whole family of TEM enzymes that exhibit resistance to a growing number of β-lactam-based antibiotics. The design and synthesis of new β-lactamase inhibitors (which bind to the active site of the enzyme, and

block binding, and so inactivation, of the antibiotic) is therefore important for the design of potential drugs.

The researchers used the crystallographic coordinates of the acyl-enzyme intermediate of TEM-1 bound to penicillin G to design and synthesize a novel boronic acid-based inhibitor that interacts specifically with conserved catalytic groups in the active site of group 2B β-lactamase enzymes. The new molecule's design principles and structural analysis, as well as the resulting mechanistic implications, are discussed, with the analyses suggesting that the inhibitor is "among the most potent small-molecule reversible inhibitors of β-lactamase described to date". (Source: *Biotechnology Business News*, 28 August 1996)

Iron, marine bacteria and the carbon cycle

Iron availability limits phytoplankton growth in large areas of the world's oceans, but less is known about the iron requirements of heterotrophic bacteria, which also play an important role in carbon cycling. Tortell et al. now report that oceanic bacteria have a higher iron content per unit of biomass than do phytoplankton, and that iron deficiency in laboratory cultures inhibits respiratory electron transport, resulting in slower growth and assimilation of carbon. Heterotrophic bacteria may therefore have a significant effect on oceanic carbon cycling through the role they play in the biogeochemical cycling of iron. (Source: *Nature*, Vol. 383, 26 September 1996)

Research instrumentation

DNA "computer" successfully negotiates the basics of addition

The design and development of a computer able to perform mathematical calculations, but based literally on test tubes of DNA, may not be as far-fetched as it first appears, following the publication of a study which could be considered to represent a step in the right direction.

The feasibility of designing a DNA-based computer was demonstrated in 1994 by Adleman, who harnessed the ability of single DNA strands to bind to one another according to the order of bases (adenine, thymine, cytosine, guanine) in each strand.

Adleman used DNA effectively to solve the problem of how best to link a series of imaginary cities by different routes. However, as the authors of the latest study, Frank Guarnieri, Makiko Fliss and Carter Bancroft (at the Department of Physiology and Biophysics, Mount Sinai School of Medicine, New York), admit in their paper, for a computer to be useful in a wide range of applications it will need to be able to perform mathematical calculations, such as addition, rather than just "search" procedures.

In their approach to the development of a "generally useful DNA-based computer", the team present a DNA-based algorithm for addition, and the results of "a simple example" that was carried out biochemically, through the generation and application of a paradigm for "making DNA add any two rational non-negative binary numbers".

The addition was achieved by combining in a test tube primer extension reagents plus DNA strands appropriately representing the two numbers to be added. The result was 1+1=10 (i.e., 2 in binary notation).

Although correct, the authors admit that use of their general algorithm to add two large binary numbers may require "some technical modifications". (Source: *Biotechnology Business News*, 17 July 1996)

Stretched to the Max: FISH mapping on DNA fibres

A new technique based on applying FISH techniques to linear stretched DNA molecules may help researchers resolve issues critical to large-scale DNA sequencing efforts.

Heinz-Ulrich Weier (Resource for Molecular Cytogenetics) says the recently developed technique, called quantitative DNA fibre mapping (QDFM), can help researchers construct high-resolution physical maps and minimal tiling paths, assess gap sizes and devise closure strategies, and provide quality-control checks during map- and sequence-assembly steps.

QDFM combines molecular combing techniques to attach and stretch DNA molecules across a glass microscope slide. FISH is used to hybridize fluorescently tagged probes to the straightened DNA fibres. Digital image technology records and analyses images from the fluorescence microscope and measures the position of the DNA sequence of probe along the DNA fibre.

QDFM is rapid and provides a high spatial resolution of 1 to 2 kb, up to 1 Mb. Throughput of QDFM could be increased dramatically with automated image analysis that includes algorithms for finding the fibres, autofocusing, and handling multiple slides.

With as many as 20 clones combed on a single microscope slide, early results look promising, but QDFM's impact on genome research will depend on how well it scales up. The technique is amenable to automation, notes Weier, which could increase its throughput manyfold. Berkeley Lab plans to integrate QDFM into the large-scale sequencing process. (http://rmc-www.lbl.gov/ and http://www.lbl.gov/~weier/). (Source: *Human Genome News*, April/June 1996)

General

Smallest stable human chromosomes created

By truncating normal chromosomes, a research group has created the smallest human chromosome fragments that remain stable throughout the cell cycle. The "minichromosomes" are potentially small enough to be inserted into yeast cells for genetic studies.

Minichromosomes, which in some cases are less than one-tenth the size of the smallest normal human chromosome, could have implications for research on chromosome properties and behaviour. They also suggest the possibility of synthesis of artificial chromosomes from relatively simple genetic elements.

Minichromosomes were created by Raoul Heller, Karen E. Brown, Carola Burgtorf, and William R.A. Brown, of the biochemistry department at the University of Oxford, UK.

The researchers fragmented the human Y chromosome into six stable minichromosomes using three rounds of telomeredirected chromosome breakage.

The human Y chromosome is an estimated 50 million to 75 million base pairs (Mb) long, whereas the minichromosomes are about 4 to 9Mb in length. Chromosomes in the commonly studied yeast *Saccharomyces cerevisiae* range up to 3Mb. So the minichromosomes are about the right size to be integrated into yeast, the simplest eukaryotic organisms, in which they could be studied more easily. Chicken lymphoid cells might also serve as an effective host system for minichromosomes.

Yeast artificial chromosomes already can be built up from simple functional chromosome elements. The larger size of human chromosomes and a lack of detailed knowledge of the requirements for their assembly have up to now prevented the construction of human artificial chromosomes from small modular parts. Use of mini-chromosomes to learn more about human chromosome structure and function could potentially bring de novo synthesis of human chromosomes closer to realization. (Extracted from *Chemical and Engineering News*, 22 July 1996)

Team set to research synthetic DNA production

Cambridge Research Biochemicals (CRB), a business unit of Zeneca LifeScience Molecules, has set up a team of researchers to identify generic methods for the production of DNA medicines. Using a new facility at Gadbrook Park, Northwich in Cheshire, UK, the team will focus R&D effort on developing a solution-phase method for production of synthetic DNA.

Synthetic DNA—composed of chemically synthesized nucleic acids—is attracting attention because of its ability to hinder disease pathways in cells.

One of the most studied approaches is antisense technology, in which a short stretch (about 20 residues) of synthetic DNA is taken up by cells. Here it recognizes and binds to a region of messenger RNA destined to produce an aberrant protein and thus trigger the disease state. With the DNA bound to it the RNA is no longer able to be processed to produce the protein.

Manufacture of synthetic DNA has been possible since the early 1980s, using a solid-phase process. In this technique, the growing chain is covalently bound to a solid support and chemistry is performed by flowing a stream of reagents over the support. When the required length of DNA has been produced, it is cleaved away from the solid substrate.

This method has been satisfactory for producing the milligram amount needed for basic research, but the challenge now is to find cost-effective methods of manufacture for the hundreds of kilograms that will be needed for these molecules to realize their potential fully as therapeutic agents.

Solution-phase methods, where the syntheses are performed in solution rather than on a solid support, are more efficient and more amenable to scale up than solid-phase processes.

Alongside the research effort CRB will continue its core DNA production work with existing customers. The firm has claimed leadership in the synthesis and purification of DNA for companies active in the area of antisense and DNA therapies. (Source: *European Chemical News*, 16-22 September 1996)

Leptin stars in blood production

A hormone that controls body fat may also be involved in producing blood cells, say US scientists. Researchers seeking treatments for obesity involving this protein may have to rethink their approach. The discovery may also advance medical knowledge of blood cell cancers.

William Matthews and colleagues at Genentech were investigating how the body regulates the production of blood cells. They were looking for any receptor molecules that signal blood cells to grow. To their surprise, the researchers found a receptor that was the same as the one for the hormone leptin. This hormone, which is produced by the obesity (ob) gene in mice, controls levels of stored fat and may be involved in regulating body weight.

The team found that the leptin receptor is expressed in a type of bone marrow cell called a stem cell, which can produce all types of blood cells. Bone marrow also contains fat cells, but scientists are not sure why they are there.

The findings offer a new perspective on the role of fat cells in producing blood cells, says Matthews. Leptin appears to encourage stem cells to grow and produce several blood cells including red blood cells, and two types of cell that are important for the body's immune system. Matthews believes that fat cells in bone marrow may act as "nurse-maids", supplying the stem cells with the leptin they need to grow and produce blood cells.

The findings have implications for leukaemias, where scientists have known there was a connection with marrow fat cells. For example, several reports have shown that some patients have reduced fat levels and are less efficient at producing fat cells. Matthews believes that the role of the fat cell will attract much greater attention now.

This work also suggests the need for more research on leptin before it is used therapeutically. It indicates that the biological effects of leptin are far more complex than previously believed. (Source: *Chemistry & Industry*, 16 September 1996)

"Mini" protein for Genentech

Researchers at the US company Genentech have managed to substantially reduce the size of a protein without reducing its activity. The creation of an active "mini-protein", smaller than any natural protein, is a breakthrough which could lead to a new generation of pharmaceuticals, taken by mouth rather than by injection.

Staff scientists James Wells and Andrew Braistead, in the company's protein engineering department, reduced the active part—the "domain", of Protein A, widely used for the purification of antibodies, from 59 amino acid residues to 33.

As pharmaceuticals, natural proteins of between 50 and several hundred amino acids are too large to get through the digestive tract into the bloodstream and must be injected.

Wells and Braistead's method, if applied widely, could offer the possibility of making proteins containing "unnatural" amino acids. (Source: *European Chemical News*, 8-14 July 1996)

Deciphering the signal for cell suicide

Scientists in Israel have found the "missing link" in a biological process that controls whether cells live or die. The discovery could lead to drugs that control diseases, such as multiple sclerosis, where this mechanism has gone wrong.

One way that cells can die is by a "suicide" process called apoptosis. In one mechanism, the immune system detects an infected cell and issues a "suicide instruction", which a cell wall receptor recognizes and passes on to the cell's internal machinery. Scientists have identified the cell wall receptors but they did not know how the message triggered the final suicide act. David Wallach and colleagues at the Weizmann Institute in Rehovot have now found the killer molecule.

The researchers have identified an enzyme called MACH which they say responds to the signal directly. It has two sections: one recognizes the incoming suicide message, the other cuts up vital cell proteins, causing the

cell to die. They also note that by using "adapter" molecules, MACH can do the same job for different types of receptors.

This is the first example of a complete signalling mechanism for cell death, and unlike other message systems, it is very direct, says Wallach. He expects more such molecules will now be discovered. (Source: *Chemistry & Industry*, 1 July 1996)

Yeast genome sequenced

An international consortium of scientists announced at the end of April that they had achieved a major goal of the Human Genome Project—the complete sequence of a eukaryote, the single-celled *Saccharomyces cerevisiae* strain S288C. The 16 yeast chromosomes were sequenced from tip to tip with no gaps, and both strands of the DNA double helix were analysed, resulting in an accuracy rate higher than 99.99 per cent. The biggest surprise of the project was that more than half the genes uncovered during sequencing were previously unknown, despite decades of intense scrutiny by yeast geneticists. Another unexpected discovery was the degree of redundancy in the genome, with several genes often appearing to have homologous sequences and functions. The full yeast sequence has been publicly available since the end of April, but access formerly was limited to the laboratories involved in the sequencing project, those in the follow-up functional analysis programme (Eurofan), and companies in the Yeast Industry Platform, Brussels.

Yeast data web sites:

- *ftp.mips.embnet.org* (directory/*yeast*)
- *ftp.ebi.ac.uk* (directory/*pub/databases/yeast*)
- *genome-ftp.stanford.edu* (directory/*yeast/genome seq*)
- BLAST and FASTA searches: *http://genome-www.stanford.edu/Saccharomyces/*

(Extracted from *Human Genome News*, April-June 1996)

Acidifying ion transport

Coupling genetic engineering with the powerful technology of microphysiometry has allowed a research team at Bristol-Myers Squibb (Princeton, NJ) to develop a prototype drug screen for the analysis of effectors of ion transport. By engineering channels into potassium transporter-defective yeast cells, Stephen Kurtz's group has shown that extracellular acidification can be used to measure transmembrane ion and proton flux, thus developing the rationale for a high-throughput screen. (Source: *Nature Biotechnology*, Vol. 14, July 1996)

Metalloproteinases antibody distortion

Researchers at the Scripps Research Institute in California have found a way of using antibodies to distort the structure of metalloproteinases. In a paper published in *Nature* they show how it is possible to create a new class of metalloproteinases by using this technique. These metal containing enzymes have a wide variety of synthetic uses and the discovery could broaden the range of their applications. (Source: *European Chemical News*, 29 July to 11 August 1996)

PNA method for study of telomeres

Scientists have discovered a new application for Peptide Nucleic Acid (PNA) technology in the area of telomere biology. One group of investigators at the Terry Fox Laboratory (Vancouver, BC) used PNA-based probes to quantify the length of telomeres. Relationships between telomere length and diseases such as cancer are being studied by a number of research teams. (Source: *Genetic Engineering News*, 15 June 1996)

Total synthesis of antitumour compound is achieved

Researchers at Harvard University have completed the first total synthesis of the antitumour compound FR-901,228. The molecule belongs to a small group of potential anticancer compounds called detransforming agents because they can reverse the morphological effects of oncogenic transformation. Unlike current anticancer drugs, detransforming agents are not intrinsically toxic, offering a new avenue for cancer treatment. Chemist Julian A. Simon, at the Fred Hutchinson Cancer Research Center in Seattle, carried out the synthesis with former Harvard undergraduates Khan W. Li, Jerry Wu, and Wenning Xing. The team prepared both enantiomers of a key building block, a thiol-containing β-hydroxy acid, by using a catalytic asymmetric aldol addition developed by Erick M. Carreira, associate professor of chemistry at California Institute of Technology. And they tried two modes of cyclization in the final step. They obtained better yields by using the enantiomer with orientation opposite to that in the final product. Inversion during the ring-closing step yielded the correct stereochemistry. (Source: *Chemical and Engineering News*, 5 August 1996, p. 25)

Cell culture shows promise as source of anti-cancer drug taxol

Cell culture may be a commercially viable way of producing large quantities of the anticancer drug taxol. A study by Yukihito Yukimune and colleagues at Mitsui Petrochemical Industries, Yamaguchi Prefecture, Japan, indicates that the taxol-producing plant species *Taxus media* can synthesize 110 mg of taxol per litre in two weeks in cell cultures. This productivity is far better than the best so far achieved in another cell culture—153 mg of taxol per litre in six weeks. Yukimune says the high productivity is maintained even in a 200-litre culture. The high yields are made possible by methyl jasmonate, which the Japanese scientists found is a strong promoter of the biosynthesis of taxol and related taxanes. Taxol is used to treat ovarian and breast cancer and is under clinical investigation for treatment of other cancers. It was originally isolated from the bark of the Pacific yew tree in tiny amounts (0.007 per cent yield), and obtaining the drug from this source alone would have seriously depleted the Pacific yew tree population. Currently, demand for the drug is being met by partial synthesis from precursors produced by needles and twigs of the European yew. (Source: *Chemical and Engineering News*, 2 September 1996, p. 23)

Combinatorial approach yields killer substrate for tumour cells

Using combinatorial mutagenesis, researchers at Worcester Foundation for Biomedical Research, Shrewsbury, MA, have expressed mutant α-haemolysin polypeptides that are preferentially activated by cathepsin B, a protease linked to cancer metastasis. The mutant haemolysins are designed to punch holes in the malignant cells that activate them. Unlike normal cells, which store cathepsin B intracellularly, cancer cells wear it on their surface so it can clear a path for them through the extracellular matrix. Led by Hagan Bayley, the Worcester Foundation group constructed a library of inactive

haemolysin mutants that contained two complementary polypeptide chains rather than the usual single chain. Removal of a redundant central peptide from one of the chains by cathepsin B triggers pore-forming activity from some of the mutants. Fifteen of the mutants were more readily activated by cathepsin B than was the control. (Source: *Chemical and Engineering News*, 15 July 1996)

Supramolecular assemblies

Two independent research teams have made a hybrid of tagged gold nanoparticles with DNA strands and used base-pairing interactions between the strands to organize the particles into supramolecular structures.

