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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

GENETIC ENGINEERING AND BIOTECHNOLOGY MONITOR

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

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

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TO OUR READERS

In the last issue of the *Monitor*, we mentioned that we were in the process of preparing the Second Task Manager's Report on Chapter 16 of Agenda 21: Environmentally Sound Managemment of Biotechnology. This second report will focus on more recent developments and trends in biotechnology and its application and make available to developing countries a general body of comprehensive and well-balanced information on the ways biotechnology interacts with other factors in achieving the goal of sustainable development.

In this context an information consultation was held by UNIDO in October to deliberate on strategic issues and discuss innovative measures to address them. During the course of the short two-day consultation, many areas were discussed, from the need to integrate biotechnology concerns into national sustainable development policies to create and build national capacities, to safety in biotechnology, matters related to intellectual property rights, the need to establish an institutional mechanism for the further development and implementation of an international policy on biosafety, and the need to promote a greater awareness of biotechnology issues. The general tone of the discussions centred around those items of greatest concern to the participants, namely the matters of biosafety regulations and their implementation, intellectual property rights, awareness building at all levels, including training, and the necessity for institutional mechanisms within developing countries to foster the development of national biotechnology businesses through licencing, joint ventures, etc. The main elements of this consultation will be reflected in the Second Task Manager's Report, along with inputs from contributors. This Second Task Manager's Report will provide key information for a related event, an interagency and governmental Round Table on Biosafety to be held by UNIDO in 1996 as a follow-up to the discussions of the Third Session of the Commission on Sustainable Development.

In line with the current concern on biosafety and related issues, a workshop on strengthening institutional capacity in biosafety is planned to be held in Moscow from 15-19 January 1996. This workshop, which is co-sponsored by the United Nations Environment Programme, the International Centre for Genetic Engineering and Biotechnology and the COBIOTECH Information Centre, will focus on policies and institutional support mechanisms for the safe application of biotechnology and the regional harmonization of regulatory oversight.

Many of our readers will be interested in knowing that all the Monitors will soon be available on the Internet. The UNIDO World Wide Web (WWW) server (http://www.unido.org) was opened to public access on 24 November, with some 140 documents available so far. Any document may be located via an integrated full text searching facility. Interaction is made possible by a growing number of on-line forms and clickable e-mail addresses provided in every document. The system has been designed to accommodate by e-mail delivery service at a future stage of development. The next issue of the *Monitor* will include a more detailed description of this system.

While on the subject of the access to UNIDO information sources, we would like to draw the attention of all our readers to the new access numbers for BINAS (the Biosafety Information Network and Advisory Service). BINAS is available on the Internet Gopher and World Wide Web (WWW). Gopher clients can access BINAS by pointing at: binas.unido.org. Mosaic and Netscape clients can access BINAS by pointing at: gopher://binas.unido.org or http://binas.unido.org/binas/binas/html

Virginia Campbell
Scientific Editor

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A. SPECIAL ARTICLE

GENETIC DIVERSITY IN SOUTH AFRICA — CONSERVATION AND SUSTAINABLE UTILIZATION

Professor Ralph Kirby
Department of Biochemistry and Microbiology
Rhodes University, P.O. Box 94
Grahamstown, South Africa

Introduction

Africa and southern Africa as part of the continent have a series of pressing and important problems with respect to the conservation of genetic diversity. South Africa has an additional one because it is the country with the world's third most abundant biodiversity covering only 0.8 per cent of the world's land surface, but South Africa has more than 8 per cent of the world's higher plant species, 8 per cent of the world's bird species, 5.8 per cent of the world's mammal species and 4.6 per cent of the world's reptile species. The biodiversity of lower animal, lower plant, fungi and bacteria in South Africa's many diverse environments is unknown. The problems revolve round the need to support an ever rising population with increased expectations of improved living standards by exploitation of the natural resources of the continent. Physical natural resources have a finite life-span when exploited and their value depends on the benification of those resources within the place of origin as to their overall value to the population. Biological natural resources, by contrast, are renewable and represent a permanent natural asset which should be exploitable in the long term by the country containing the asset.

However, mankind is part of the biosphere and therefore interacts directly with biological natural resources and the very pressures that require the exploitation of Africa's natural resources also directly put pressure on the biological resources by competition. Like physical resources, biological resources can be split into two groups: firstly, those resources which are known and accessible; and secondly, those resources which are unknown and require discovery. In the case of physical resources, the two groups are obvious: the first group is the visible and already exploitable resources, for example, gold in South Africa, diamonds in Namibia and oil in Nigeria; the second group consists of minerals, etc. which have yet to be found. Many companies spend millions of US dollars on exploration for the second group of resources with vast returns to the company and the country that finds such a resource. Biological resources of the former type consist of known biological species with a variety of known uses. However, outside of academic circles, with a few notable exceptions, very little is done to identify unknown biological entities such as new species and subspecies. In this article, I wish to explore the approaches available to African scientists to study, enumerate and monitor the biological resources of Africa both on the land, in its inland waters and in its coastal area, with particular emphasis on the approaches being used in South Africa to analyse these problems. Also under consideration will be the methodologies presently used in South Africa that can be transferred simply and cheaply to other African countries. It is patently obvious that African scientists, and preferably scientists from within the country under study, should be responsible for the evaluation of the biodiversity within Africa rather than scientists from the Western world. The biological resources of an African country belong to that country and even though part of those resources may be exploitable by a multinational company, only if the initial discovery, research and evaluation is done by an African scientist do the research funds, scientific reputation and any monetary value return to the scientist, his institution and his country. In many cases, especially with ongoing evaluations of biodiversity, a scientist from outside the country is at a disadvantage and repeated travel to and from an outside country significantly increases the cost of such research. The International Union of Biological Societies adopted the *Diversitas* programme at its 24th General Assembly in 1991 to study species diversity at all levels including animals, plants, micro-organisms, cells, species, communities, ecosystems and landscapes. The specific scientific themes include:

(1) Ecosystem function in biodiversity;
(2) Origins, maintenance and loss of biodiversity;
(3) Biodiversity inventorying and monitoring;
(4) Conservation of the wild relatives of cultivated plants and domesticated animals;
(5) Marine diversity;
(6) Micro-organism diversity; and
(7) The human dimension of biodiversity.

Although European, North American, West Pacific Asian and Ibero-American regional programmes have been set up, Africa lags behind in this programme and other UNESCO based programmes. Funding is mostly country based, which means that in poorer nations, biodiversity must have a lower priority unless profit can become a driving force.

Genetic diversity and sustainable development: the problems

The known species

The problems falling into this group tend to be associated with macro-organisms for the most part. These organisms are the ones with the highest profile in the human mind and have been studied and analysed for many years. The need to conserve these organisms has been at the forefront of Governments' minds for many years and South Africa has done its part in the preservation of these ecosystems, with two examples coming to mind, the creation of the Kruger National Park and the Addo Elephant National Park, which have been extremely important in the preservation of two distinct populations of elephant in South Africa. However, the impact of man on the environment continues to fragment wild populations creating a number of problems that must be addressed.

This is particularly important as the number of private game reserves in Africa increases. In the 1970s in the Northern Transvaal of South Africa, Mala Mala, Londolozi and Sabi Sabi removed the cattle from their large ranches and began bush clearing to restore open grasslands previously encroached by bush due to overgrazing. The result was game lodges commanding tariffs up to US$ 500 per night, which have become significant employers. As this type of enterprise has spread through all of southern Africa, many new jobs based on eco-tourism have been created. However, the long term viability of this type of job creation depends on sustainable ecosystems, which become more difficult to maintain as the size of the game ranch becomes smaller. On-line management of this type of ecosystem is required and some of the problems are described below.