The work, which merges the disparate fields of DNA chemistry and inorganic colloids, offers a promising solution to the problem of organizing nanoparticles into complex arrays or materials in which the size and shape of each individual particle is preserved.

Because of their nanometer dimensions, colloidal particles of metals and semiconductors have potentially useful optical, optoelectronic, and materials properties, which are tunable by changing the particle size. These properties might be put to work in applications such as chemical sensors, signal enhancers for spectroscopy, and fabrication of nanostructures such as electronic devices. (Extracted from: *Chemical and Engineering News*, 19 August 1996)

AFM reveals details of protein crystallization

The possibility of understanding crystal growth at the most fundamental level is behind work in several laboratories to use atomic force microscopy (AFM) to probe the growth and structure of protein crystals. Some researchers are beginning to take the technique one step further to actually watch the movement of individual protein molecules.

So far only a handful of laboratories have applied this approach to studying protein crystallization and movement, but those that have are enthusiastic about its promise.

AFM provides a window to watch crystal growth on the nanometer scale. For many proteins, that means the images reveal the crystal lattice as well as the steps and planes on the crystal surface.

The first studies of protein crystallization using AFM were performed in 1992 in the laboratory of physics Professor Stephen D. Durbin at Carlton College, Northfield, MN, on the protein lysozyme. Since then, about 10 other virus and protein crystals have been examined in several laboratories. (Extracted from *Chemical and Engineering News*, 26 August 1996)

Researchers mimic peptide

A small peptide mimic of the blockbuster biotechnology drug erythropoietin (EPO), allowing chemical synthesis and production of a version which can be taken orally, has been produced by US researchers.

The joint team from the Affymax Research Institute, the Scripps Research Institute and the Robert Wood Johnson Pharmaceutical Research Institute, was able to isolate small peptides of under 20 amino acids to bind and activate the receptor for cytokine EPO.

According to Nick Wrighton, staff scientist at the Affymax Research Institute, the peptides are far from the potency of EPO, but peptides with the potency of EPO could be produced in the future. (Source: *European Chemical News*, 9-15 September 1996)

New methods get DNA all bent out of shape

Researchers have demonstrated two new methods that can be used to bend DNA. Such bending plays a key role in transcription, replication, recombination, and other processes, but the molecular mechanisms of bending remain unclear. Work by Christopher Switzer of the University of California, Riverside; L. James Maher III of the Mayo Foundation, Rochester, MN; and co-workers now shows that DNA can be induced to bend 4 to 8° by attaching ammonium ions to one face of the helix. The studies confirm earlier results in which DNA was bent by substituting neutral methylphosphonates for DNA phosphates, and they help substantiate the hypothesis that DNA-binding proteins change the shape of DNA by asymmetric neutralization of phosphate charges. The results are also of potential importance for the design of artificial DNA-bending proteins. David A. Liberles and Peter B. Dervan of California Institute of Technology bend DNA with an oligonucleotide that binds to two DNA sites 10 base pairs apart. Bent angles of 38 to 61° were obtained by adjusting the length of the oligonucleotide linker. The researchers believe the work could lead to "a new class of reagents for use in biology and human medicine". (Source: *Chemical and Engineering News*, 9 September 1996, p. 31)

E. APPLICATIONS

Pharmaceutical and medical applications

Molluscs offer pain relief

Drugs that can treat strokes and pain could be produced from Australian cone shells, a predatory marine mollusc found in the Great Barrier Reef.

Paul Alewood and his team at the University of Queensland are studying conopeptides, a group of small peptides of between 10 and 30 amino acids produced by the mollusc.

Cone shells produce a mixture of peptide toxins to paralyse their prey. They work by preventing the exchange of ions, which affects nerve transmission. Alewood believes that information on how conopeptides block ion channels could be used to develop drugs to treat illnesses such as strokes that involve calcium ion channels. (Source: *European Chemical News*, 9-15 September 1996)

Cellular mechanism of oral tolerance shown

Researchers at Brigham and Women's Hospital have reported on studies demonstrating that white blood cells from multiple sclerosis patients receiving AutoImmune's Myloral (oral bovine myelin) produce immune-regulating hormones that may suppress their disease. The studies are the first to demonstrate the cellular mechanism of oral tolerance in humans, said an AutoImmune official.

Myloral's clinical efficiency and safety as an orally administered treatment for MS is currently being evaluated in a Phase-III clinical trial, slated for completion in the spring of 1997, said the official. (Source: *McGraw Hill's Biotechnology Newswatch*, 15 July 1996)

Sickle-cell disease

In a report just published in the *New England Journal of Medicine*, Mark Walters and Keith Sullivan, from the Fred Hutchinson Cancer Research Centre and the University of Washington, in Seattle, describe how they and their colleagues in America and Europe have cured 16 children who were suffering from sickle-cell disease by adapting a bone-marrow transplant technique. As in all transplants of foreign tissue, the donor has to be immunologically compatible with the recipient or the transplant is likely to be rejected. Bone marrow is particularly difficult to match. The best donor is therefore a patient's healthy sibling. And, because their immune systems are not fully developed, the most successful transplants are those carried out between children.

The team carried out 22 transplants in children with advanced sickle-cell disease. The patients first underwent chemotherapy to destroy their defective bone marrow. They were then injected with new marrow taken from healthy siblings. The new marrow, not being genetically pre-disposed to develop sickle-cell disease, then went on to generate healthy blood cells. Four patients rejected the transplants but survived. One died of a brain haemorrhage. And one succumbed to graft-versus-host disease, in which the immune cells generated by the transplanted marrow attack the body of the patient. But, after two years, the remaining patients are still healthy.

Even when it succeeds, however, the treatment is not without problems. Still, the success of the latest trial should encourage more research. It may be possible, for example, to use less severe pre-transplant chemotherapy. That would allow some of a patient's marrow to survive and thus make the whole experience less traumatic. To this end, Suzanne Ildstad, of the University of Pittsburgh, in Pennsylvania, is working on breaking down genetic barriers to bone-marrow transplants. (Extracted from *The Economist*, 17 August 1996)

Anaphylaxis vaccine work gets funding

UK-based Peptide Therapeutics has been awarded a grant of £450,000 ($720,000) by the Department of Trade and Industry to aid development of a vaccine against anaphylaxis, an extreme form of allergic response that can lead to respiratory obstruction or vascular collapse and death.

If successfully developed, the vaccine would be the first against a life-threatening disease which is not caused by an infectious agent.

The vaccine is directed against the mechanism that causes mast cell degranulation and works by generating an antibody which locks on to IgE preventing the allergen from triggering the release of chemical mediators, primarily histamine.

The vaccine has shown potential in Phase II trials of 13 patients with severe food allergies. (Source: *European Chemical News*, 16-22 September 1996)

New drug protects against heart attacks

A new drug appears to halve the risk of dying from a heart attack, scientists reported at the annual Congress of the European Society of Cardiology in Birmingham last month. It also seems to halve the risk of suffering a heart attack. Clinical trials of the drug were stopped early so that all patients could benefit.

Abciximab, made by the US firm Centocor under the name *ReoPro*, is a monoclonal antibody which helps to stop blood clots from forming. It does this by targeting receptors on the surface of platelets, the tiny particles involved in blood clotting.

The clinical trial of abciximab involved 1,266 patients in centres around Europe. They were all suffering from unstable angina.

The patients received abciximab or a placebo before, and immediately after, undergoing angioplasty. But the trial was stopped early because major, significant benefits of the treatment were clearly apparent on interim analysis of the data.

Abciximab is a large protein so it can only be given by injection. But medical scientists are investigating small molecule drugs which have a similar effect. Although details of these trials remain confidential, potential drugs are likely to be petptides based on the abciximab antibody. (Extracted from *Chemistry & Industry*, 16 September 1996)

Agreement for development of oral insulin

The British drug delivery and diagnostics specialist Cortecs International has entered into an agreement with Osteometer Biotech and the Centre for Clinical and Basic Research (CCBR) both based in Denmark, for the clinical development of an oral formulation of insulin.

The technology developed by Cortecs uses a lipid-based carrier attached to the insulin molecule, protecting it

against degradation in the gut. Trials with pigs have shown a high level of consistency of delivery with oral insulin, something that is important in human diabetes. (Source: *European Chemical News*, 8-14 July 1996)

Gene team finds test for brittle bones

A simple blood test that will identify women at risk of osteoporosis has been developed by British scientists. A team of experts from Aberdeen and London has found that osteoporosis is strongly associated with an abnormality in the gene responsible for bone production.

The discovery allows millions of women at risk to be identified before the disease takes hold. Treatment, including diet changes and hormone replacement, can then be used to prevent occurrence of the crippling condition.

The announcement follows a four-year research programme involving 300 patients carried out by doctors at Aberdeen and Guy's Hospital, London. (Extracted from *www.telegraph*, 31 August 1996)

Brain cancer treatment

The world-wide rights for *Gliadel*, a new implant treatment for the most common form of brain cancer, have been sold to Rhône-Poulenc Rorer by Guildford Pharmaceuticals.

Gliadel is a biodegradable polyanhydride polymer wafer which is implanted in the brain cavity after a tumour has been surgically removed. Once in place, the wafer erodes slowly and releases the chemotherapeutic drug carmustine directly and specifically to the tumour site. (Source: *European Chemical News*, 1-7 July 1996)

Conjugate eradicates human colon tumours in mice

Human colon tumours in mice disappeared after treatment with a highly toxic cancer killer linked to an antibody, according to a new study.

The drug, C242-DM1, was developed by ImmunoGen Inc., Cambridge, MA.

In the study, reported in the *Proceedings of the National Academy of Sciences*, researchers treated eight mice that had implanted human tumours with daily injections of the conjugate at a high dose of 300 micrograms per kilogram for five days. The tumours disappeared and the scientists said the mice did not show signs of the major side effect, weight loss. The mice remained tumour-free for 200 days.

The researchers also tested the drug at lower doses, and in comparison to 5-FU, the standard in colon cancer chemotherapy, and saw better, longer term, tumour control. (Extracted from *McGraw Hill's Biotechnology Newswatch*, 19 August 1996)

DNA test measures CMV in cells

Researchers at the Instituto Ludwig de Pesquisa do Cancer in São Paulo have developed a DNA test capable of measuring the amount of cytomegalovirus (CMV) present in the cells of patients. CMV is a high-risk factor for patients who have just undergone organ transplant, the new born, and patients with tumours or AIDS. The test, which identifies the presence and size of CMV in patient DNA, was a by-product of another, yet unfinished, study at the institute to establish the number of copies of the herpes virus associated with uterine cancer. The CMV test is to be patented and a diagnostic kit will be developed by medical analysis company, Hemagen. (Source: *Biotechnology Business News*, 11 September 1996)

New genetic test

A new genetic test could be used to positively diagnose Alzheimer's disease while the patient is still alive, according to US researchers. The discovery could help clinical trials of potential treatments.

Diagnosis of Alzheimer's currently relies on subjective physical assessment and can only be confirmed by autopsy. Some symptoms can appear to stem from Alzheimer's but actually result from other conditions. Allen Roses and colleagues at Duke University Medical Centre have shown that testing for a gene called APOE e4 can strongly support the presence of Alzheimer's.

In the study, 67 patients diagnosed as probable Alzheimer's cases were tested for the gene and the results compared with brain examinations after death. Three-quarters of those whose brains showed the characteristic nerve fibre tangles of Alzheimer's had the gene, but none of those who were not Alzheimer's cases had it.

The team points out that potential Alzheimer's drugs can now be tested in genuine Alzheimer's sufferers. Researchers will be able to include only those people with Alzheimer's symptoms and the APOE e4 gene and be more certain that they are studying the right group of patients. (Source: *Chemistry & Industry*, 15 July 1996)

Proteus gets go-ahead for cancer vaccine trials

Proteus International has been given the go-ahead to start testing its cancer vaccine in patients. A Phase II trial with the GnRH immunotherapeutic vaccine for prostate cancer will begin immediately and preliminary data confirming safety and efficacy are anticipated in the last quarter of the year.

Clearance to conduct the study under a Clinical Trial Exemption Certificate was given by the UK Medicines Control Agency in June 1996, followed by further approvals from National Health Service ethics committees. (Extracted from *Biotechnology Business News*, 17 July 1996)

Vaccine against human papilloma virus enters trials

The first clinical study to evaluate whether a human papilloma virus (HPV) vaccine could be used to treat cervical cancer showed that the vaccine is safe and in at least one patient induced a strong immune response.

Eight patients with invasive cervical cancer received the vaccine, a recombinant vaccinia virus encoding modified forms of cancer-causing proteins found in HPV types 16 and 18.

Although the study was too small to reach any firm conclusions about the vaccine's therapeutic effect, one patient did mount a cytotoxic-T-cell response to a specific HPV type found in the vaccine, according to the study in a recent issue of *The Lancet*.

That patient remains disease-free 15 months after the vaccination following years of recurring disease and traditional cancer treatments.

However, it is unclear whether the vaccine is responsible for ridding her body of cancer. Another patient who did not exhibit a T-cell response remains free of cancer 21 months after the vaccination. None of the patients developed any significant side effects to the vaccine.

The research was led by L.K. Borysiewicz of the University of Wales College of Medicine, Cardiff, UK, and Cantab Pharmaceuticals of Cambridge, UK.

"The results are encouraging and do not warrant further investigation", said Michael Steller, an investigator

at the National Cancer Institute, where the Cantab vaccine is also being tested in a Phase I study.

Vaccine therapy is seen as a promising avenue for treating cervical cancer because the disease is almost invariably associated with HPV infection in nearly all cases and chemotherapy and radiation are not very effective for treating advanced disease. (Extracted from *McGraw Hill's Biotechnology Newswatch*, 15 July 1996)

Combination therapies yield positive results

Combination therapies have shown that by using a cocktail of drugs AIDS can be brought under control, if not completely cured.

Glaxo Wellcome released news of successful trials with its drugs, *Epivir* and *Retrovir*, more commonly known as 3TC and AZT. These showed that used in a three-way combination with a protease inhibitor, known as 141, the level of HIV became undetectable in patients after periods of between 12 and 48 weeks.

Although the number of patients involved in the studies was small, the effect was achieved in different population groups, varying from those with early infection through to patients with more advanced disease who have previously been treated with anti-retrovirals. The anti-viral effect was achieved without significant increase in side effects compared with single drug therapy.

The company also released information about a new reverse transcriptase inhibitor, 1592U89, which is said to be three times as potent as AZT. The new drug also has the advantage that unlike most other drugs used against AIDS it appears to be able to penetrate the central nervous system.

The recent acquisition of the rights to protease inhibitor 141, developed by Vertex Pharmaceuticals, gives Glaxo Wellcome the option of producing its own combination therapy. Again this has been found to be able to penetrate the central nervous system, an important property as it has been speculated that brain tissue could act as a reservoir for infection during therapy.

Glaxo Wellcome appears to be in a strong position as it already supplies two of the components which are required in the combination therapies, AZT and 3TC. (Source: *European Chemical News*, 22-28 July 1996)

Livestock applications

Transgenic animals in the news

A second generation of transgenic piglets are the most crucial generation in a five year generic engineering project at the University of Illinois. The project involved the injection of a cow gene that increases milk production into hundreds of swine embryos. Al, the only boar produced following the procedure which had the gene intact, has sired 19 piglets. Nine of these retained the desired gene. Once this generation produces its own piglets, it will be possible to determine whether they produce more than the average amount of milk. If so, it could lead to a new line of pigs that gain weight faster before weaning. (Source: *The AgBiotech Bulletin*, July 1996)

Cloning may lead to year-round soft-shelled crab supply

In a recent project expected to revolutionize the soft-shelled crab industry, Sea Grant researchers have successfully cloned genetic material that allows blue crabs to regulate moulting and establish their protective shell. Understanding the chemical mechanisms that control this process is a key discovery in an effort to manipulate crab development to produce a dependable supply of soft-shelled crabs (which are actually crabs that recently shed their protective cover).

The cloning experiment—led by Mississippi/Alabama Sea Grant researcher Doug Watson—focused on a gene that codes for a protein known as moult-inhibiting hormone (MIH).

At normal concentrations, MIH blocks shell shedding and maintains the crab's protective cover. However, as a crab develops, it continually outgrows its shell and must replace it with a new, larger one. At that time, concentrations of MIH fall and the crab enters moulting.

Under natural circumstances, this process occurs irregularly, limiting the industry's ability to take full advantage of potential soft-shelled harvests. However, now that MIH genetic material has been cloned and the MIH hormone can be produced in large quantities, researchers can experiment with substances that could block the hormone's activity and force the crab into moulting. This ability could produce an "abundant, year-round, and controllable supply of soft-shelled crabs for the Gulf of Mexico soft-crab industry and consumers of seafood", Watson said. (Source: *Sea Technology*, June 1996)

Research provides weapon against shellfish disease

Modified viral particle (called retroviral vectors) have been used for the first time to alter the genes of a marine inveterbrate. This research may provide a new tool for marine biologists to use against the diseases that attack commercial stocks of oysters, clams, mussels and abalone, according to Dr. Jane C. Burns of the University of California at San Diego's department of pediatrics and school of medicine.

Burns collaborated with Dr. Thomas Chen, director of the University of Connecticut's Biotechnology Center, to genetically modify the dwarf surf-clam *Mulinia lateralis*. Results of the experiment are published in the 16 April edition of the *Proceedings of the National Academy of Sciences*.

Once the genes responsible for protecting cultured shellfish from disease have been identified, retroviral vectors could be used to deliver these protective genes directly to brood stock, Burns said. (Source: *Sea Technology*, June 1996)

Leptin regulates neuroendocrine changes in starved animals

"Regulation of the neuroendocrine system during starvation could be the main physiological role of leptin", rather than its more widely studied role in preventing obesity, according to a team of researchers at Harvard University Medical School. Rexford S. Ahima, Jeffrey S. Flier, and their colleagues base their proposal on the effects of giving a recombinant form of the protein to male and female mice deprived of food for 48 hours. Restoring leptin to normal levels in the blood did not alter weight loss or glucose or insulin levels in the mice. It did, however, largely ameliorate drops in hormones involved in reproduction and in thyroid and adrenal function. The findings suggest that leptin may exert its effects on the hypothalamus. The leptin-mediated changes "including limiting procreation, decreasing thyroid thermogenesis, and increasing secretion of stress steroids...together are likely to

have survival value during prolonged nutritional deprivation", the researchers note. (Source: *Chemical and Engineering News*, 22 July 1996)

Agricultural applications

Calgene developing coloured cotton

Calgene has been issued a US patent (US5,530,185) for transgenic colour alteration in cotton plants. After two years of research, Calgene is growing plant prototypes in greenhouses. John Callahan, vice president of Calgene's cotton division, says he "expects brown, black and blue transgenic cotton to be on the market by 1999", with red to follow. Similar research is also being done by CSIRO, the Australian Government's scientific and industrial research organization.

While naturally occurring coloured cotton has previously been cross-bred to produce bolls in various shades of brown and light green, yields have been low—less than half that of white cotton from the same number of plants. And largely because the fibres are short and weak, it was about twice as expensive to produce. However, the technology described in Calgene's patent could yield coloured cotton with the physical properties of white cotton.

The patent covers gene constructs incorporating the pZ promoter, first characterized in tomato, linked to genes involved in the production of melanin, a dark brown or black pigment. The pZ promoter is tissue-specific in plant ovary cells, and temporarily specific during flowering. As a result, the transgenic cotton fibres, which are seed hairs, are dark brown or black. Calgene's future research will focus on enhancing the brown/black shade of colour, and on development of blue and red cotton fibres, using other such naturally occurring pigments as indigo. (Source: *Nature Biotechnology*, Vol. 14, September 1996)

Plant growth promoting rhizobacteria (PGPR)

Plant growth promoting rhizobacteria (PGPR) can induce systemic plant resistance to disease pathogens and insect pests, according to an item in *IPM Practitioner*. The report cited the work of an Auburn University researcher, G. Zehnder, who studied bacterial wilt disease in curcubits caused by *Erwinia tracheiphia*, a pathogen spread by cucumber beetles. The pathogen cannot be controlled with fungicides, so insecticides are used to control the insect.

Zehnder found that when cucumber seeds were treated with PGPR, the resulting plants grew faster. The soil rhizobacteria also reduced cucumber beetle numbers better than standard insecticides. It is thought that PGPR induce systemic changes in the plants that improve growth and encourage insect resistance. PGPR have also been found to increase nitrogen fixation, increase root growth, increase above-ground plant growth, and enhance biological disease control. (Source: *The AgBiotech Bulletin*, July 1996)

New from the laboratory

• Mogen International has developed transgenic canola plants that produce enzymes, such as phytase, which are used in the feed industry to reduce the amount of phosphorous excreted by livestock. According to a report in Canola Guide, the enzyme helps single stomached animals such as pigs and chickens to digest and utilize natural phosphate, a mineral necessary for bone development.

• *Olpidium* zoospore fungus, a common soil fungus, has been used by US Agricultural Research scientists to transfer market genes into wheat. The process has now been patented, according to an item in ISB News Report. Use of the fungus provides an option to *Agrobacterium* or various gene guns.

• The same source notes that American Cyanamid has applied to the US Environmental Protection Agency to field test a genetically engineered baculovirus as an agent against cabbage loopers and tobacco budworm. The baculovirus was altered to encode an insect-specific toxin protein from scorpion venom. (Source: *The AgBiotech Bulletin*, July 1996)

Bacterial treatment to prevent root disease

USDA researchers are developing a bacterial treatment to prevent root diseases, according to an item in *Industrial Bioprocessing*. Researchers are selecting bacteria strains by an enrichment process and screening for antibiotic production. By coating wheat seeds with a liquid containing the selected bacteria, and then drying them, increased wheat yields of 10 to 30 per cent have been achieved. Researchers are also genetically altering various bacteria to enhance adaptability to various locations, and to develop strains with a wider spectrum of antibiotic activity.

Contact: R. James Cook, Root Disease and Biological Control Research Unit, Agricultural Research Service, USDA, Pullman, WA 99164, USA. Tel.: 509-335-1116; Fax: 509-335-7674. E-mail: rjcook@wsu.edu (Source: *The AgBiotech Bulletin*, July 1996)

Chilling resistance

Cold susceptibility makes tobacco a warm-climate crop, but Ishizaki-Nishizawa and colleagues at the Central Laboratories for Key Technology (Kanazawa, Japan) have attempted to change that. By expressing a cyanobacterium $\Delta 9$ desaturase gene transgenically, *cis*-double bonds were introduced into saturated fatty acids linked to plastid membrane lipids, reducing the levels of saturated fatty acids in plant membranes. The transgenic tobacco plants, unlike wild-type plants, resisted short-period exposures to temperatures of 1° C, and they germinated and developed normal chloroplasts at temperatures 15° C lower than optimal for wild-type plants. (Source: *Nature Biotechnology*, Vol. 14, August 1996)

First release of engineered arthropod

In late February, the US Department of Agriculture (USDA) approved the first field test of a genetically engineered arthropod—a mite that feeds on other mites. The approval cleared the way for a University of Florida entomologist to release about 1,400 transgenic mites on bean plants in a small research plot in Florida's Alachua County. The mite was engineered to contain a bacterial gene which acts as a marker to make it easy for researchers to track the mite in the environment. Using the new marker, scientists will monitor the transgenic mite's ability to control spider mites under field conditions.

USDA's approval came despite recommendations from the Union of Concerned Scientists (UCS) and others that the test be delayed pending full public participation in the risk review process and a public discussion of the risks associated with engineered arthropods. (Source: *The Gene Exchange*, June 1996)

True potato seed

Crises affecting two of the world's most important food crops—potato and wheat—are presenting challenges

to germplasm research scientists that have global repercussions affecting everyone from the farmer to the consumer.

Potato blight (*Phytophthora infestans*) is again on a rampage throughout the world, this time in even more virulent forms than in its earlier incarnation which precipitated the infamous Irish potato famine of the mid-1800s.

Karnal bunt (*Tilletia indica*), which has continued to threaten South Asian wheat growing areas since it was discovered in 1931, has been discovered for the first time in several growing areas of the USA, the world's largest wheat exporter. In response to the discovery, US Secretary of Agriculture Dan Glickman has declared an "extraordinary emergency" to cope with the outbreak.

A threat to the existence of either of these crops is a calamity the world cannot afford. There are a few similarities in the spread of the diseases, both of which provide the staple food supply to millions, if not billions of people around the world. In both cases, the diseases have become more difficult to control or eradicate. And, in each case, germplasm researchers have been working for years to develop resistant varieties to replace the susceptible seed varieties now prevalent in the growing areas. For both crops, fungicides are limited in effectiveness and availability to fight the diseases on the chemical warfare front. (Source: *Diversity*, Vol. 12, No. 2, 1996)

Developing country farmers

True potato seed (TPS), the small seeds produced by the flower of the potato plant, may help provide the answer to *P. infestans*. Though still in the experimental stage, International Potato Centre (CIP) scientists are optimistic that TPS will accelerate the development of late blight-resistant cultivars. With TPS, large quantities of disease-resistant planting materials can be ready in one season, whereas using conventional tubers takes nearly 10 years to move from research station to farmers' fields.

Mahesh Upadhya, CIP's programme leader for propagation and crop management, believes developing country farmers will more widely accept the TPS technology. Asian farmers are already using TPS because it is cheaper than traditional seed potatoes and produces better. One hundred grams of TPS, enough to plant a hectare, cost about US$ 80, whereas the two tons of tubers needed to plant the same field costs well over US$ 1,000.

TPS offers several advantages for developing country farmers. Producing small tubers from TPS is labour intensive—a plus in rural areas that are short of jobs. TPS populations are homogenous enough to meet market demands but still contain a mixture of genes that protect them from a variety of viruses and plant diseases. The resulting potato crops are made up of numerous gene combinations rather than a monoculture of genetically identical potato clones, as is the case for crops grown from traditional tuber seed of a cultivar. TPS also provides planting flexibility, allowing farmers more control over timing. For instance, in the Red River Delta of Viet Nam, farmers plant TPS between two plantings of rice for a highly profitable potato crop.

In India, the world's sixth-largest potato producer, farmers are growing more than 10,000 hectares of potatoes derived from TPS planning material. Six TPS hybrids produced in India were bred by a CIP team and extensively evaluated by India's Central Potato Research Institute. India's Ministry of Agriculture has provided funding to state governments to increase TPS production facilities to alleviate the country's chronic shortage of quality seed. TPS production in India is proving commercially successful as Indian producers are selling portions of their seed to potato programmes in Viet Nam, Egypt, the Philippines, Sri Lanka and Bangladesh.

For further information contact: Dr. Peter Gregory, Deputy Director General for Research, International Potato Center, Apartado 1558, Lima 100, Peru. Tel.: +51-1-436-6920/435-4354; Fax: +51-1-435-1570. E-mail: cip@cgnet.com or cip@cipa.org.pe.(Source: *Diversity*, Vol. 12, No. 2, 1996)

Food production and processing

Biosensors and their applications to food processing

Quantitative measurement of specific chemical compounds is becoming increasingly more important in the food processing and quality control industries. In the past, conventional methods were time consuming, often requiring pre-treatment, such as the elimination of unwanted compounds from the sample. Biosensors—the amalgamation of signal transducers and biomembranes with high molecular selectivity—pose one solution to this problem. For example, a bioreactor functioning in an organic solvent has been developed for the production of a highly polymerized oligo-saccharide using hydrolase.