Inbreeding

As populations have become fragmented by urbanization and the building of fences, the natural migrations of individuals and groups has been disrupted. This is true for plants as well as animals where vast areas of cultivation have isolated individual plants and plant populations from nearby relatives. This phenomena is exacerbated by the trend towards private game parks where animal populations are isolated by fences for economic reasons. Small populations give rise to two genetic problems—inbreeding and loss of heterozygosity. Both can lead to depressed levels of reproduction and the appearance of aberrant individuals, as genes which are normally recessive within the population are expressed. It is important that these phenomena are monitored and populations maintained in as viable a condition as possible

Translocation

This leads on from the previous point. If one is to maintain a large number of relatively small populations, it is essential that individuals be translocated from population to population to maintain gene exchange. It is also important when establishing new populations, for example in a private game park, that when the animals are chosen for this park, the greatest genetic diversity possible is obtained Thus, in any case where translocation takes place, the maximizing of the genetic diversity of the populations undergoing translocation is carried out. In many cases this can be done empirically, by bringing in animals or plants from populations which are not known to be related to the population receiving them. However, in some cases where the populations are small and interrelated, a means of establishing genetic diversity should be used.

Local adaptation

Translocation can give rise to other problems. Particular populations, especially those that are highly isolated by physical barriers can become genetically adapted to a particular environment, this being a step in the evolution to new species. If there is an introduction into such a population, or such a population is translocated to a new environment where it interbreeds with another population, this can potentially give rise to the loss of those genes particular to the local environment. Thus, it is necessary to establish if natural populations are highly genetically distinct, and that therefore their local gene pools should be preserved, perhaps by captive breeding.

The unknown species

Separate from the above problems, but linked to increasing urbanization and destruction of habitats, are the problems arriving from unidentified levels of genetic diversity. These can be divided into two groups:

Cryptic species

These occur where isolation and other evolutionary genetic effects have created what amounts to new species or subspecies undetected by classical morphological means. Any type of environmental impact on such small unique populations could result in an unwitting extinction. In many respects, the smaller the organism, the more difficult it is to detect such cryptic species; however, in general, most such species are eukaryotes.

Novel organisms

The microbiological world probably contains millions of yet undiscovered organisms which may be capable of producing novel useful compounds and processes. Modern medicine is dependent on antibiotics isolated from soil micro-organisms and molecular genetics depends for many processes on enzymes isolated from organisms from extreme environments. Detection of such organisms from environmental samples is exploitation of the resources of the country from which the sample originated.

Molecular genetic methods and their applications

The above problems require studies on individuals and populations which are rapid, relatively cheap, functional in an African environment and allow analysis of the individual genetic structure of members of the population and comparison between individuals. The molecular genetic techniques described below make this possible and their suitability is commented on.

Allozyme analysis

This method of analysis involves the isolation of active enzymes by non-denaturing gel electrophoresis, usually using starch gels but sometimes using acrylamide gels. The proteins are separated on both charge, shape and molecular weight, such that these parameters cannot be estimated from the mobility. Once separated, the proteins are detected using specific chemical stains which produce a colour reaction at the position of the band due to the specific activity of the enzyme. A very wide range of such stains have been developed for enzymes, such as dehydrogenases, amylases, nucleases, etc. A number of different bands can be identified from one gel representing either different mutant versions of the same gene in a polypoid organism, or different genes making the same type of enzyme at different genetic locations in the genome of the organism. In complex higher organisms, the enzymes present are tissue specific and only samples from the same pure tissue can be directly compared with each other. Because enzyme activity must be retained, the samples must be treated very carefully and repeated freezing and thawing or storage at high temperatures must be avoided. Analysis is usually carried out manually due to the complex nature of the interpretation needed. Some problems are associated with this method, particularly in the context of southern Africa: firstly, sampling of specific tissues tends to require dead

specimens and for rarer species this can be a major problem; secondly, the collection and transportation of delicate samples over long distances can be a problem in Africa where a cold chain can be difficult to maintain; thirdly, separate gels must be run for each enzyme although methods of reducing the workload due to this have been established; fourthly, in animals and plants with a large number of isoenzymes and which are of two or higher ploidy, interpretation of gels can be difficult even for an experienced scientist; and finally, the availability, transportation and cost of the specialist chemicals required for each enzyme detection system can be problematic. The method has two major advantages. Firstly, that it allows a direct measurement of the heterozygosity at specific loci and an overall estimation of the average heterozygosity for the loci studied. Inbreeding and small populations are characterized by low levels of heterozygosity. Secondly, that specific alleles of a particular gene can be traced from population to population, which can allow conclusions to be drawn on how populations are or were connected by interbreeding.

SDS acrylamide gel electrophoresis of proteins

This method also uses protein samples and requires them to be taken from specific tissues in higher animals and plants. However, the proteins are separated by electrophoresis on acrylamide gels in the presence of sodium deodycle sulphate (SDS), which is a charged detergent. SDS denatures the proteins randomizing their shape and binds to them, equalizing their charge. Thus separation on the gel is accomplished on molecular weight alone. Staining is carried out using generalized protein stains, such as commassie blue or silver stain, which means that specific functions cannot be linked to particular protein bands, unlike above. Different proteins of the same molecular weight will run to the same point in the gel, meaning that they can superimpose. However, samples are not as vulnerable to damage from changes in their environment although a good cold chain is still needed.

Changes in molecular weight of specific proteins occurs more slowly in genetic terms than changes in charge and therefore changes in the proteins in a population measured by SDS acrylamide gel electrophoresis must take a longer time to occur. Thus, although they can be used to intra-population and inter-population genetic variability, they become more useful at the discrimination level of subspecies and species. Analyses can be carried out either manually or electronically and are usually calculated as a percentage of the band shared between two individuals. This method's major advantages are firstly: its simplicity, requiring relatively few tools and chemicals, and secondly, that it is fast and can be used cost effectively for preliminary studies.

RFLP analysis of complete organelle DNA

Mitochondria and chloroplasts are subcellular organelles that contain their own genetic material in the form of organelle specific circular DNA molecules. The size of these DNA molecules vary and can be as small as 18,000 base pairs in many vertebrate mitochondria but can be as large as 200,000 base pairs in the chloroplasts of higher plants. The organelles and DNA are, in general, maternally inherited and thus can be used to trace maternal lineages. Changes to the DNA sequence in the organelles occurs from time to time by mutation and these changes are perpetuated from generation to generation if they do not directly affect the function of the organelle, which many do not. Such changes can be detected if the whole circular DNA molecule is isolated and subjected to a battery of type II DNA restriction endonucleases, which cut the DNA at specific sequences in the DNA, ranging from four base pairs to eight base pairs. Thus, a change within a specific site could either eliminate a so-called restriction site already present or create a new site. The pieces of DNA produced by the restriction endonuclease are separated on agarose or acrylamide gels and the fragments detected either using the interchelating agent ethidium bromide or silver staining. The bands produced can either be used to deduce a complete two dimensional map of the circular organelle (easily possible with 18,000 base pairs of the vertebrate mitochondrion), or allowing the calculation of percentage band shared between individuals. The changes are called restriction fragment length polymorphisms or RFLPs. In either case, it is possible to estimate the sequence divergence between individuals and the average sequence divergence within and between populations. It is also possible to trace mitochondrial types from one population to another. The rate of mutation of organelle DNA is about ten times higher than for nuclear DNA and it thus changes quite rapidly with time. Large diverse populations contain many different RFLP types within their organelle populations. Inbred, bottlenecked, small or recently evolved populations contain few organelle types.

The advantages of this approach rest on the fact that good methods of isolation of organelle DNA, and particularly vertebrate mitochondrial DNA, have been developed and that this type of analysis can rapidly give an indication of populations that are under threat. The disadvantages are tissue sampling and storage, which can be important in getting a good yield of analysable DNA. The analysis is relatively time consuming if done to completion and covers a limited part of the genome of the complete organism, which is specialized and maternally inherited.

Analysis of polymerase chain amplified fragments of organelle DNA

The complete and partial DNA sequences of a significant number of mitochondrial and chloroplast DNAs are known and detailed comparisons of such DNAs have been carried out so that it is possible to identify conserved regions of such DNA and other regions, which are subject to greater variability. Polymerase chain reaction allows the amplification of as little as a single molecule of DNA to microgram quantities of identical DNA if two specific priming sites can be identified which flank the area to be amplified. This is possible for a number of regions in organelle DNA, but in particular, the D-loop region, the rRNA region and the cytochrome oxidase II region of mitochondria are commonly used for this purpose. Once such a sequence has been amplified, it can be analysed either using the RFLP technique described above, which is relatively easy and rapid, or by DNA sequencing of the complete fragment, which is more costly, time-consuming and difficult. Either way, the results can be analysed to provide sequence divergence between individuals, within populations and between populations for these maternally inherited sequences.

RFLP analysis on such small pieces of DNA (about 1,000 base pairs in size) is not highly efficient but can give

good results. The more complex approach to DNA sequencing is more difficult to set up and more costly to run in an African context although it gives better results. An example of this is the identification of meat from protected whales in shops in Japan by PCR amplification using a portable thermocycler. This emphasizes one major advantage of this approach, which is that it can be carried out in the field using a generator and minimum equipment. The amplified sample can then be returned to the laboratory for analysis thereby avoiding the need to transport samples. However, this method is probably the least vulnerable to sample deterioration, and preservation using freezing, drying or alcohol have been successfully used. It can also be used on museum specimens, mummified samples and samples preserved in other ways, for example, in amber. This allow studies of genetic variation in both the physical and temporal dimensions for the same criteria as complete organelles. Its major disadvantage is the same as for complete organelle analysis, which is that it studies an even more limited range of maternally inherited genes.

Randomly Amplified Polymorphic DNA Sequence (RAPDS) fingerprinting

This is another polymerase chain reaction based technique in which short (10 base pair long) single primers are used to amplify random fragments from the complete genome of an organism. The genome size of organisms vary from $2x10^6$ base pairs for the smallest bacteria up to 10^9 base pairs upwards for higher plants and animals. Thus, under the conditions of amplification applied, the primers allow random DNA sequences, usually less than 1,000 base pairs in size to be amplified. The resulting DNA fragments are separated by either agarose or acrylamide gel electrophoresis, detected and their size measured. Each band represents a particular pair of 10 base pair sites with a unique sized piece of DNA between the two primer sites. Thus, each band samples the organisms genome for variation in that region. Percentage band sharing between organisms and within between populations can be easily estimated and even sequence divergence can be calculated with a few assumptions. Heterozygosity cannot easily be estimated because DNA bands are dominant and paired alleles from the diploid chromosome pairs are hard but not impossible to find. RAPDS fingerprinting allows identification of unique populations and the measurement of genetic diversity within them. It can be used to relation different populations to each other and to do limited phylogenetic analysis at the subspecies and closely related species level. It cannot be used to study distant phylogenetic relationships, which is possible with organelle DNA.

The advantages of RAPDS fingerprinting are: that it is quick and cheap, allowing large numbers of samples to be processed; that it gives excellent information on the structure and relationship within and between populations; and that it covers a significant area of the total organisms genome. As there are thousands of ten base pair primers available, the coverage is only limited by the number of primers used in the study. A minimum of four and usually between six and ten are adequate. Depending on the questions being asked, then one or two primers giving significant genetic variation can be targeted for the complete study. The technique's disadvantages are that it is laboratory and instrument dependent, sample preservation can be a problem but usually is not and analysis of the data objectively for a large number of samples requires an electronic data capture and analysis system.

Microsatellite DNA fingerprinting

This is another polymerase chain reaction based method which examines the variation in specific very short repeats found in the eukaryotic genome. A cloned chromosomal DNA library of the organism under study is made in a high copy number bacterial plasmid vector with an insert target size of about 500 bp. This library is probed using a radioactively labelled short oligonucleotide synthesized to contain the repeat motif which has been targeted. Clones that give a strong signal with the probe using autoradiography are identified and the plasmid DNA extracted from them. The inserted DNA within these plasmids is then sequenced and the repeat motif found within the cloned sequence. This motif will be flanked by unique DNA sequences, which are then used to design two primers for polymerase chain reaction amplification of the repeat motif. Repeat motifs within the eukaryotic DNA are subject to slippage on replication and the number of repeat units within the motif can increase or decrease over a number of generations. Thus, when a number of individuals from a population are analysed using the pairs of primers and polymerase chain reaction on an acrylamide gel system, variation in the overall number of repeat units in the specific locus of the organism can be detected. Overall genetic variability can be estimated and heterozygosity measured as the two alleles in the diploid can be identified, unlike with RAPD fingerprinting. Furthermore, a limited amount of multiplexing can be carried out allowing up to three or four different loci to be analysed in one polymerase chain reaction.

This process can give the most detailed results for a specific species and population, including the heterozygosity within populations, the variation in heterozygosity between populations, genetic variation within populations and genetic variation between populations, all at the DNA level. However, in the context of Africa, the method has a number of disadvantages. Firstly, the microsatellite repeats that are studied are not characteristic of the whole of the genome of the organism and may not, in some cases, reflect the variation in the unique genes, which are genes most important to the organism. Secondly, this system works for higher eukaryotes and not for prokaryotes and some lower eukaryotes. Thirdly, the primers for each locus must be identified and sequenced for each species studied; although some primers may be used in a number of closely related species, results are much better if the primers are targeted directly at the species from which they came. Finally, the technology required to carry out a microsatellite project is relatively high, not easily transportable into a low technology environment and expensive from the point of view of the work required to obtain only one set of primer between 10 and 20 are required for a good study. However, if suitable target primers have been identified elsewhere, the microsatellite analysis of a population using polymerase chain reaction is a good option.

Analysis of targeted polymerase chain reaction amplified genes

This method gets round one of the disadvantages of microsatellites in that unique genes are targeted for amplification by specific pairs of primers using polymerase

chain reaction. Again, heterozygosity and genetic diversity within and between populations can be estimated for each targeted unique gene. However, this process requires that the sequence of the gene in question is available. This requires either the cloning and sequencing of the gene in question or the sequence of the gene to be available from other workers in the DNA sequence data banks. This approach is viable for sequences from well studied organisms of all types, such as the great apes, and the ability to identify polymorphism can be increased by using such techniques as thermal gradient gel electrophoresis. However, for the majority of organisms in Africa and any novel species, this method is not really practical.

South African molecular population genetic research groups

Below is a list of the major research groups in molecular population genetics in South Africa, with their areas of technical expertise and their major research interests. The list is not complete and departments of genetics, zoology or botany exist at a number of other universities having specific interests in certain problems.

Department of Biochemistry and Microbiology, Rhodes University, Grahamstown and JLB Smith Institute of Ichthyology, Grahamstown.