Measuring alcohol content is often required in food processing. The enzymes alcohol oxidase and alcohol dehydrogenase have both been employed in such sensors. In both cases, the enzyme is immobilized on the surface of an electrode and the reaction products—hydrogen peroxide or a redox dye—can be measured by the flow of electric current, which correlates directly with the alcohol content.

Similarly, fish freshness can also be measured by an enzyme sensor. As a fish decomposes, ATP is degraded into ADP, AMP, IMP, inosine, hypoxanthine, xanthine, and finally uric acid. Thus, fish freshness can be estimated by measuring the relative concentration of ATP and its derivatives. Enzyme sensors measure IMP, inosine, and hypoxanthine concentrations. The ratio of these relative concentrations then gives a quantitative measure of freshness.

Gaseous compounds such as alcohols and esters can be measured with an odorant sensor. Piezoelectric quartz crystal is coated with phospholipids resembling those found in the human nose. The lipids absorb the odorant gas, causing a mass change on the surface of the crystal. The resonant frequency of the piezoelectric crystal is subject to this mass change, so the odorant concentration can be measured via the shift in resonant frequency. By applying various types of lipids to piezoelectric crystals, it is possible to make a multi-channel odorant sensor. Identification of the odorant gas can then be performed by the unique pattern of the multi-channel sensor. (Source: *Science & Technology in Japan*, No. 59, 1996)

Chemical applications

Biotechnology patent could lead to polyester harvests

Scientists at Massachusetts Institute of Technology have received a US patent that could lead to harvesting polyesters from plants. The patent covers insertion of genes for polyhydroxybutyrate polymerase into bacteria and crop plants. It is the sixth in a series of biotechnological patents for making biodegradable polyester resins to be obtained by

biology professor Oliver P. Peoples and former MIT research fellow Anthony J. Sinskey. Sinskey is now vice president for research and development at Metabolix in Cambridge, MA, which has licensed the patents. The patents cover insertion of thiolase genes that mediate condensation of acetate to acetoacetate, and reductase genes for conversion of acetoacetate to β-hydroxybutyrate, as well as the polymerase genes. Harvesting polyhydroxybutyrate from transgenic corn could lower production costs of the polyester, according to Metabolix. The transgenic bacteria and plants can also copolyesterify β-hydroxybutyrate with β-hydroxyalkanoates up to C_{12}. Monsanto currently produces the Biopol brand of β-hydroxybutryrate/valerate copolyester by fermentation of *Alcaligenese eutrophus*, a process originally invented by ICI. (Source: *Chemical & Engineering News*, 29 July 1996)

Synthetic polymer acts as anticoagulant

A "heparinoid" methacrylate resin that inhibits blood coagulation has been synthesized by researchers at Kagoshima University in Japan. Naturally occurring anticoagulant heparin is made up of a string of sulphated disaccharide units. The new material—poly(glucosyloxyethyl methacrylate) sulphate—carries pendant sulphated sugar groups [*Bioconjugate Chem.*, 7, 393 (1996)]. The team's work could lead to synthesis of anti-thrombogenic biomaterials that could adhere to damaged blood vessel walls or implanted medical devices and inhibit clot formation on-site. Heparin itself is not easy to immobilize onto solid surfaces, the researchers note. Led by Mitsuru Akashi at the university's department of applied chemistry and chemical engineering, the group discovered the more sulphur groups the sugar groups carried, the longer the methacrylate resin delayed blood-clotting time. By comparison, sulphated polymers containing no sugar groups had little effect. Heparin was the most effective anticoagulant, leading the group to conclude that the potency of a heparinoid anticoagulant is linked to the number of sugar groups and their degree of sulphation. (Source: *Chemical & Engineering News*, 26 August 1996)

Industrial microbiology

Metalwork breakthrough

Monsanto claims to have developed the first metalworking fluid to be based on proteins rather than oil or synthetics, thus offering benefits of biodegradability and low toxicity.

A researcher working on the company's programme in protein technology, normally aimed at pharma, agricultural and food businesses, discovered a product that looked, felt and worked like oil.

The company recognized it could have useful applications as a metalworking fluid because of advantages of superior cooling, treatment of waste and improved worker safety.

Glacier has a long useful life and does not turn rancid. Its cooling properties enable machines to run faster and promote longer life. (Source: *European Chemical News*, 16-22 September 1996)

Therapeutic molecules from microalgae

Heliosynthese SA (Aix-en-Provence, France) and Scotia Pharmaceuticals (Stirling, UK) have received an EEC Eureka award for their three-year joint programme to establish microalgae as the source for a new generation of polyunsaturated lipids, particularly arachidonic acid and docosahexanoic acid. It is anticipated that these fatty acid-based compounds will find wide application as nutritional and pharmaceutical products.

Heliosynthese announced the production of a new form of superoxide dismutase containing manganese (Mn-SOD) from *Porphyridium cruentum* at the Oxidative Stress and Redox Regulation Congress that took place at the Institut Pasteur, Paris, France from 21-24 May 1996. SOD has proved effective as an adjuvant therapy in AIDS; however, SOD of animal origin carries the risk of viral contamination.

Heliosynthese is able to produce industrial-scale quantities of Mn-SOD in continuous flow, sterile, autotrophic conditions using a bioreactor and processes patented by the company. (Source: *Microbiology Europe*, Vol. 4, No. 4, July-August 1996)

Extraction industry applications

Micro-organisms liquefy coal

An international research group centered around the German firm Rhein Braun Co. is working on the basic research of the development of a coal liquefaction technology that employs micro-organisms.

The group is looking at the use of micro-organisms, which include bacteria, to biologically liquefy coal, with the aim of making inexpensively a liquid fuel similar to petroleum.

According to the group, micro-organisms used in its research have produced several litres of a liquid intermediate substance from lignite.

However, the liquefaction rate is only 50 per cent, which has prompted the group to continue with research for the discovery of more effective micro-organisms. In addition, because the intermediate substance is still too costly to use as a fuel, the group says that technological development of a more efficient processing method is crucial. (Source: *McGraw Hill's Biotechnology Newswatch*, 16 September 1996)

Energy and environmental applications

Water treatment technologies using natural materials

When using river water for domestic use, it is important to remove suspended material such as silt, solids and micro-organisms. This is normally done using chemical coagulants, but in some developing countries the chemicals may be unavailable or too expensive. An alternative is to use natural coagulants, usually from plants.

The potential use of natural coagulants for water treatment in developing countries as full or partial replacement for conventional chemical coagulants has been studied by Leicester University's Environmental Engineering Group for 10 years. The work has focused on using crushed seeds from the widespread tropical tree Moringa oleifera Lam. This is a high yielding and fast growing tree originating in northern India, and whose seeds provide suspensions that act in similar fashion to proprietary chemicals. Laboratory studies at Leicester and field trials at Thyolo in southern Malawi have shown that the seeds can be as effective as aluminium sulphate in the treatment of a wide range of raw water qualities.

Moringa oleifera is a truly multi-purpose tree. The seeds contain 40 per cent (by weight) high quality

vegetable oil. After this has been extracted the press-cake still contains the active coagulant material.

Furthermore, the seed pods, leaves and flower can be used as a highly nutritional food source. There are many other uses as well, a recent finding by the Civil Engineering Department at Edinburgh University, who along with the University of Malawi are collaborating in this project, is that activated carbon suitable for water treatment can relatively simply be obtained from the seed husks.

Present studies are aimed at development of robust water treatment processes using Moringa oleifera (at Leicester) and further development of the activated carbon process (at Edinburgh). Widespread promotion of the tree by Leicester University has led to implementation projects in Africa and South America.

Contact: Department of Engineering, (Attention Dr. Geoff Folkard), University of Leicester, Leicester LE1 7RH, United Kingdom. Tel.: (0) 116 252 2538; Fax: (0) 116 252 2619. E-mail: gkf@leicester.ac.uk. ODA Project R6179, Theme W4. (Source: *ODA*, No. 2, p. 3, 1996)

Automated system for recycling mushroom culture sawdust as carbon

Orii Co. Ltd. has started marketing an automated system for recycling mushroom culture sawdust for reuse as carbon. Waste sawdust is sterilized with dry hot air and carbonized, and the treated carbon is used as activated carbon (for purification, deodorization and dehumidification), and as an organic fertilizer of high added value. The system is also applicable to treating coffee dregs and construction waste timber, so the company plans a series of recycling systems.

The carbon produced by the system contains nutrients added in the mushroom culture process, so poultry excrement and other substances are added to produce agricultural organic compost. Field tests are also in progress to use the carbon as a feed ingredient, which is anticipated to reduce the cost of manufacturing feeds.

Three systems are already in operation, through which field tests are being conducted and highly satisfactory results confirmed. These systems can treat 5 m^3 of sawdust in 8 hours, and operate at a fixed temperature of less than 600° C.

Further details from: Orii Co. Ltd., Public Relations Department, 6 Suzukawa, Isehara City, Kanagawa Pref. 259-11. Tel.: +81-463-93-0811; Fax: +81-463-93-3102. (Source: *JETRO*, April 1996)

Biofermentation type raw garbage treatment system

Sanyo Cookery Equipment Co. Ltd. is marketing a raw garbage treatment system by biofermentation, called the "Biolister". The biolister utilizes microbes that exist in the atmosphere to ferment and convert the raw garbage into compost.

The design is compact and utilizes two methods, namely, the Direct type and the System type. The Direct type is fed directly with raw garbage collected at a point. The raw garbage is converted into sludge by stirring and heating, using a water jacket built into the base of the biolister fermentation tank, followed with its air-drying and fermentation.

The System type is fed with pre-treated garbage which is first fed into a crushing machine at the site of garbage generation and converted into slurry form by crushing and mixed with a water shower. The slurry-form garbage is pumped to the dewatering system within the fermentation system, where it is compressed and the water content reduced to about 60-70 per cent, then transferred into the fermentation tank automatically.

The fermentation tank is provided in either one or two tanks with portions that permit controlled successive fermentation process.

The final compost is usable effectively in organic cultivation. The volume of the final compost is reduced to about one-thirtieth (1/30) and one-sixtieth (1/60), of the original raw garbage, by the Direct and System type biolister, respectively.

Further details from Sanyo Cookery Equipment Co. Ltd., Public Relations Department, 276 Ninomiya-Machi, Maebashi City, Gunma Pref. 379-21. Tel.: +81-272-68-1263; Fax: +81-272-68-2653. (Source: *JETRO*, August 1996)

H_2/gluconic acid route uses cheap substrates

An enzymic method for producing hydrogen and gluconic acid from cheap substrates such as waste paper has been developed by researchers at the Oak Ridge National Laboratory, Tennessee. The process could boost prospects for H_2 as a fuel, as well as providing an alternative means of manufacturing gluconic acid, a chelating agent.

The team, led by Jonathan Woodward, uses a combination of enzymes to produce H_2 and gluconic acid from glucose. The enzymes are a glucose dehydrogenase and a hydrogenase. A cellulase can be added to waste paper as the starting material.

The process concerns the recycling of a helper molecule called nicotinamide adenine dinucleotide phosphate and can be carried out at temperatures over 60° C, a big advantage in maintaining sterility. (Source: *European Chemical News*, 15-21 July 1996)

Water purification sysem uses low cost bugs

Orient Green Co. Ltd. has developed a water purification system for factories and waste water that uses microorganisms.

The technology relies on OM Nakamura bacteria to break down harmful organic and inert substances to the point where water is suitable for drinking and can be released into lakes and rivers. OM Nakamura is actually a cocktail of many different organisms and is already in use in Aomori Prefecture at a waste disposal plant as a method for reducing odors.

The new process involves no chemicals and requires only simple equipment, which keeps costs down. A team of universities and research institutions are cooperating to develop applications for the technology. (Source: *McGraw Hill's Biotechnology Newswatch*, 5 August 1996)

F. PATENTS AND INTELLECTUAL PROPERTY RIGHTS

US equivocates on Hagahai patent

The US National Institutes of Health (NIH), owner of the patent on the cell line of a Hagahai indigenous person from Papua New Guinea, is sending mixed signals about what it intends to do with the patent. NIH has been the subject of extreme criticism from Governments, indigenous people, and NGOs for patenting the cells. Confusing and incomplete reports have emerged about the patent's status, including stories indicating it will be abandoned. But despite dozens of requests, NIH has produced no written confirmation that the patent has been abandoned as of 1 October 1996.

The uncertainty began in August when in Port Moresby, just prior to an important national conference on biomedical research, a report surfaced that NIH had given the patent to the Papua New Guinea Government. ICRAF, a Port Moresby NGO, immediately forwarded the newspaper account to the US for confirmation. RAFI contacted several NIH offices, including the International Relations and Technology Transfer Offices; but officials were curiously out to lunch, away at meetings or on the phone for several weeks straight. No messages were returned.

Dr. Amar Bhat of NIH's International Relations Office finally offered comment while attending a meeting on the Human Genome Diversity Project in Washington on 16 September 1996. Bhat said that NIH first intended to place the patent in a trust for the Hagahai; but later decided it would abandon it altogether. Bhat said this would be done by the end of September.

On 22 September 1996, the Associated Press (AP) wire service circulated a story reporting that NIH had "quietly offered to abandon its rights" in the patent, and quoted a "well-placed source at NIH headquarters" as commenting "We were blindly patenting things that were patentable ... The PNG cell line certainly fell within that category." The AP article repeated Bhat's story that the idea of a trust was initially entertained; but since NIH thought the patent is unlikely to make money, the costs of transferring the patent rights and creating the trust could not be justified. Neither Bhat or AP elaborated on who the proposed trustees are/were.

At the end of September, the AP story and original Port Moresby report were widely circulated on the Internet, leaving thousands across the world wondering what exactly NIH was up to. Critics of the patent pointed out the ironies of the Hagahai, through their trustees, having to pay thousands of dollars in order to get rights to their own cells back from NIH. Still, NIH maintained a vacuum on official information and refused to confirm or deny the reports.

RAFI suspects that NIH intends to abandon the patent and that their refusal to comment or provide written confirmation is because they are desperately trying to concoct a coherent rationale for their plans. NIH is in the difficult position of trying to abandon the patent without prejudicing its continued open policy on patenting human tissues or appearing to cave in to pressure from indigenous people and NGOs. NIH may be sending out a trial balloon by citing an obscure and largely irrelevant modification to the laws governing technology transfer at NIH (made this year by the US Congress) as the official pretext for the patent's potential abandonment.