Technical Expertise:
SDS acrylamide gel protein profiling
Polymerase Chain Reaction (PCR) amplification of DNA
DNA sequence analysis
Molecular analysis of mitochondrial DNA
Randomly Amplified Polymorphic DNA (RAPD) fingerprinting
Thermal Gradient Gel Electrophoresis (TGGE) analysis of genes
Research Interests:
Population genetics of threatened species of marine and freshwater fish
Population genetics of dolphins
Population genetics of ostriches
Population genetics of endangered Fynbos plant species
Population genetics of African bees
Population genetics of marine gastropods
Identification of novel bacterial fungal species from the southern African environment
Population genetics of medically important bacteria in southern Africa

Department of Chemical Pathology, Medical School, University of Cape Town and Sir Percy Fitzpatrick Research Institute for Ornithology, University of Cape Town.

Technical Expertise:
Polymerase chain reaction (PCR) amplification of DNA
DNA sequence analysis
Molecular analysis of mitochondrial DNA
Research Interests:
Population genetics of birds
Population genetics of the rhinoceros

Mammal Research Institute, University of Pretoria.

Technical Expertise:
Polymerase chain reaction (PCR) amplification of DNA
DNA sequence analysis
Molecular analysis of mitochondrial DNA
Research Interests:
Population genetics of mammals in general and threatened species in particular

Department of Genetics, University of the Witwatersrand.

Technical Expertise:
Allozyme analysis
Theoretical population genetic modelling
Research Interests:
Speciation

Types of research projects

Below are examples of the types of projects carried out by the group at Rhodes University, which is made up of the Department of Biochemistry and Microbiology and JLB Smith Institute of Ichthyology with strong collaboration with the Department of Zoology and Entomology, Rhodes University, the Department of Botany, Rhodes University, Cape Nature Conservation, Transvaal Nature Conservation, the Port Elizabeth Museum and a number of departments from other universities and other interested bodies and companies. The overall theme of the research is measurement of genetic diversity in important species and the application of this to sustainable utilization of the genetic resources of southern Africa

Genetic characterization of small isolated freshwater fish populations

Southern Africa contains a number of habitats which, because of geographic geological and climatological factors, contain small isolated bodies of fresh water. The limited number of large fresh-water systems consist of a few major river systems such as the Vaal, the Orange and the Tugela and a number of man-made lakes, which are the result of the construction of dams. The majority of natural water bodies at the coast consist of a large number of small river systems, while inland small lakes, springs and sinkholes predominate in many areas. The relative scarcity of water supplies through the southern African region creates large-scale pressure on these resources. Many of the water bodies are unique, isolated and have not been studied in detail.

One such system is the dolomitic springs and sinkholes of the western Transvaal. The diverse and competing aspects of utilization and exploitation of these springs and sinkholes pose a major threat to the unique biota inhabiting these water bodies. A multidisciplinary project aimed at the identification and characterization of the ichthyofauna of six selected study sites in the western Transvaal was initiated by the Department of Nature and Environmental Conservation, Transvaal and set up in collaboration with the JLB Smith Institute of Ichthyology, Grahamstown. Genetic characterization of the unique members of the ichthyofauna of these sites, Molopo Oog, Wondergat, Malmani, Marico,

Schoonspruit and Klerkskraal was carried out and specific recommendations on the conservation of these species was made and on the sustainable utilization of these unique water resources for farming and recreational purposes.

Genetic characterization of known threatened and rare fish populations

Barbus andrewi is a fish species found in a limited number of rivers in the Western Cape of South Africa. It is particularly threatened for two reasons: firstly, attempts to eradicate the species to improve fishing occurred in the past; and secondly, from competition with introduced Northern Hemisphere fish species. The species is rare enough to make sampling difficult and fin clips were used to obtain tissue samples to avoid destructive sampling of the populations. Support from the Department of Nature and Environmental Conservation, Cape Province, allowed the study of two natural populations in Berg River and the Buffelsjagsdam/Breede River. A captive population bred at the Amalinda Fish Hatchery was also studied with the aim of developing a reintroduction programme. We have used RAPDS fingerprinting to make recommendations on the best approach to the conservation of this species using captive breeding and re-introduction.

Genetic variation within and between rare and common taxa of Cape *Proteaceae*

The Fynbos biome is unique and contains a complete floral kingdom, part of which is made up of many taxa of *Proteaceae* not found anywhere else in the world. These range from populations of plants in the 100,000 to millions, to ones which contain less than 50 individuals. These species, notwithstanding their unique place in the world's flower population, represent an economic resource for the Cape.

Harvesting of these flowers from the wild provides employment for a significant number of people and the eco-tourist potential of the floral kingdom is only just beginning to be exploited. An initial screening of a number of threatened species by molecular genetics is under way to measure both their genetic diversity and gene pool of these species and to elucidate some of the taxonomic problems associated with very rare plants. The very small gene pool that some of these species may have poses a particular threat, especially as rationalization of nature conservation resources may lead to re-designation of nature reserves. Preservation of the plants by propagation outside of the wild would require knowledge of the genetic makeup of the plants taken from the wild to maximize the gene pool and could be used to encourage the move to commercial *Protea* farming rather than exploitation of wild plant populations. Protein profiling and RAPDS fingerprinting are being used to confirm species and subspecies status for rare *Proteas* and to identify viable populations for preservation and further study. Recent results have shown us that RAPDS fingerprints can be obtained from preserved herbarium material, which opens up the possibility that changes in the genetic diversity of these rare species can now be studied over time.

Population genetics of two dolphin species from the east coast of southern Africa

Two species of dolphin are found commonly off the shores of southern Africa, the bottlenose dolphin and the humpback dolphin. Both are under threat from a variety of human agencies including pollution, overfishing and the use of shark nets to protect swimmers. Although not confined to the southern African coast, they are an important element of the coastal ecosystem as well as being an eco-tourist attraction. Two questions concerning these species are being researched. Firstly, what is the genetic diversity of the populations along the southern African coast and are these populations unique compared to the rest of the world. Secondly, as the degree of threat to the dolphin populations varies along the coast from being high close to Durban in Natal/Kwazulu to relatively low off the coast further south, do the dolphins form one continuous interbreeding population or are there only relatively few individuals that move from one distinct population to another. Finally, can we discover something about the breeding and social structure of dolphins. Mitochondrial DNA studies, RAPDS fingerprinting and possibly, microsatellite analysis could in the future answer these questions and make recommendations on how best to stabilize the populations of these two dolphin populations and retain their ability to attract eco-tourists.

Identification of Microbial Population Diversity in Environmental Samples

Since the discovery of antibiotics during the 1940s, pharmaceutical companies have collected samples from a massive number of different environments in almost every country of the world and screened these samples for the presence of organisms that make new antibiotics. Almost all the groups of antibiotics in use today were discovered this way and in almost every case the country of origin of the organism is lost in obscurity unless preserved in the species name, such as *Streptomyces natalensis*. More important, the country of origin, which in most cases was not the country of the company which exploited the discovery, received no monetary reward for the exploitation of its natural resource. The United Nations Treaty on the Environment has changed this to some degree, but it is up to each country to protect its own resources. We have developed a RAPDS fingerprinting-based method for studying the genetic diversity within the actinomycetes found in soil samples. Thus, unique organisms can be identified against a database for further study if necessary by commercial companies, and the organisms can be protected from unwanted exploitation by those not permitted so to do.