Though the end of the Hagahai patent boondoggle is possibly at hand, indigenous people and NGOs are quick to point out that if NIH abandons the Hagahai patent, the controversy surrounding patenting of human tissues will be far from over. The US Patent and Trademark Office, as well as the patent offices of most other Northern countries, are continuing to allow the patenting of human tissues, and NIH abandonment of a single patent will have no effect on the thousands of other patents and patent applications on human tissues. (Source: *RAFI Communique*, September 1996)

DNA in court

In recent high-profile criminal cases, the use of DNA evidence itself seemed to be on trial. Defense and prosecution witnesses have argued about the significance of a match between a defendant's DNA profile and the DNA evidence found at a crime scene, its appropriate use as evidence, and the most effective ways to gather and process samples.

Unlike fingerprinting, where scientific consensus preceded its admission as evidence in court, the use of DNA in legal proceedings has been a work in progress. Scientific techniques and legal opinions often have been at odds since DNA evidence first was introduced into the courtroom in the mid-1980s.

Despite the controversy, DNA analysis promises to be the most important tool for human identification since the development of fingerprinting, both for implicating and for exonerating suspects in criminal cases, says a Research Council committee in a new report requested by the US Federal Bureau of Investigation. This follow-up to a 1992 Research Council report examines the latest advances in forensic science and technology, and offers a new look at issues that have been misapplied or misunderstood since the first report was issued.

Most prominent among these is the "interim ceiling principle", a formula for calculating the likelihood of a match irrespective of the defendant's race or ethnic makeup.

Since then, data have been gathered that make use of the interim ceiling principle unnecessary. The new report offers formulas that factor in the known similarities among population subgroups. These calculations are still designed to be conservative, statistically underestimating the chance of a match rather than exaggerating it, which should reduce the chance of a false conviction.

The committee underscored the importance of proper handling of evidence, and emphasized that laboratories must follow procedures to ensure high-quality DNA work. For example, the rights of defendants are best protected if DNA evidence is divided, with the unused portion to be used for additional, independent testing if necessary. And laboratories should participate regularly in proficiency

tests and make every effort to gain accreditation from professional organizations for performing DNA analysis. (Source: *News Report* of the US National Research Council, 1996)

Biotechnology patent examination harmonization frustrated

Discussions between the United States, Japan and the European Patent Office aimed at harmonization of patent examination standards for biotechnology-related patent applications in the three Patent Offices have stumbled because of an unexpectedly great divergence in views. The division between the European Patent Office on one side and Japan and the United States on the other side is particularly marked, partly because of differences between the member states of the European Patent Convention. A comparative study report will not be issued until after a meeting between patent officials of the three groups in November 1996.

An informative article on patent examination practice in Japan entitled "Patentability of Biotechnology Inventions in Japan" by Yusuke Hiraki may be found in *Patents and Licensing* (1996)26(3)7. (Source: *Australasian Biotechnology*, Vol. 6, No. 4, 1996)

G. BOOKS, JOURNALS, REVIEWS AND BIOINFORMATICS

New publications on biotechnology ethics

Three new publications on biotechnology regulations, ethics and public debate are available from the International Centre for Human and Public Affairs in the Netherlands:

• *Coping with Deliberate Release: The Limits of Risk Assessment*, edited by *Ad van Dommelen*, maps promises and perils in the emerging social and political landscape of modern biotechnology. It includes the perspectives of 15 distinguished authors.

• *Contested Technology: Ethics, Risks, and Public Debate*, edited by *Rene von Schomberg*, offers critical reflection on procedures for technology assessment.

• *The Social Management of Biotechnology: Workshop Proceedings*, edited by *Peter Wheale*, discusses the ethic and moral aspects of biotechnologies.

Contact: International Centre for Human and Public Affairs, Pastoor Smitstraat, 25, 5014 RH, Trilburg, The Netherlands. Tel.: 31-13-5360751; E-mail: R.von Schomberg@kub.nl;web site at http://www.kub.nl:2080/FWW/EnvEthics/Intro.html

The world health report 1996—fighting disease, fostering development

Infectious diseases are the world's leading cause of death, killing at least 17 million people a year. Most of these deaths are preventable—nevertheless, the struggle to control infectious diseases has become a global crisis. No country is safe. Many new diseases, some of them incurable, are surfacing around the world. Others are re-emerging to pose bigger threats than before. Life-saving drugs are becoming less and less effective in combating bacteria and other microbes.

The World Health Report 1996—Fighting Disease, Fostering Development[1] provides an expert assessment of the world health situation in all its complexity, giving particular attention to infectious diseases. It combines the latest health statistics with an analysis of the many factors that have shaped the current situation—and created an unprecedented crisis.

By showing where we stand today in the fight to control infectious diseases, the report aims to help the world comprehend both the alarming implications of recent trends and the need for immediate action. Over 50 old and new diseases—from malaria, tuberculosis and cholera to AIDS, plague and Ebola haemorrhagic fever—are profiled in terms of their incidence, causes, opportunities for control, and impact on health and socioeconomic development.

The report opens with an overview of the state of world health at the end of 1995, including a concise analysis of global economic, political, social, and demographic trends relevant to health in general and infectious diseases in particular. Also included are the most up-to-date statistics on life expectancy, mortality by age group and sex, and causes of death and disease. Against this background, the report turns to an in-depth analysis of infectious diseases. General problems considered include the emergence of several new diseases, the spread of epidemics, a sharp rise in antimicrobial resistance, and the growing number of hospital-acquired infections. A special section on cancer concludes that up to 15 per cent of all new cancer cases per year are linked to infectious agents.

The most extensive section analyses over 50 diseases organized according to mode of transmission: person-to-person, contaminated food and water, insect bites, and contact with animals. By focusing on the way diseases spread, the report is able to trace how the present situation arose and identify the human interventions needed for prevention or control.

Throughout this analysis, the picture that emerges is one of a world poised to conquer some diseases soon, yet gravely threatened by many others, losing its arsenal of effective drugs, creating more and more opportunities for diseases to emerge or flourish, and above all paying a high price for past complacency. As the report repeatedly argues, the price of continued complacency will be higher yet, especially since socioeconomic development cannot move forward while so many of the world's people are disabled by disease.

To show the way forward, the report explains what WHO is doing to fight disease and foster development by combating these and many other problems. A final chapter, on charting the future, describes the precise actions needed to eradicate or eliminate diseases such as poliomyelitis, leprosy, neonatal tetanus, and guinea-worm infection, to tackle old diseases such as tuberculosis and malaria, and to cope with several newer threats.

[1] Available from Distribution and Sales, World Health Organization, 1211 Geneva 27, Switzerland (or any WHO sales agent), price Sw.fr. 15.- (developing countries Sw.fr. 9.-)

Tropical disease research

Progress 1975-94; highlights 1993-94
assembled by R. Walgate, with contributions from J. Turner, P. Parker & N. Cater, 1995, v +167 pages [E, F] ISBN 92 4 156179 3, Sw.fr. 26.-/US$ 23.40

This book provides a lively account of the ambitions and obstacles, successes and setbacks that have characterized the fight against tropical diseases over the past two decades. The report, which also describes the current state-of-the-art in tropical disease research, commemorates the twentieth anniversary of the UNDP/World Bank/WHO Special Programme for Research and Training in Tropical Diseases (TDR). Established in 1975, TDR is devoted to the development of applicable, appropriate, and affordable methods to control the major tropical diseases.

Chapters focused on each of the major tropical diseases—malaria, schistosomiasis, lymphatic filariasis and onchocerciasis, leprosy, African trypanosomiasis, Chagas disease, and leishmaniasis—provide a journalistic, objective, and sometimes critical review of what 20 years of investment in TDR means in terms of tangible outcome. Throughout the report, the personal experiences related by hundreds of scientists and other TDR collaborators enliven this account of steady, impressive progress in combating some of humanity's most terrible—and neglected—diseases.

Gene Delivery Systems

A State-of-the-Art Review

After a century of progress in medicine, we are still heavily afflicted by the continuing scourges of inherited disease, cancer, and new virus diseases such as AIDS. All are caused by malfunction or subversion of our genetic machinery. The crucial breakthrough, in which huge efforts, hopes and finance are now being invested, is gene therapy—the effort to fix or replace broken genes.

At the core of gene therapy stands the problem of gene delivery—getting the new genes to the right place, to do the necessary job, without unwanted side effects; killing the tumour regenerating the supply of the deficient enzymes within the patient's cells and tissues. But gene delivery is difficult, expensive, and can easily miss the target.

The OECD's new report combines state-of-the-art science from an international workshop of leaders in this field, with assessments and insights of experienced scientists and policy advisers. They grappled with finding the right balance between basic research and clinical trials. The book asks if we are trying to do too much, too soon. It examines the respective responsibilities of Government, academia, the private sector, and the clinician, and tries to define the right steps, and the current priorities for public policy.

This report is designed for specialists and non-specialists alike. Included with the workshop papers are more general overviews of what gene therapy means, and what regulatory frameworks are in place, to ensure safe practices from laboratory and factory to the clinic. Panel discussions and summary reports also address the economic challenges, and related issues such as intellectual property rights.

The report is the latest in a long series of OECD publications on modern biotechnology, looking simultaneously at the leading edges of new science and advanced technologies, and at the policy problems which they raise, or help to resolve. A list of related publications is available on request.

"*Gene Delivery Systems. A State-of-the-Art Review*", 446 pages, OECD, Paris 1996. France only: FF 230; all other countries: FF 300; US$ 59; DM 87. ISBN 92-64-14887-6 (93 96 04 1)

Wider application and diffusion of bioremediation technologies. The Amsterdam '95 Workshop

Bioremediation—the use of micro-organisms to clean pollution in soil, air and water—is increasingly recognized as the technology of choice.

Although bioremediation still lacks some of the reliability of chemical and physical methods, the versatility of biological systems allows for the treatment of a very wide range of pollutants. The relatively low maintenance costs make bioremediation a powerful and economically competitive tool in solving environmental problems.

The OECD has made a major contribution to the wider understanding of this eminently environment-friendly technology, particularly in Government circles, and to improved international cooperation.

The new OECD publication, *Wider Application and Diffusion of Bioremediation Technologies—The Amsterdam '95 Workshop*, focuses more closely on detail than previous workshops. Presentations cover bioremediation for air/off-gas and soil, and particularly industrial application and diffusion. In fact, in a relatively short time, bioremediation has evolved from a collection of technologies into an expanding business. Not all problems have been solved; future progress of bioremediation will continue to depend critically on improving the scientific underpinnings and on an appropriate public policy framework.

The book reports the discussions of the workshop—attended by more than 100 international experts and participants—on seven key issues: business opportunities and bottlenecks for bioremediation in air/off-gas and in soil; efficacy, reliability and predictability in air/off-gas and in soil; focus and trends in R&D; information transfer and dissemination; and standardization and best practice.

The Amsterdam workshop followed two previous examinations of bioremediation: the 1994 report *Biotechnology for a Clean Environment—Prevention, Detection, Remediation* and the subsequent Tokyo workshop and report *Bioremediation: the Tokyo '94 Workshop* have received international attention.

Further information is available from: Sonia Guiraud, Biotechnology Unit, Directorate for Science, Industry and Technology, 2 rue André Pascal, 75775 Paris cedex 16, France. Tel.: (33 1) 45 24 16 54; Fax: (33 1) 45 24 18 25. E-mail: Sonia.Guiraud@oecd.org

Journalists may obtain a copy of the reports from the OECD Communications Division (requests by fax only).

"*Wider Application and Diffusion of Bioremediation Technologies. The Amsterdam '95 Workshop*", 456 pages, OECD, Paris 1996, France only: FF 290; all other countries: FF 365; US$ 72; DM 106. ISBN 92-64-14869-8 (93 96 031). Available from the OECD Publications Distributors.

Biodiversity and the Law

In 1991, the US Environmental Protection Agency identified species extinction and habitat destruction as two of the four greatest environmental threats to human welfare. As a result, conservation advocates must learn to better utilize existing law to protect biodiversity, and lawmakers must respond with new laws that are necessary for the challenge of building biodiversity policy.

Biodiversity and the Law, edited by William J. Snape III of Defenders of Wildlife, is a timely and provocative volume that combines historical and cutting-edge legal analysis in an attempt to explain the importance of biodiversity law to those inside and outside the conservation profession. It argues that the law should adapt to protect all species of life, since these species are vital to human survival.

Contents include:

- The roles that science and policy will play in establishing a legal regime that protects biodiversity;
- A description of the only US law, the Endangered Species Act, that actively protects species;
- An analysis of the importance of combining the requirements of various public land statutes and the National Environment Policy Act of 1970;
- Multilateral efforts to globalize biological resources;
- Discussion of the need for innovative interpretations of existing law.

In stimulating essays, contributors explain the importance of biodiversity law as it relates to all aspects of everyday life and explore its major scientific and legal angles. Throughout, they argue that the preservation of biodiversity, which by definition includes all species of life on Earth, should be recognized as the main objective of environmental law and policy.

Contributors include Mollie Beattie, Donald M. Waller, Jason Patlis, Lindell L. Marsh, Todd G. Olson, Peter Jenkins and David R. Downes.

William J. Snape III is director of the legal division at Defenders of Wildlife, where he manages all legal programmes and provides legal counsel on programme policies.

(*Island Press* 1718 Connecticut Avenue, N.W. Suite 300, Washington D.C. 20009)

Research confirm risks predicted in new UCS book

Recent studies have confirmed predictions made in a new Union of Concerned Scientists book, *The Ecological Risks of Engineered Crops* (MIT Press), that engineered genes in crops may transfer to wild plants or weeds, resulting in gene-altered weeds that are more difficult for farmers to control and potentially disruptive to natural habitats. In their book, biologists Jane Rissler and Margaret Mellon propose a scheme for assessing the risks of gene flow, as well as the risk that genetically engineered crops may themselves become weeds. In March, the journal *Nature* published a report that showed that herbicide-tolerant genes from genetically engineered canola moved quickly to nearby weeds, transferring the herbicide tolerance to the weeds. Another recent report in *Nature* focused on the risks posed by gene movement from genetically altered canola and emphasized the need for prudence and a case-by-case approach to risk assessment of genetically modified plants.