Conclusions

Conservation and sustainable development require that genetic diversity be identified, measured, analysed over time, exploited where possible and protected from threats where possible. Modern methods of studying genetic diversity at the organism are becoming increasingly complex, but lack two important features. Firstly, this approach does not usually find a vast range of new resources. It is an extension of the classical approach to species identification although it is very good as an overall measurement of total resources available. Secondly, it tells the observer almost nothing about the genetic structure of the population and does not have a direct predictive ability on how well the population will survive. Only molecular genetic tools are now able to some extent to make such predictions, identify easily new cryptic species, analyse what happens to a population over time, and protect any novel organisms identified from unauthorized exploitation.

Of the range of molecular genetic tools available to study population genetics in an African context, three have decided advantages over the rest in ease of application in a difficult environment, cost and large-scale sample analysis. These are SDS acrylamide gel electrophoresis of proteins for rapid analysis of population diversity, RAPDS fingerprinting for detailed analysis of diversity between and within populations, subspecies and species, and microsatellite analysis if detailed analysis and heterozygosity measurements are required of specific species in a long-term study. Mitochondrial analysis using polymerase chain reaction also has its place in studies of the systematics and taxonomy of species especially as it can be easily applied to museum specimens.

There are two specific emotional problems in genetic diversity and conservation within southern Africa: these are the elephant and the rhinoceros. In the case of the African elephant and the white rhinoceros, the success of their conservation within the public and private game parks of South Africa have created major problems of overpopulation and environmental degradation. The South African Government's request to CITES to allow a limited trade in some of the products of these two species has met with a mixed reception. This highlights the major problem of sustainable utilization of rare species within a biodiversity problem. Only by utilizing the protected species in as many ways as possible can the economics of protecting the whole biodiversity of the region be made to balance. This must include the products of the animals as well as eco-tourism, because without culling or removal, large-scale environmental damage occurs, especially with large herbivores, and eco-tourism is harmed.

The South African Government asked for trade in elephant parts other than ivory to be allowed and this was rejected. In fact, with DNA fingerprinting, certification of such products can be 100 per cent accurate. In contrast, the trade in live white rhinoceros and white rhinoceros trophies was agreed to under specific conditions. This is a step forward for conservation when an animal can move from a complete ban on trade back to trade under specific conditions as it becomes less threatened. Of the highly endangered animals in the world which are poached for a saleable product, both the white and the black rhinoceros could easily be exploited in a true sustainable utilization system. Unlike ivory, the removal of the horn from a rhinoceros is about as painful as cutting one's toenails and the horn grows back to full size in about five years. At whatever price such a horn could be sold in a real marketplace, farming rhinoceros for horn is probably one of the more economically viable possibilities for marginal bushveldt farms in southern Africa. The market for rhinoceros horn in the Middle and Far East could probably be sustained by 100,000 farmed rhinoceros putting 20,000 horns on the market per year at a value probably between US$ 100 and 400 million per annum. A CITES controlled and directed market would eliminate poaching as uneconomic once the price dropped and stabilized. It should be noted that most domestic animals are extinct in the wild, e.g., horse, cattle, sheep, etc. because real economic value makes them property, not wild animals. A similar thing has occurred in South Africa over the last 150 years with the ostrich, where very few wild ostrich still exist and conservationists do not want domestic ostriches, which have been genetically manipulated to be released into the wild population. Such a situation could be envisaged for the two species of rhinoceros. The elephant is more difficult, but directed and controlled trade once a stable farmed population is established should be the way.

South Africa is not unique in Africa in having the expertise to use molecular population genetics but it is a resource centre which is already being exploited in Namibia Botswana, Malawi and Zimbabwe. The research and training resources in South Africa should be used to the advantage of the whole of Africa. However, the lack of a specific government policy on biodiversity and conservation, including direct funding to support research on these areas remains a problem. Recent meetings involving UNESCO concerning the Biodiversity Treaty hopefully mean that such a policy and funding is being considered.

B. NEWS AND EVENTS

UN and other organizations' news

New United Nations AIDS strategy

The United Nations is on the verge of launching an initiative which could determine the way the world responds to the AIDS epidemic.

The proposed joint initiative between United Nations agencies "is different from anything the United Nations system has ever tried to do", says Mina Bail of the United Nations Development Programme (UNDP).

With a budget expected to be more than $100 million a year, the new organization will be the biggest spender in the international struggle against the disease, and could influence the way individual Governments spend their own AIDS budgets.

A too-narrow focus on the medical aspects of the disease has been a recurring criticism of official programmes, but as five United Nations agencies and the World Bank jostle for a slice of the action, there are concerns that the Joint Co-Sponsored United Nations Programme on HIV/AIDS may end up as just another United Nations mega bureaucracy.

The need for a coordinated approach stems from the continuing spread of the epidemic: the World Health Organization (WHO) estimates that the total number of AIDS cases jumped by 60 per cent—to 4 million from 2.5 million—in the 12 months to July 1994. Allowing for under-reporting and under-diagnosis, WHO estimates that there are 14-15 million people infected with HIV in the world today. Most will develop full-blown AIDS within the next decade, taking a heavy toll on health services, social networks and, in some cases, national economies. WHO figures estimate 40 million people will be infected by the year 2000, but looking at dependency ratios (relatives of the sick, particularly the young and the old), between 200 million and 250 million will be affected, with many aged between 20 and 40.

WHO accounts for 70-80 per cent of the world body's spending on AIDS, with the UNDP, UNFPA, the United Nations Children's (UNICEF), the United Nations Educational, Scientific and Cultural Organization (UNESCO) and the World Bank spending the rest. The new body scheduled to start in January 1996 will bring them all under one umbrella. But while the new plan is a logical development in the AIDS fight, it is not yet a marriage of minds. Currently, the basic plan is for the new programme to work on two levels. Globally, the programme will be administered from Geneva, in place of WHO's Global Programme on AIDS which will be closed down at the end of 1995. A key test will be money: greater efficiency from coordination is good, say many of those involved in tackling AIDS outside the United Nations system, but must not be used as an excuse to cut funding. The second test of the programme will be at the other level – on the ground. On a country-by-country basis, the six agencies are to tailor services to individual countries' needs, coordinating their work through special committees which will consult with national Governments and community groups. The aim is to end the notorious duplication between United Nations programmes and to help national Governments set their own priorities.

Nevertheless, bringing together the six agencies, each with its own approach to the disease and its own particular territory, is proving a monumental task.

Much of the concern surrounds the tug-of-war over which agency will dominate the new programme. WHO has been the lead United Nations agency, and has been seen as focusing on the medical aspects of the disease. When it became clear that people living in poverty were especially at risk, UNDP began to focus on country-level activities, addressing poverty, homelessness and women's empowerment.

UNICEF aims at young people and mothers; the United Nations Population Fund concentrates on sexual health and family planning; UNESCO's interest is in education and public information on HIV and AIDS. The Bank, which claims to be the largest source of finance for AIDS prevention in developing countries, is motivated by the need to stop the epidemic becoming a brake on development. (Extracted from *Development and Cooperation*, February 1995)

IPGRI News

An action plan to cover all aspects of collecting, conservation, evaluation, and utilization of Asian tropical fruits has been developed as a result of an expert consultation organized by the International Plant Genetic Resources Institute (IPGRI). The participants also agreed to conduct more basic studies on patterns of genetic diversity and to publish a report that will be issued by IPGRI. The International Centre for Underutilized Crops and national programmes had cooperated with IPGRI prior to the meeting which was hosted by the Malaysian Agricultural Research and Development Institute. For additional information, contact: Dr. Nazmul Haq, International Centre for Underutilized Crops, School of Biological Sciences, University of Southampton, SO16 7PX, UK. Fax: 44-703-594-269. (Source: *Diversity*, Vol. 10, No. 4, 1994)

Global meeting on biotechnology

An international meeting on the role of patents in biotechnological inventions, one of the fastest growing areas of patent applications, took place in New Delhi, India, in November 1994, with experts stressing the need to strengthen the information system in this field.