The book is available from UCS, 2 Battle Square, Cambridge, MA 02238, for $16.95 plus 20 per cent for postage and handling (Source: *Biotech Bulletin*, 15 May 1996)

Integrating biotechnology in agriculture Incentives, constraints and country experiences

by Carliene Brenner

World-wide concern for more environmentally friendly agriculture has provoked interest in agricultural biotechnology, particularly in developing countries. While many have embarked on biotechnology research, few biotechnology applications have yet to reach the farmer's field. This study, based principally on country experiences, calls for an integrated approach to biotechnology in which national priorities for research are firmly linked to the objectives and problems of agriculture. It also argues in favour of public/private sector partnerships and, on the part of the donor community, for long-term funding.

A growing number of developing countries are investing in agricultural biotechnology research and some have created special biotechnology research institutes. However, biotechnology has often been embarked upon in isolation from the overall national context in which it is being developed, from the problems confronting agriculture and from the obstacles in the way of technology development and diffusion. This can lead to unrealistic expectations with respect to the pace and extent of biotechnology development and applications in developing country situations. Given the potential of biotechnology to contribute to more sustainable methods of plant production and protection, it is important to create the conditions which would enable developing countries to take full advantage of that potential.

This research, which draws and builds on earlier Development Centre research in this field, was motivated by the following concerns: first, that the potential contribution of biotechnology to developing-country agriculture, at least in the short term, has been overstated; second, that the current economic, political and environmental context, which differs significantly from that which inspired the widespread diffusion of the earlier Green Revolution technologies, may be less conducive to the transfer of biotechnologies from developed to developing countries; third, that the enhanced role of private-sector interests, together with the strengthening of intellectual property rights in agricultural biotechnology is likely to weaken the earlier "public good" aspect of agricultural technology; finally, that the factors which in the past have inhibited the widespread diffusion of new technologies in developing-country agriculture are not only poorly understood, but have generally been overlooked in expectations for biotechnology.

Against this background, the Development Centre has sought to review developments with respect to biotechnology for plant production and protection in selected countries. Not only have the nature and scope of the research effort been examined, but also the policies, practices and mechanisms in place which would facilitate or impede the development of biotechnology-based products and their diffusion in the farmer's field. An effort is also made to determine the kinds of institutional arrangements and policies which would enable developing countries to take full advantage of the potential of biotechnology to contribute to more environmentally friendly approaches to crop production and protection.

The project has a number of different components, including an analysis of publicly funded international initiatives to facilitate the introduction of biotechnology in developing-country agriculture. It also includes comparative analysis of the situation in six countries—India and Thailand in Asia; Colombia and Mexico in Latin America; and Kenya and Zimbabwe in Africa—which have focused on biotechnology for plant production and protection. A feature of these studies is that they have not only examined the "state-of-the-art" with respect to biotechnology research, but also provide information on the different phases in the whole process from basic research to the marketing and widespread diffusion of a biotechnology product.

In general, the biotechnology research reported on the country studies suffers from a lack of clear priorities and focus and has not been firmly integrated with the priorities and problems confronting agriculture. Countries cite both financial and human resources as major constraints in research. However, in the absence of clear objectives and priorities, it is difficult to determine with any accuracy what would be an appropriate level of resources to be diverted to biotechnology rather than to other, perhaps equally or more important, problems.

The crucial area of "development"—midway between the laboratory and the field—emerges as a major obstacle in most country studies. Contributing factors are: weak or inexistent linkages and feedback among the different public and private actors and institutions concerned with the development of biotechnology; lack of effective demand for the biotechnology product(s) under development; and inadequate provision—or lack of provision—in research budgets for product development, large-scale testing and up-scaling.

With structural adjustment and liberalization policies under way, there are strong pressures in most countries to reduce public expenditure—including the financing of agricultural research—and to give greater rein to market

forces. Although private-sector organizations, such as producer groups, play a significant role in some countries for specific crops, in most countries R&D investment in biotechnology by commercial firms is very limited. It will therefore be necessary to provide incentives to local firms to encourage participation in biotechnology research, or in public/private sector research collaboration. The alternative would require greater effort on the part of public research institutes towards "finished" products, closer to potential commercialization.

Another possible constraint to the development and diffusion of biotechnologies is that of inadequate national capacity in the complementary or underpinning technologies and capacities necessary to ensure the transition from laboratory to end user. For example, in the countries included in the study, while the seeds industry is well developed for the major commercial crops, with private local and foreign firms supplying and selling seed, for other crops—and in particular for food crops grown by low-income farmers—the seeds sector is less developed. Indeed, for some crops, seed is not commercially produced but is mainly reproduced, saved and exchanged among farmers.

The study says that when it comes to the ultimate phase in the research, technology development and diffusion cycle, again there are major constraints to be addressed. Most of the biotechnology products already being commercialized are the products of tissue culture and micropropagation. Disease-free planting material is now available for a growing number of crops and is supplied by a growing number of local firms. Other biotechnology products, such as biopesticides, have met with less commercial success at a time when public extension services which, in the past, have facilitated the diffusion of new technology at the farm level, have fewer resources or are being privatized.

This raises the problem of "public good" technologies which Governments may wish to promote for reasons of equity, as a measure in favour of poor farmers, or as a means of alleviating environmental pollution. These may be situations where there is a perceived **need** for the technology, but where **demand** in an economic sense is not strong and where the socioeconomic and/or environmental benefits of the technologies would be realized only in the long term. This raises difficult issues of devising ways in which Governments could, at one and the same time, keep short-term costs to a minimum, while at the same time supporting the development of public-good biotechnologies and creating conditions for their production and diffusion by commercial companies in the longer term.

One of the most important lessons which emerged from the country studies on which this book is based is that little economic information is available, whether on the costs of biotechnology research or the comparative cost of final biotechnology products. Even more importantly, very little evidence is available on the actual or potential cost-benefit of biotechnology products to farmers which will, in the long run, determine their success or failure. The fragmentary evidence generated by the country studies indicates a pressing need for more in-depth analysis of short- and long-term economic and social costs and benefits of technology.

Another important issue raised by the research is the need for assessment of the comparative cost/benefits of importing or purchasing biotechnology techniques and/or products, versus local development. Clearly this is not an "either-or" issue, as even importing biotechnology requires, at the least, the capacity to identify technologies suitable for transfer or purchase, but it does raise the question of the extent to which developing countries should conduct their own research and develop their own biotechnology applications.

In certain situations, it may make eminently good sense, in both scientific and economic terms, to purchase, license, or import particular elements of technology or finished biotechnology products rather than "reinventing the wheel". There are undeniable advantages in being a late-comer, or follower, rather than attempting to "catch up" with a moving target: the technology which is acquired has been tried and tested, and can be obtained at lower price and with less risk. However, the biotechnology products (herbicide-tolerant crops) being developed in industrialized countries may not be the most appropriate for resolving the particular problems confronting agriculture in the countries included in our project, or for developing country agriculture in general.

In the final analysis, the question of the extent to which a country undertakes its own biotechnology research and the extent to which priority is given to biotechnology over other research methods should be linked, first and foremost, to country priorities and objectives in agriculture and in agricultural research, as well as to environmental concerns. Equally important, it should be linked realistically to the scientific and technological capacities and level of agricultural development in the country concerned.

Clearly, each country will need to make its own decisions with respect to policies and priorities for the development of agricultural biotechnology. At the same time, it is important that biotechnology policies and programmes are closely integrated in the framework of the problems confronting agriculture and agricultural research, with a clear sense of the specific problem areas to which biotechnology could best contribute.

Given the scarcity of resources, effort should be made to create conditions whereby research effort is not wasted and to improve the chances that successful research will lead to the diffusion of a biotechnology product. This would require concentration on a few, selected problem areas rather than a proliferation of research projects and dispersal—or even duplication—of research effort, as is the case at present. It would also require that the constraints to technology transfer and diffusion—whether regulatory procedures at the production level, inadequacies in the seeds sector or problems of acceptance by farmers—be taken into account and addressed. Finally, it would require strengthening of the linkages and interaction which can facilitate and/or accelerate the research, technology development and diffusion process. It is also crucial that these linkages—or "networking"—be strengthened not only at national level, but at the regional and international as well.

Evidence from the country studies suggests that regional collaboration in biotechnology has been most successful so far in the biotechnology policy arena. This has been particularly noteworthy with respect to workshops on biosafety and intellectual property rights, which have been evaluated as extremely useful by participants. It is important that countries make progress in these policy areas as the lack of adequate institutions constitutes a barrier to investment and progress towards the introduction and spread of genetically altered materials. Regional and/or international initiatives in these two areas should receive continued support, as they provide momentum for countries within a given region to organize follow-up activities.

Many countries lack both the resources and the capacity to take advantage of biotechnology. There is a special role to be played by aid in helping to strengthen this capacity. The research points to a wide range of options for donor agencies in supporting biotechnology initiatives in developing-country agriculture.

It is also now becoming abundantly clear that, if biotechnology projects are to be brought to fruition—particularly if that implies the ultimate diffusion of a biotechnology product—long-term financial support and commitment will be required.

A final policy conclusion which emerges from the project is that, in those situations where public-sector systems are no longer fulfilling that role and where markets have not yet emerged, alternative technology transfer and diffusion mechanisms may be needed in the future for "public good" technologies in developing-country agriculture. These would need to involve a diversity of public and private partners. This is a matter which will require reflection on the part of developing countries, relevant NGOs, the donor community and the international agricultural research community as a whole.

(ISBN 92-64-14901-5). Copies may be ordered from OECD, Mail Orders, 2 rue André Pascal, 75775 Paris cedex 16, France, or any of the main sales outlets of OECD publications.

Biotechnology Information Center

The Biotechnology Information Center, an Information centre of the USDA-National Agricultural Library, has developed a rich source of current biotechnology-related information available via Internet.The files at the site include bibliographies, resource guides and educational resources. Numerous links to other biotechnology-related gophers have also been included.

Contact:Accessathttp://www.inform.umd.edu/EdRes/Topic/AgrEnv/Biotech

European innovation on-line

Europe's Innovation and Technology Transfer programme now has a Home Page. The site introduces the Innovation Programme and its objectives, and, through a "What's New" section, provides news of the latest developments. Other main sections are Innovation Programme Activities, Innovation Programme Services; Participation in the Innovation Programme, the Green Paper on Innovation, European Policy Developments; and Frequently Asked Questions.

Contact: The home page is available at http://www.cordis.lu/innovation/home.html

Bioinformatics on the net

Oxford Molecular (Oxford, UK) and GlaxoWellcome (London, UK) have formed an alliance to deliver an on-line bioinformatics library free for non-commercial use. The site will offer public access to software, databases, and on-line resources for the storage, retrieval and analysis of genetic information. Based on COMMS MANAGER, Oxford Molecular's newest software architecture, the company is offering this service—complete with five post-doctoral bioinformatics researchers to design new software algorithms for the library—in an effort to become the open standard of choice for pharmaceutical and academic researchers. The two companies will maintain the on-line library at the GlaxoWellcome Stevenage Medicines Research Centre and will provide service and support, initially for three years. Oxford Molecular will also provide a variety of resources, including bug fixes and new releases. According to the two companies, the bioinformatics library will act as a repository of the most popular algorithms derived from existing code from GlaxoWellcome, Oxford Molecular Group, and other WWW public domain sources, as well as new algorithms designed by the library's postdoctoral contributors. (Source: *Nature Biotechnology*, Vol. 14, September 1996)

European bioinformatics initiative

The European Bioinformatics Institute has launched an initiative to support industry in the field of bioinformatics.

The first project, to be known as BioStandards, is funded jointly by the EBI, the EU (under their DGIII Information Technology programme), and several leading European pharmaceutical and biotechnology companies involved in the project—Astra, Biocine, British Biotech, Ciba, GlaxoWellcome, Hoffmann-La-Roche, Merck KGaA, Novo Nordisk, Pfizer, Rhône-Poulenc Rorer, Sandoz, SmithKline Beecham and Zeneca.

...Helping industry to adapt

The main focus of the initiative will be to help industry adapt quickly to the rapid changes in bioinformatics, in order to gain the maximum benefits. BioStandards will comprise training, education and the development/adaptation of databases, software and information structures which are of particular importance to industry. There will be particular emphasis on the promotion of existing standards and the development of new ones.

The EBI is part of the European Molecular Biology Laboratory, an international research organization, headquartered in Heidelberg, Germany. The EMBL is backed by 14 European Governments and Israel.

The EBI is based on the Wellcome Trust Genome Campus in Hinxton, near Cambridge, UK. It shares the site with the Sanger Centre and the UK Medical Research Centre's Human Genome Mapping Programme Resource Centre. These three institutes represent one of the greatest concentrations of genomics and bioinformatics expertise in the world, notes the EBI.

The Gene Letter now online

Volume 1, Issue 1 of *The Gene Letter* (http://www.geneletter.org/) went on-line in July. Developed and published by the Shriver Center with a 2-year grant from DOE, the bimonthly electronic newsletter is designed to inform consumers and professionals about advances in genetics and to encourage discourse about emerging policy dilemmas. Regular columns are Science, Medicine, Ethics, Law, International Developments, Student Corner, and Resources. Editors are Philip Reilly and Dorothy Wertz (Shriver Center) and Robin Blatt (Massachusetts Department of Public Health). *The Gene Letter* also operates an uncensored chatroom (http://www.geneletter.org/genetalk.html).

Video on genetic testing

Promise and Perils of Biotechnology: Genetic Testing is the third videotape in the *Winding your Way through DNA* educational series. An outgrowth of the 1992 symposium of the same name, the series was developed in response to teachers' interest in videotapes and curriculum materials based on the symposium's topics. The 25-minute classroom video and teacher's guide educate students about inherited disorders, their prevalence in society, and the

benefits and drawbacks of genetic testing. Through the narration of a genetic counsellor, the documentary follows three people: one young woman with a family history of Huntington's disease who decides to be tested and a mother and daughter who change their lifestyles to deal with familial hypercholesterolemia. For high school, college and public education classes in genetics, biotechnology and bioethics.

Contacts for scientists and individuals: Cold Spring Harbor Laboratory Press (800/843-4388 or 516/349-1930, cshpress@cshl.org); teachers and educational institutions: Pyramid Media (800/421-2304 or 310/828-7577, rwright@pyramedia.com).

Dealings with the media
Briefing Paper 5 October 1996

- What do the media want?
- Being interviewed;
- Appearing on radio and television;
- Causes of dissatisfaction.

The media world, in which journalists work, is very different from the world of scientific research—and even from that of scientific communication through journals and conferences. So while scientists and biotechnologists can collaborate effectively with journalists, such collaboration needs to be based on mutual understanding. Unrealistic attitudes on either side can be a recipe for dissatisfaction, or worse.