The meeting was organized by the World Intellectual Property Organization (WIPO). The topics for discussion included the role of intellectual property in promoting technological innovations, aspects of legal protection, micro-organism deposit systems and application of patents and special features of licensing. (Extracted from *The Times of India*, 9 November 1994)

WHO establishes cytokine reference standard

At a symposium on "Laboratory Testing of Cytokines" during the General Meeting of the Japan Society of Clinical Pathology in Morioka in October 1994, Masayuki Kohase, head of the Laboratory of Cytokines, Department of Vaccine Control, National Institute of Health, said that a World Health Organization (WHO) expert committee aimed at establishing international reference standard

at establishing international reference standard interferons (IFN) and cytokines will be formally inaugurated.

Dr. Kohase reported that WHO has finally determined that the one Japanese reference standard unit (1 JRU) of the cytokine interleukin 2 (IL-2) is convertible to one international standard unit (1 IU). In the future, it will be possible to us IU in scientific papers, etc. and this fact should be widely publicized among health professionals.

The Japanese National Institute of Health is one of the WHO research facilities gathering data for the establishment of international reference standard IFN.

In addition to IFN alpha, beta, and gamma, WHO plans to establish international reference standards for new recombinant and modified types of IFN, but the WHO expert committee will discuss which international reference standards will be established. Since international reference standard cytokines are supplied via the National Institute of Biological Standards and Control (NIBSC) in the United Kingdom, WHO has requested that these reference standard cytokines should be used by mixing with the reference standards established in each laboratory. Dr. Kohase also insisted that the time has come for Japanese manufacturers to consider support in this field aimed at making an international contribution. (Source: McGraw Hill's *Biotechnology Newswatch*, 5 December 1994)

United Nations Conference on Straddling Fish Stocks and Highly Migratory Fish Stocks

The third substantive session of the United Nations Intergovernmental Conference on Straddling Fish Stocks and Highly Migratory Fish Stocks (the United Nations Conference), which was held in New York in August 1994, provided the first opportunity for the negotiating text of a key fishing agreement to be discussed as a legally binding document.

The mandate of the United Nations Conference is to develop a regime to regulate fishing of Straddling Stocks (SS) and Highly Migratory Species (HMS) on the high seas. Australia was represented by officials from the Department of Foreign Affairs and Trade, the Department of Primary Industries and Energy and the Australian Fisheries Management Authority.

The key outcome from the third session was a Draft Agreement for The Implementation of the United Nations Convention on the Law of the Sea, 10 December 1982, Relating to the Conservation and Management of Straddling Fish Stocks and Highly Migratory Fish Stocks.

For the first time, the session provided members with the opportunity to discuss the negotiating text under the form of a legally binding document. Coastal States, including Australia and other Forum Fisheries Agency (FFA) member countries, including Canada, United States, Argentina, Chile, Peru, Norway and Iceland had previously indicated their strong support for a legally binding outcome. Distant water fishing nations (DWFNs), including Japan, Korea, China, the European Union and Poland were seeking a non-binding outcome such as a General Assembly Declaration, and expressed concern that the negotiating text was now in legally binding form. However, Australia expects that the draft agreement will form the basis of future negotiations.

The provisions of the draft agreement have not yet been debated in plenary. The preliminary review indicates that the draft agreement is generally favourable to coastal state interests, as it provides detailed provisions on flag state responsibility—including an annex on data collection; precautionary approaches to fisheries management; monitoring; control and surveillance; compulsory dispute settlement, by catch; and requirements for cooperation with regional fisheries management organizations. The UN Conference aims to complete its work in 1995 and has two further sessions plus an intersessional scheduled. (Source: *Environment*, No. 14, December 1994)

GRAIN

Genetic Resources Action International Network (GRAIN) has announced a three-year project entitled *Harnessing Diversity* to consolidate GRAIN's activities as an international organization. GRAIN has established and currently directs three special projects: "Agri-research" on making international agricultural research relevant to the needs of small-scale southern-hemisphere farmers; "The Fight for Rights" on the legal and political battle over who can own or benefit from genetic resources world-wide; and "Growing Diversity" on strengthening community conservation and use of agricultural biodiversity. For more information, contact: Ms. Renée Vellvé, GRAIN, Jonqueres 16 6°D, E-08003 Barcelona, Spain. Tel.: 34-3-310-5909. Fax: 34-3-310-5952. E-mail: grain@gn.apc.org. (Source: *Diversity*, Vol. 10, No. 2, 1994)

ICBG to explore African rain forest

The Walter Reed Army Institute of Research will launch a mission to Africa to explore the rich biodiversity of the second largest continuous rain forest in the world, as a source of new molecular leads for drug development and as an important economic resource for communities inhabiting the area.

The collaborators include the University of Yaoundé, Cameroon, the Smithsonian Institute, the Biodiversity Support Programme, Shaman Pharmaceuticals, Bristol Myers, and Squibb Pharmaceutical Research Institute forming an International Cooperative Biodiversity Group (ICBG). The ICBG strategy is to use data from field ethnobotanical and ethno-medical studies as well as existing chemotaxonomic and pharmacologic publications, thus generating a prioritized list of plants for investigation.

A large quantity of biological samples will also be mass screened to identify active compounds to be isolated and characterized for further development. The regions to be explored include the rain forest of Oban Hills in Southern Nigeria and the Korup forest range of Cameroon, covering some 2.8 million sq. miles in the West and Central African Region.

Group members from the Smithsonian Institute will install a large-scale permanent forestry plot. The Korup National Park of Cameroon will provide the sites for forest dynamic research which these scientists will conduct to assess the local abundance, distribution and dynamics of trees and shrubs with medicinal properties including the feasibility of sustained collection or harvest of these species from the natural forest or plantations. Systems for cultivating the medicinal plant *Ancistrocladus*, source of the anti-HIV agent Michellamme B, will also be developed through this project. Africans will be trained in relevant areas through organized courses and participation in the installation of the forest plot.

As in many parts of the African Region, the traditional medical system in this area is still the prevalent form of

medical care for the majority of people. Users of the traditional medicines will be interviewed, and ethnobotanical information evaluated to support the computerized literature search and chemotaxonomic studies that these scientists will be employing to establish a prioritized list of plants for collection and further study.

According to an ICBG press release, natural products extracted from these plants will be evaluated for use against malaria, leishmaniasis, African sleeping sickness, trichomonad infections and new anti-parasitic chemotypes will be identified and developed into orally active, readily available safe and effective drugs.

For more information, contact: Dr. Brian G. Schuster, Walter Reed Army Institute of Research, Division of Experimental Therapeutics, Washington, DC 20307-5100; Tel.: (301) 427-5411; Fax: (301) 427-6514. (Source: *African Diversity*, No. 10, October 1994)

WHO promotes onchocerciasis control

In a resolution adopted in May 1994, the World Health Assembly (WHA) asked the Director General of the World Health Organization (WHO) to "pursue actively the initiatives taken for onchocerciasis control through ivermectin distribution". It is expected that ivermectin will become available during 1994 in all communities in Latin America where onchocerciasis is endemic. Extended availability will take longer in Africa.