The purpose of this briefing paper is to explain, particularly for scientists working in biotechnology, how the media operate. It shows how specialists and journalists can work together in ways that are constructive and may be mutually beneficial. This briefing paper therefore differs from most others in the series, which aim to review in a balanced way the various areas of biotechnology together with their related issues and implications.

What do the media want?

Newspapers and magazines, radio and television companies, receive a vast quantity of material every day of the year. It comes in many different forms. These include announcements from companies, Government departments, research institutes and other bodies; material from national and international news agencies (*Reuters*, for example); and releases from public relations firms representing their clients' interests. The lay media also gain ideas from specialized publications such as *Nature* and other major journals of science. Sheer pressure on space and broadcasting time means that journalists can use only a tiny proportion of the information they receive through these various channels. How, then, do they choose what to cover?

Journalists and their gate-keepers (see below) are receptive to novelty. Significant developments in science and technology—for example, major advances in the treatment of a particular disease—provide many examples of such novelty. As well as developments with concrete applications now or in the future, the media report discoveries that are simply inherently interesting. So while much "normal research" goes unreported, developments with practical implications for, say, medicine or agriculture will attract journalistic attention. The same is true of discoveries that are counter-intuitive or have an element of the unexpected.

The general media also feed off each other to a surprising degree, and they work to unwritten menus of topics that appeal to them at any one time. Stories about environmental pollution, for example, may be keenly sought this year but may be less popular with journalists and their editors next year. In engaging the interest of the media, it is helpful to be aware of what subjects are currently favoured on their agenda. Some of the most skilful initiatives in "placing" stories in the media are taken by people who see opportunities for providing new angles on stories that are already running strongly.

There is fierce competition within the media. Newspapers, for example, compete for readers and for advertising revenue. Nevertheless, their science correspondents often work closely together, attending many of the same conferences and discussing what they are planning to report. Many journalists also have an appetite for occasional "exclusive" stories—which, if they are considered to be sufficiently important, their competitors will then have to follow up.

Journalists and their gatekeepers

Journalists dealing with fields such as biotechnology do not work in isolation. Like their peers in other areas, they work to agendas that are determined by "gatekeepers" in newspaper, magazine and broadcasting offices. News Editors in newspapers, for example, largely determine the topics which they believe we all, as readers and listeners, wish to know about. The space allotted to any one topic can also change, even between one edition of a newspaper and the next, as other news breaks and is given higher priority.

The majority of major newspapers in Europe employ a Science Editor. Many of these have a first degree in science, and some a PhD, while others have specialized after being general reporters. Like local newspaper journalists, general reporters (who also cover science and technology) can be expected to have little or no background knowledge on the topics they cover. However, both science editors and general reporters need to "sell" their ideas for news stories to a News Editor, who in addition will ask them to cover stories that have been initiated through other channels.

Features Editors are responsible for the longer "feature" articles in newspapers and magazines. Many of them welcome timely suggestions from outside contributors—for example, a proposal for a review of hay fever and its treatment from a specialist in this area. Such proposals should be made well in advance—not only for the idea to be considered and the article commissioned and written, but also for it to appear in sufficient time for readers to make use of information it contains. There are numerous opportunities for scientists and their organizations to be pro-active in this way—though many are unaware of such openings, or believe (wrongly) that the media will not be interested in such proposals.

Radio and television

Broadcasting channels are like newspapers in having newsrooms to monitor the news. Science specialists, based in those news departments, provide appropriate coverage for news bulletins. They also work for current affairs programmes, responding to requests from their Editors.

Although precise titles vary in different parts of the broadcasting world and in different countries, the Editor is usually the person in overall charge of weekly and other regular science programmes, with one or more producers responsible for individual programmes in the series. The Editor principally sets the agenda, though particular producers may be especially interested in specific topics

within the general field covered by the programme. In radio, presenters often work closely with their producers in making editorial decisions. Local radio programmes, like local newspapers, are always keenly interested in stories with a local angle.

In most countries, independent production companies are now responsible for a substantial proportion of "dedicated" science programmes.

As with the print media, editors and presenters of programmes dealing regularly with science, medicine and applied disciplines invariably welcome suggestions about topics they may care to cover. Again, they are keenly interested in "pegs" on which to hang a story, so as to give the idea topicality. Examples of pegs are the publication of a paper in a major journal, the appearance of a report with public interest and the anniversary of an event such as a great discovery or the birth or death of a famous scientist. To be of use, contacts regarding topics and pegs of this sort need to be made weeks and preferably months in advance.

Dealing with journalists

Journalists, and certainly those dealing with news, are invariably in a hurry. For those working in newspapers and broadcasting, this haste is entirely genuine. They may well be pursuing several stories in a single day, against the clock. But rapidity is also built into the media culture, so that anything (an interview, a photograph...) tends to be wanted instantly.

There are also more practical considerations if your story or message is to appear in the media when you want it to and if at all. Newspapers usually have two internal news conferences to determine what will be in the paper the next day. If a press release misses the early evening conference, your story is unlikely to make it to print the next day unless it really is important. The best time of the day to contact a news desk is early to mid morning, yet this may not be suitable for an evening paper or a lunchtime radio or television news bulletin. The shelf-life of a story is also painfully short: a long-term research project releases its result on a Friday afternoon; by the time of the next possible major news outlet on Monday, it will be considered old news and unlikely to get a place in the schedule. Afternoon press conferences are not a good way of getting communications into the media, and especially not on a Friday.

In reality, while journalists greatly appreciate an immediate response, it is perfectly reasonable that anyone approached by a reporter should ask for time to consider the request and how to respond.

If a journalist approaches you, in person or by telephone, make sure from the outset that you really understand what they want, what publication or programme they represent and how they propose to use any comments you make. In the case of radio and television, you should find out whether a proposed interview will be live or recorded, what is the format of the programme and who else will be taking part.

Even if you are satisfied on these points, you may want to collect your thoughts. Ask the caller to ring back in 20-30 minutes. Alternatively, say that **you** will return the call—but be absolutely sure that you do so. During the interim, you can also consult colleagues. Press officers in companies, universities and elsewhere can also be invaluable in providing guidance about particular journalists, publications and programmes and their past track record.

In the long term, some scientists find it mutually rewarding to become acquainted with individual journalists who deal with scientific issues, whether nationally or locally. While this should certainly not provide automatic channels through which to gain media publicity, such relationships can be of value to both parties and increase mutual confidence.

Being interviewed

There are several scenarios in which you may find yourself dealing with the media. These range from a scientific conference at which you are delivering a paper, to a telephone call from a journalist asking about your own work or seeking guidance about some development in your field. If there is a choice, it is more satisfactory and reassuring to meet a journalist face-to-face than to respond to a voice on the telephone. Paradoxically, some of us are more easily tempted on the telephone into saying more than we would have wished.

Ten Golden Rules

- Be well briefed;
- Plan the points you wish to make and your responses to standard questions and arguments;
- If you are in doubt, be prepared to say "I don't know";
- Be as open as possible and never lie;
- Do not say "No comment"; there is always something more useful which can be said;
- Show concern if there is a genuine problem;
- Show that your organization is addressing the situation or issue;
- Be as positive as possible without sounding callous and uncaring;
- Beware of admitting liability;
- Have a list with contact details of trained spokespeople available to make statements on specific questions.

A scientist may, on very rare occasions, be best advised not to speak to a journalist at all—for example, one who has a long record of serious misrepresentation. There are obvious dangers in declining an interview, however. bear in mind too that it is entirely reasonable that a journalist should wish to talk to you. Be very cautious about total refusal.

If you are tempted to decline an interview simply because you are busy and can scarcely spare the time, remember that the journalist will go elsewhere. He or she may turn to someone who is less qualified to speak with real authority on the subject. Either way, you may wish to seek guidance from a press officer in your institute, company or university.

Even when you are speaking to specialist reporters who cover areas such as science and medicine regularly, remember that terms and ideas which are very familiar to you may be new to them and thus require careful explanation. A general reporter will know very little science at all. So do not assume much knowledge on the part of the interviewer, and do not worry about "talking down" to a journalist. It is far better to do this than to use technical jargon without any explanation. Choose commonplace words wherever possible. If technical terms

are unavoidable, explain them—perhaps using metaphors or analogies to get over difficult concepts.

Remember that a journalist is unlikely to stick solely to technical matters. He or she may also pose questions about the funding of your research, the repercussions of biotechnology for consumers or its implications for exports or imports. In preparing for the interview, think about the questions a reader or listener would expect to be raised and to have answered.

The most satisfactory basis for an interview—from the standpoint of both parties—is "on the record". This means that the journalist can use and quote anything that you say. But there may be occasions when you prefer to conduct an entire interview, or part of it, "off the record", or "non-attributably". It is important to reach an unambiguous agreement **in advance** about the conditions of the interview. Ninety-nine journalists out of 100 **will** respect any form of confidence you agree. Never use the expression "No comment". There is always something less evasive you can say.

If you are working in collaboration with a company or institute other than your own, as part of a joint research project, you must discuss journalistic enquiries and requests for interviews with your partner organization and agree on what you will say.

Appearing on radio or television

Some scientists, even those with initial anxieties, prove to be natural performers on radio and television. Others fare less well. Television is a particularly demanding medium, especially in the unfamiliar environment of the studio. There are some dependable pieces of advice that are usually helpful. Be prepared—be absolutely clear about what you want to say and what is the purpose of your appearance. Always try to be positive. Never be angry or dismissive towards an interviewer, however difficult this may be, because there is a danger that this will alienate viewers or listeners.

While these guidelines are useful, practical experience is much more so. For those whose work and/or position in biotechnology mean that they are likely to be approached at any time for a broadcast interview, practical training is invaluable, especially for television. When embarking on media training, make sure that you are in the hands of people who currently work, or have very recently worked, in the medium. Some courses of this sort are run by trainers who themselves have had little or no practical experience in television or radio. They are scarcely likely to be in a good position to advise you.

A key question about a radio or television appearance is whether it is recorded or live. Each has its advantages and disadvantages. While some people are more nervous about a live interview, others appreciate the opportunity to say exactly what they wish to say, without any possibility that their words will be edited before transmission. Remember that, **in a news or current affairs programme**, the interviewer may wish you to crystallize your viewpoint/comments in a "sound bite" of at most 30 seconds. Remember too that, as with public speaking, a little nervousness actually helps.

Can I check the copy?

If you help a journalist who is writing a **news** story, it is not usually realistic to expect to see and approve the final text. There is usually insufficient time, and the copy may well be edited much later in the day when it is beyond the writer's control, let alone your influence. However, journalists are usually willing, in the interests of accuracy, to phone you back to check any quotes they wish to use. This can be part of your agreement with them beforehand. Remember that, while such quotes should be accurate, they cannot carry all of the fine distinctions which are appropriate to statements made in a paper in a learned journal.

It is much more realistic to expect to see a text, or a rough-cut of a programme, if you are dealing with a journalist who is working on a longer time-scale. Examples include a writer preparing a feature article for a magazine or newspaper and a radio or television journalist making a documentary. Again, ensure that you agree on this beforehand. Writers and producers will always be grateful to you for correcting blatant inaccuracies. They do not wish to be seen to be making mistakes.

Will I be paid?

Newspapers and magazines do not usually pay for interviews, whereas radio and television programmes may offer a fee or respond positively if asked for one—especially if they wish to take up a substantial amount of your time. However, there are no universal rules. On the one hand, you can reasonably expect to receive a modest fee if you are asked to go into a radio studio for a live or recorded interview. On the other hand, a television news crew may want to come to your laboratory and, despite the inevitable disruption, film you with no payment whatever. You will then have to weigh the time and inconvenience against the attendant benefits in publicity. There is often some flexibility for you to receive a fee even when it is not normally offered. Ask at the outset, not afterwards.

Television "researchers" pose particular problems. A researcher is not the producer or editor of a programme but a more junior member of staff who is employed to contact many different experts and develop a programme idea. Helping researchers can be beneficial to an organization—not least on those occasions when a scientist manages to influence a programme, plans for which were moving in some unsatisfactory direction. But dealing with researchers can also turn out to be unproductive. Much will depend upon your personal inclination and the policy of your institution. Again, press officers can help in resolving a decision about whether to help researchers.

Press conferences and releases

At a formal press conference—during a scientific meeting, for example—journalists are invited to hear about new developments in research. Such occasions must be accompanied by a "hot-line", open for at least 24 hours, so that journalists unable to attend can phone for information. Before a press conference, a press officer may ask for your help in preparing a "hand-out"— a sheet giving key points and the background to the announcement. Written notes of this sort are invaluable, as they are also on other occasions when you are interviewed by an individual journalist. As well as your name and position, a briefing sheet can contain information such as names of organisms and a summary of experimental results. This will be particularly useful for the general reporter who knows virtually nothing about the subject—for example, a local newspaper or radio journalist (who may even welcome a short list of key questions that he or she should ask you).

Press releases should also contain information about how to contact the key individual(s) involved—who **must** be available to be contacted through telephone or e-mail at the time as indicated. They are usually embargoed, with a date and time before which the contents of the release must

not be used. Journals such as *Nature* issue press releases every week, highlighting key papers in their next issue. Publication of an institute's annual report is another occasion when press releases are used to draw attention to work described in the report.

The importance of effective press releases can hardly be exaggerated. Releases which describe developments of timely interest to journalists, which are clearly written and which contain all of the formal ingredients outlined above, are used far more widely than those which are deficient in these respects. Moreover, a company or institute that issues only well-prepared releases, carrying genuine news, encourages journalists to pay immediate attention to future releases from the same place. Press releases are not usually published verbatim, but they should be written in a style such that they could be—when time is extremely short, for example.

Causes of dissatisfaction

There are, inevitably, occasions when scientists feel unhappy about the outcome of their dealings with a journalist—in a newspaper article or television programme, or indeed the non-appearance of an article or broadcast item. If this happens to you, first pause and consider exactly why you are concerned. Is it because you gave your time to help with an article or programme that has been aborted? If so, while common courtesy may mean that you had a right to have been informed, there is invariably nothing else to be done. Many articles and radio and TV recordings are never used—for logistical reasons quite unconnected with quality.

Again, if you believe that you have been misrepresented in an article or programme, consider carefully **why** you believe this to be so. Do you have a genuine grievance? Or are you really bothered because, for example, too much prominence has been given (in your opinion) to the ideas or achievements of another research group? In the latter case, discuss the matter with a colleague not involved in the work, wait until the next day and if you still feel as strongly, write a letter to the journalist setting out your point of view. This **will** be taken seriously.