Since it was launched in 1974, WHO's Onchocerciasis Control Programme in West Africa has protected over 30 million people from this tropical disease, also known as river blindness. Countries concerned are parts of Benin, Burkina Faso, Ghana, Guinea, Guinea-Bissau, Côte d'Ivoire, Mali, Niger, Senegal, Sierra Leone and Togo. Some 9 million children born in the last 20 years in the area covered by the Programme consequently no longer risk blindness. Moreover, 1.25 million people already infected by the parasite—called Simulium or blackfly—have been able to get rid of it.

"Before the arrival of an effective drug, ivermectin, at the end of the 1980s it was impossible to consider large-scale chemotherapy for onchocerciasis", emphasizes WHO. The outcome of productive WHO collaboration with the pharmaceutical industry, ivermectin is supplied free of charge by its manufacturer, the US company Merck & Co. in White House Station (NJ). When administered orally, generally once a year, ivermectin kills the parasitic microfilariae and substantially reduces their numbers in the body.

Jointly run by WHO, UNDP, FAO and the World Bank and led from Ouagadougou by Dr. Ebrahim Samba, the strategy of the Onchocerciasis Control Programme is to reduce the blackfly population to a level where parasite transmission is excluded and to maintain that level until the parasites in humans die out.

So far, 25 million hectares have been liberated from onchocerciasis, according to Dr. Samba, however, vector control will have to continue. Close collaboration between the countries will also be necessary especially to detect any cases of transmission. Blackfly ignores frontiers and an imported reinfection can never be completely ruled out.

Dr. Samba recognized the contribution of private industry to the success of WHO's Programme and named companies, especially Merck & Co., for "giving us ivermectin free", Abbott Laboratories for "selling *Bacillus Thurengiencies* at a reduced price", Ciba Geigy, Wellcome, Takeda, Bayer, Janssen, "all and many more (that) have contributed to the results".

Ivermectin is at present being distributed in small-scale projects in virtually all countries where onchocerciasis is endemic. According to WHO, however, the overall coverage of populations infected is still low and there is a need to better define priority areas for intervention. Existing and planned arrangements for ivermectin distribution in countries where onchocerciasis is endemic should permit rapid progress, WHO concludes. (Source: *Health Horizons*, No. 23, Autumn 1994)

AMBO/AMBL

Two Australian scientists have initiated a movement to form the Asian Pacific Molecular Biology Organization (AMBO) to promote molecular biology in the Asia-Pacific region, ultimately leading to the establishment of an international laboratory, the Asian Pacific Molecular Biology Laboratory (AMBL). Keith Stanley (Sydney) and David James (Brisbane) have obviously been influenced by the very successful EMBO EMBL model in Europe and believe a similar approach would benefit the development of bioscience in the Asia-Pacific region. The action plan envisages the establishment of AMBO by the end of 1994 and then enlisting government support with the eventual aim of establishing AMBL by the year 2000. The role of AMBO will be to sponsor travelling and research fellowships, organize practical and theoretical workshops, organize an annual symposium, establish an effective electronic network for information exchange, establish a top-ranking scientific journal, and setting up a working party to decide on the best model for AMBL.

It is envisaged that AMBL will concentrate on *basic* research in cell and molecular biology with four major areas of emphasis tentatively identified: genes and development, molecular cell biology, molecular structure and instrumentation. This emphasis on basic research is intended to complement many existing research institutes in the region which have a more *applied* goal. (Extracted from *Australasian Biotechnology*, Vol. 4, No. 5, October 1994)

International trade in endangered species re-examined by CITES Convention

Representatives to the Ninth Conference of the Parties to the Convention on International Trade in Endangered Species (CITES)—called the most successful treaty ever for the protection of global natural resources—met in Fort Lauderdale, Florida, during 7-18 November 1994 to evaluate the status of wild species whose survival is endangered by human activities including trade. Their most important activity, and the main purpose of the biennial CITES meetings, was to decide which species should be placed on or removed from the three CITES Appendices that guide international trade in wild species.

CITES, which entered into force in July 1975, was created to stem the unrestricted commercial exploitation of wild animals and plants, which is the second major threat to survival of some species. The first is habitat destruction. The representatives of the Parties to the Convention meet every two years to review implementation of the Convention, to revise its procedures, and to list (or remove) protected species in light of current information. CITES is now part of the United Nations Environment Programme (UNEP).

CITES and the Biodiversity Convention Work Together

UNEP Executive Director Elizabeth Dowdeswell explained to the delegates that CITES will remain in place and is a necessary complement to the Convention on Biological Diversity (CBD).

CITES Appendices

The three appendices to CITES list a total of 37,000 species according to degree of endangerment. Their annual turnover, according to CITES, is estimated at millions in US dollars.

Appendix I lists species whose international trade is prohibited. Import and export are possible only if the import is for non-commercial purposes, and import and export permits are required. Among the 500 animals species listed in appendix I are all anthropoid apes, great whales, and giant salamanders. Among the 150 plants are some cacti and orchids, including slipper orchids.

Appendix II lists species whose international trade is controlled. While import and export are possible, an export permit must be issued. In addition, special restrictions may apply, such as export quotas and marking of specimens. Among the animals on appendix II are flamingoes and medicinal leech. All carnivorous plants and snowdrops are also on this list.

There is also a third appendix which lists species whose trade from certain countries is restricted unless an export permit is issued and a certificate of origin is presented.

The CITES delegates also considered new listing criteria, drawn up by the International Union for the Conservation of Nature (IUCN), which drew vigorous debate. The purpose of the new criteria was to create a more "scientific" and "objective" classification scheme based on statistical thresholds (for example, the number of animals and the size of the remaining habitat). Delegates worked out a compromise whereby the numerical thresholds were advisory only.

Other actions taken by the CITES delegates included: defeat of efforts to weaken control of elephant products; formulation for the first time of steps to protect sharks; defeat of Norway's efforts to open trade in minke whales; and agreement to allow limited trade in live white rhinos. Significant steps to combat the recent appearance of organized crime in the wildlife trade were also taken.

Involvement of organized crime

Delegates approved a draft enforcement resolution to strengthen the Convention that includes formalizing a link between Interpol and customs officials to facilitate exchange of confidential, enforcement-related information. Among the provisions are increasing training and technical assistance to the parties on enforcement matters, establishing an Enforcement Working Group to provide a "reservoir of experience" for technical advice on enforcement matters, and supporting and encouraging formation of regional enforcement agreements. Financing will come through external funding to the Enforcement Project already established within the CITES Secretariat, located in Switzerland.

The new, recently signed Lusaka Agreement is an example of States agreeing to work together to fight wildlife smuggling. Signed in early September, the agreement between the African range states was praised by numerous speakers.

The United States Interior Secretary told the delegates of his country's initiatives aimed at stemming criminal exploitation of wild species:

- Several United States agencies have announced a pilot programme, beginning this January, through which representatives from five Asian countries will be trained in CITES implementation and enforcement;
- The United States is offering assistance and training to countries trying to improve CITES compliance. In July, the Fish and Wildlife Service conducted a course in undercover wildlife enforcement techniques, designed especially for CITES officials. That practice should continue, and we should make our wildlife forensics laboratory available to more foreign entities.

The next meeting of the CITES COP will be in Zimbabwe during the first half of 1997. For additional information on CITES, contact: CITES Secretariat, 15, Chemin des Anémones, Case Postal 456, CH-1219 Chatelaine-Genève, Switzerland. Tel.: 41-22-979-9139/40. Fax: 41-22-797-3417. (Source: *Diversity*, Vol. 10, No. 4, 1994)

Scientific interaction hallmark of 5th World Livestock Congress

Over 1,400 delegates from 85 countries attended the 5th World Congress on Genetics Applied to Livestock Production (5th WCGALP), held last August at the University of Guelph, Canada. The attendance was double that of the 4th WCGALP held in Edinburgh, Scotland, in 1990.