In a particularly serious case, and again after talking to colleagues and/or your press officer, it may be appropriate to complain to the editor and/or to send a letter for publication. Even when not published, such letters **are** considered carefully and may well be taken on board when that subject is covered in future. Finally, there are options of reporting the journalist and publication to the official body in your country that deals with complaints about the press, or to take legal action if you believe that you have been defamed.

Be realistic

Some journalists are sometimes mischievous—as are some people in other walks of life. Journalists also make mistakes—as do some biotechnologists. Some of them sensationalize new developments—as do some biotechnology companies. Yet the vast majority of journalists do not set out to be mischievous, to make mistakes or to sensationalize their material. They work to the best of their ability and—especially given the pressures on their time—their output is of a high standard. Moreover, writers who specialize in areas such as science, medicine and technology have done so because they are keenly interested in those topics. They need your help, just as you may need theirs.

Further sources of information

Hitting the Headlines—A Practical Guide to the Media by Stephen White, Peter Evans, Chris Mihill and Maryon Tysoe, British Psychological Society, Leicester, 1993

Surviving the Media—How to Appear Successfully on TV, Radio or in the Press by Diana Mather, Thorsons, London, 1995

Can I Quote You on That? by Frank Albrighton, Conference of University Administrators, Birmingham, 1986

Presenting Science to the Public by Barbara Gastel, ISI Press, Philadelphia, 1983

The Role of the Media in Science Communication edited by Kate Akrill, Ciba Foundation, London, 1994

For further information concerning Briefing Papers and other publications and activities of the European Federation of Biotechnology, Task Group on Public Perceptions of Biotechnology, contact:
Chairman: Professor John Durant, Research and Information Services, National Museum of Science & Industry, GB-SW7 2DD London
Tel.: +44 171 938 8201; Fax: +44 171 938 8213; E-mail: j.durant@ic.ac.uk
Secretary: Dr. D.J. Bennett, Secretariat, EFB Task Group on Public Perceptions of Biotechnology, Schuytstraat 12, NL-2517 XE Den Haag. Tel. and Fax: +31 70 365 3857. E-mail: efb.cbc@stm. tudelft.nl (Reproduced with the kind permission of the European Federation of Biotechnology, Task Group on Public Perceptions of Biotechnology)

TECHNOLOGY AND INVESTMENT OPPORTUNITIES

SELECTED INVESTMENT/TECHNOLOGY REQUESTS

MANUFACTURE OF CHITIN/CHITOSAN

The company is an established manufacturer-exporter of marine products with its own seafood processing and freezing plant. It is 100 per cent export oriented, processing and exporting frozen fish and fishery products. Current sales are US$ 3.5 million. The proposed project is to manufacture chitosan and chitin as a joint venture with a foreign partner. Chitin/chitosan is a versatile polymer applicable in the medical and pharmaceutical industry, agriculture, food and nutrition, paper, textiles, etc. The raw material is a by-product of the seefood exporting unit. It is intended to export 75 per cent of this high value product, with the remaining 25 per cent for the local market.

Estimated investment: US$ 0.15 million.

Preferred mode of cooperation: Joint venture.

(For further information, please contact: Mr. K. S. Jayakrishnan of Mr. K. S. Jayarajan, Relish Foods, Valanjavazhi, Alappuzha 5, Kerala, India. Tel: 91-477-272029; Fax: 91-477-272229.

MANUFACTURE OF SPIRULINA ALGAE

The proposal is to set up a new project to manufacture 50 tons per annum of spirulina algae for the pharmaceutical industry as a joint venture with a foreign partner who would also provide the technology and access to markets for the product.

Estimated investment: US$ 1 million.

Preferred mode of cooperation: Joint venture.

(For further information, please contact: Mr. T. A. Krishnamoorthy, Project Manager, Kerala State Industrial Development Corporation Ltd., Keston Road, Kawdiar P.O., Thiruvananthapuram 695 001, Kerala, India, Tel: (0471) 438922; Fax: (0471) 435893; E-mail: ksidc@giasmd01.vsnl.net.in)

MANUFACTURE OF TAMARIND POLYSACCHARIDE TAMARIND GUM

The proposed project is to set up a new facility to manufacture 600 tons per annum of tamarind polysaccharide, which is a natural gum with a wide range of uses, as a joint venture project with a foreign partner who could provide the technology and access wo markets worldwide, with a buy-back arrangement.

Estimated investment: US$ 2.75 million.

Preferred mode of cooperation: Joint venture; technology transfer; market access.

(For further information, please contact: Mr. P.J. Kunjachan, Managing Director, Arjuna Natural Extracts Ltd., Khaders Centre, By-pass Road, Aluva 683 101. Tel: 91-484-622204; Fax: 91-484-532404)

MANUFACTURE OF TISSUE CULTURE PRODUCTS

The proposal is to set up a project to manufacture five million items of tissue culture products as a joint venture project with a foreign partner who could also provide the technology for the project with a buy-back arrangement.

Estimated investment: US$ 1 million.

Preferred mode of cooperation: Technology transfer; joint venture.

(For further information, please contact: Mr. T.A. Krishnamoorthy, Project Manager, Kerala State Industrial Development Corporation Limited, Keston Road, Kawdiar P.O., Thiruvananthapuram 695 003, Kerala, India. Tel: (0471) 438922; Fax: (0471) 435893; E-mail: ksidc@giasmd01.vsnl.net.in)

MANUFACTURE OF CANNED WHITE BUTTON MUSHROOMS

The project envisages establishing a 100 per cent export-oriented company to produce canned white button mushrooms at an annual capacity of 2,400 tons. Since the world demand is high and steadily growing and local labour and material costs are low, the proposal is expected to be successful. The promoters have considerable experience in managing agro farming, including coconuts, rice, sugar cane, fruit and vegetables.

Estimated investment: US$ 6 million.

Preferred mode of cooperation: Technology transfer; joint venture; market access; compensation agreement.

(For further information, please contact: Mr. M. Settu, Executive Director, Kumar Kalinga Agro-farming Ltd., Vellimadaikulam, Zamin Uthukule Post, Pollachi 642 004, Coimbatore District, Tamil Nadu, India. Tel: 91-4259-25471; Fax: 91-4259-24613)

CAFFEINE FROM TEA WASTE

The caffeine is extracted using a multi-stage countercurrent extraction technique. Caffeine is used in the drug and pharmaceutical industries as a stimulant.

Status of technology offered: Pilot plant.

Preferred mode of cooperation: Joint venture/know-how

(For further information, please contact: Mr. N.K. Sharma, National Research Development Corporation, 20-22 Zamroodpur, Community Centre, Kailash Colony, New Delhi 110 048, India. Tel: 91-11-6432121; Fax: 91-11-6449401)

SELECTED TECHNOLOGY OFFERS

LIQUID GLUCOSE
The substance is produced from crude starch. The process uses and enzyme to convert starch into glucose in two stages and replaces the traditional acid hydrolysis route.
Status of technology offered: Commercialized.
Preferred mode of cooperation: Licensing; know-how.

(For further information, please contact: Mr. N.K. Sharma, National Research Development Corporation, 20-22 Zamroodpur, Community Centre, Kailash Colony, New Delhi 110 048, India. Tel: 91-11-6432121; Fax: 91-11-6449401)

HIGH GRADE PECTIN FROM LIME PEELS
Technology is offered to process high grade pectin from lime peels. The process is economical as it utilises food waste to make a value-added product. It is used as a jellying and thickening agent in the preparation of jams and jellies. It also has applications in pharmaceuticals.
Status of technology offered: Commercialized.
Preferred mode of cooperation: Licensing; know-how; consultancy.

(For further information, please contact: Mr. N.K. Sharma, National Research Development Corporation, 20-22 Zamroodpur, Community Centre, Kailash Colony, New Delhi 110 048, India. Tel: 91-11-6432121; Fax: 91-11-6449401)

SPICE OIL AND OLEORESIN
Various kinds of spices such as ginger, chillies, cardamon, pepper, etc., are dried, powdered and then distilled to obtain spice oil. The residue is extracted with a suitable solvent.
Status of technology offered: Commercialized.
Preferred mode of cooperation: Licensing; know-how.

(For further information, please contact: Head, Technology Transfer & Business Development, Central Food Technological Research Institute (CFTRI), Mysore 570 013, India. Tel: 91-821-22304; Fax: 91-0821-37453)

OYSTER MUSHROOMS
Cultivated under normal temperature conditions of 21-28^{0}C, and a relative humidity of 55-75 per cent for a period of six to eight months in a year. They can also be cultivated in summer months by providing extra humidity.
Status of technology offered: Commercialized.
Preferred mode of cooperation: Licensing; know-how.

(For further information, please contact: Head, Technology Transfer & Business Development, Central Food Technological Research Institute (CFTRI), Mysore 570 013, India. Tel: 91-821-22304; Fax: 91-0821-37453)

CASTOR OIL
Production of pharmaceutical grade, hydrogenated and commercial grade castor oil and castor cakes. The castor oil project has two plants: a castor oil mill and a castor oil refining/hydrogenation plant. The plant will also have a deodoriser to be used for vegetable oil refining for edible purposes in case of shortage of castor oil. The process involves crushing the castor seed by a cold press in the first stage and hot pressing at the second stage to remove about 60 per cent of the oil from the castor seeds. The design of the cold press is unique and is a proprietary item. This is a renewable vegetable oil and has applications in pharmaceuticals, allied chemicals, lubricants, textiles and the locomotive industries.
Status of technology offered: Commercialized.
Preferred mode of cooperation: Joint venture, know-how, licensing.

(For further information, please contact: Mr. R. Bhattacharjee, Jagadhguru Engineers and Consultants Pvt. Ltd., "Om Muruga Illam", 39/7 Sarojini Street, Chennai 600 017, India. Tel: 91-44-452537; Fax: 91-44-4825277)

DIAGNOSTIC TESTS FOR TUBERCULOSIS IN VETERINARY MEDICINE
Patents and know-how are available for three gene probes and monoclonal antibodies which have been isolated for the rapid detection of TB for use in a diagnostic kit. Can identify specific TB type, therefore very effective epidemiology tool. The test can also be used for Mycobacterium Bovis as well as M.T.B.
Status of technology offered: Laboratory.
Preferred mode of coopertion: Licensing.

(For further information, please contact: Mr. Brian Padgett, Managing Director, The Technology Exchange Ltd., Wrest Park, Silsoe, Bedford MK45 4HS, United Kingdom. Tel: 44-1525-860333; Fax: 44-1525-860664; E-mail: tech-ex@dial.pipex.com)

MOULD GROWTH MEASUREMENT
An accurate method for quantifying mould growth has been developed. Tests can be performed under controlled humidity conditions in the company's laboratory. Licences to utilise the method available.
Status of technology offered: Laboratory.
Preferred mode of cooperation: Technical expertise; know-how; consultancy.

(For further information, please contact: Mr. Brian Padgett, Managing Director, The Technology Exchange Ltd., Wrest Park, Silsoe, Bedford MK45 4HS, United Kingdom. Tel: 44-1525-860333; Fax: 44-1525-860664; E-mail: tech-ex@dial.pipex.com)

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INTECHMART

Bahia (Salvador), Brazil
11 – 13 June 1997

INTERNATIONAL BUSINESS FORUM

Organized jointly by the Government of the State of Bahia and UNIDO, the Bahia Intechmart will be held in the State's capital Salvador. The main purpose of this Intechmart will be to match the investment and technology requirements of Bahian enterprises with the assets of potential foreign partners and thus facilitate business transactions, such as joint ventures, licensing agreements and technology transfer arrangements. This is the first Intechmart staged by UNIDO in Latin America, following a string of successful similar events in Asia and Africa since 1991, when this promotion formula was adopted.

Over 70 projects identified, evaluated and profiled by UNIDO are currently being advertised worldwide by the Organization's Investment Promotion Service Offices and its other honest-broker conduits. Most projects, whether they entail new ventures or the expansion or upgrading of existing ones, are in the chemical/petrochemical, agro industrial, tourism and mining sectors. The project profiles include information on the business background of the Bahian companies and local promoters involved, the main features of the projects, and the foreign resources sought by their proponents.

Direct negotiations between potential investors and Bahian project proponents of their choice will be arranged by the Forum organizers upon request. Representatives of financial institutions, business associations, contracting companies and Government agencies will also take part in the event to provide support services.

For further information, please contact:

- Project Manager, Investment Services, Latin America and Caribbean Unit (ITPD), UNIDO, P.O. Box 300, A-1400 Vienna, Austria. Tel: (43-1) 21131-4830, Fax: (43-1) 21131-6808, E-mail: bahiaforum@unido.org
- UNIDO Office in Brazil: SCN, Quadra2, Bloco A, Ed. Corporate Financial Centre 6^0 andar, 70712-900 Brasilia – DF, Brazil. Tel: +55-61-329-2171; Fax: +55-61-329-2179; E-mail: waleska@undp.org.br
- Promoexport-Bahia: Av. Estados Unidos 14, Ed. Suerdieck, $9/10^0$ andares, Comercio, 40010-020 Salvador – Bahia, Brazil. Tel: +55-71-326-0411; Fax: +55-71-326-0520; E-mail: bahiaforum@promoba.gov.br

ENTER A WORLD OF INFORMATION

What is ITMIN?

The Industrial Technology and Market Information Network (ITMIN) is a network of databases on industrial technology and market information within Sri Lanka, with on-line international access.

Who is ITMIN?

ITMIN Limited is a public limited liability company with shareholders, set up with the help of UNIDO, UNDP and the Government of Sri Lanka to implement and operate the ITMIN project.

What can ITMIN offer?

The Business Intelligence Unit offers:
Trade information and listings;
Market research;
Company matching;
Selective dissemination of information;
Employment opportunities.

The Technology Transfer Unit assists in:
Increasing production, sales and profits;
Improving product quality;
Reducing operating costs;
Adopting up-to-date manufacturing techniques;
Accessing wider markets;
Obtaining financial assistance.

The Electronic Publishing Unit provides:
Access to electronic publications in CD-ROMs and diskettes that will help search for precise information, saving valuable time.

The ITMIN Database contains:
In-depth information on Sri Lankan companies;
Technology & research organizations;
Consultancy and expertise;
Technology and machinery offered and sought.

Apart from the above, ITMIN offers specialized integrated training in information skills for professionals, corporate staff and decision makers. And to complement all this, ITMIN is Microsoft's Internet Partner in Sri Lanka and is hence in a position to offer Microsoft Internet solutions and packages.

More information on ITMIN's services can be provided by contacting:
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