The five-day Guelph Congress provided a forum for the presentation and discussion of research and developments on conventional animal breeding and the integration of biotechnologies and molecular genetics into livestock production. Scientific research was strengthened not only by the plethora of papers presented but also by the interaction between scientists from developing and developed nations and the animated discussions held in and outside the formal sessions.

Domestic Animal Genetic Resources Focus of Symposium

A highlight of the conference was an all-day joint Congress/Food and Agriculture Organization (FAO) Symposium that attracted approximately 200 participants. Twelve papers and 14 posters were presented at the symposium, whose main objective was to review aspects of education, training, and strategies for the conservation of domestic animal resources as applied to reproductive and molecular technologies.

Working with many organizations and individuals throughout the world, FAO has begun surveying more than 40 species of domestic animals and is preparing a Global Databank on Animal Genetic Resources. The databank already includes data on about 2,800 breeds of seven species. Early analysis of the results indicates that 30 per cent or more of all animal genetic resources are currently at high risk of extinction, most breeds occurring in high risk developing regions.

There were several new developments in the scientific programme including a computer software poster session, where recently developed software was demonstrated by its author. Two related evening sessions were held by the

Biozootech Forum on industrial application of animal biotechnology, and a workshop on the de ection and mapping of quantitative trait loci (QTL) in livestock, organized by the United States National Animal Germplasm Research Program. (Source: *Diversity*, Vol. 10, No. 4, 1994)

Europeans unite to safeguard continent's plant genetic resources

Since its beginning, the European Cooperative Programme for Crop Genetic Res ces Networks (ECP/GR), a collaborative programme that coordinates European plant genetic resources activities, has stimulated European Governments' awareness the benefits of conserving genetic resources. At the same time, the general European public has increasingly realized the need for taking action to combat the global loss of biodiversity. European agricultural scientists say it is essential to maintain and develop this public awareness in order to increase recognition of the vital role that plant genetic resources (PGR) play as a fundamental component of biodiversity, and the crop scientists participating in the ECP/GR are aiding the continent's Governments to do just that. At the same time, the Commission of the European Communities (CEC) is launching a programme on agricultural crop genetic resources that will allow increased activities within the European Union.

The CEC's programme on conservation, characterization, and utilization of agricultural genetic resources could include support for European networking activities, but pure research projects would be excluded. The proposed CEC programme based on the principle of subsidiarity, is broad in spectrum and is mainly aimed at supporting collaborating activities in member countries, while the ECP/GR is essentially a coordination mechanism.

Meanwhile, the political and economic changes in Eastern Europe continue to endanger valuable germplasm collections. A 1992 mission of the Food and Agriculture Organization of the United Nations (FAO) and the International Board on Plant Genetic Resources (IBPGR) surveyed the security of collections in six countries and found that most programmes were experiencing serious difficulties as a result of drastic budget and staff cuts. Recommendations were sent to the Governments alerting them to the problem and urging them to increase their commitment to maintain the collections. As a further effort, a special activity account was opened at the Consultative Group on International Agricultural Resources (CGIAR) Secretariat to receive funds from various donors. The International Plant Genetic Resources Institute (IPGRI) is the executing agency for this initiative to safeguard the threatened germplasm of Eastern European collections.

The collaborative links forged through the ECP/GR are an important mechanism for protecting these threatened East European materials and related research. The various ECP/GR working groups are invaluable partners for IPGRI in obtaining information on potentially threatened collections, as in the case of the *Allium* field genebank at Olomouc, Czech Republic.

ECP/GR grew out of the 1975 Helsinki Conference on Security and Cooperation in Europe and began operating in 1980 as a regional joint United Nations Development Programme (UNDP)/FAO project named European Cooperative Programme for the Conservation and Exchange of Crop Genetic Resources.

Under Phase II of the programme, which began in 1983, coordination was provided by IBPGR which, as IPGRI, continues this role. At the end of 1992, 28 countries were participating in the programme, all of which contributed to the programme's funding.

For further information on the activities of the programme, contact: Thomas Gass, IPGRI, Via delle Sette Chiese 142, 00145 Rome, Italy. Tel.: 39-6-518-92221, Fax.: 6-575-0309. E-mail: e.frison *a* cgnet.com (Source: *Diversity*, Vol. 10, No. 4, 1994)

National coordinators for the European Cooperative Program for Conservation and Exchange of Crop Genetic Resources

Representatives to ECP/GR

Prof. Lufter Xhuveli, *Head*
Plant Breeding & Biology Dept.
Higher Institute of Agriculture
Rruga "Myslym Shyri" K-3
Ap-25, Tirana, Albania
Tel.: 355-42-27481 (odr: 32188)
(Home): 355-42-29147
Fax: 355-42-27481

Dr. Herman Redl
Federal Ministry of Agriculture & Forestry
Republik Osterreich Bundesminister
Stubenring 1, 1011 Vienna, Austria
Tel.: 43-1-711 00 67 66
Fax: 43-1-711 00 65 06

Mr. R. Piscaglia, *Directeur Général*
Administration de la Recherche Agronomique
Avenue de Boulevard 21, 7e Etage
1210 Bruxelles, Belgium
Tel.: 3-2-211 72 11; Fax: 32-2-211-72-16
Telex: 22033 AGRILA B

Dr. Rada Koeva
Institute of Plant Production & Genetic Resources "K. Malkov"
Sadovo, 4122 Plovdiv, Bulgaria
Tel.: 00359-32 993181 992221 992251
Telex: 86544444(IIRG BG)

Dr. L. Dotlacil
Research Institute of Plant Production
Ruzyne 507, 161 06 Praha 6
Czech Republic
Tel.: 42-2-360 851 9; Fax: 42-2-365 228
Telex: 849123 093 VURV C

Ms. Athena Della, *Director*
Agricultural Research Institute
Ministry of Agriculture and Natural Resources
P.O. Box 2016
Nicosia, Cyprus
Tel.: 357-21-30 51 01; Fax: 357-21-316 770
Telex: 8264660 MINAGRI CY

Dr. Arent B. Josefsen, *Director*
Danish Institute of Plant and Soil Science
Executive Secretariat
Skovbrynet 18
DK-2800 Lyngby, Denmark
Tel: 45-45 93 09 99; Fax: 45-45 93 08 19

Mr. Olli Rekola
Ministry of Agriculture and Forestry
Box 232
SF-00171 Helsingfors, Finland
Tel.: 358-0-1603346; Fax: 358-0-1605046

Dr. Marianne Lefort
Bureau des Resources Génétiques
57 rue Cuvier
75231 Paris CEDEX 05, France
Tel.: 33-1-47 07 15 75
Fax: 33-1-45 35 70 15
Telex: FFSPN 842260921 F
Dr. Himmighofen
Ministry of Agriculture
Postfach 14 02 70
Rochusstrasse 1
Bonn 1, Germany
Tel.: 49-228-529 3550
Fax: 49-228-529 4318
Mr. A. Zamanis
Greek Gene Bank
North Greece Agricultural Research Centre
P.O. Box 105 14
54110 Thessaloniki, Greece
Tel.: 30-31-471-110
Fax: 30-31-471-209
Dr. L. Holly, *Director*
Institute for Agrobotany
IPPQ
H-2766 Tapioszele, Hungary
Tel./Fax: 36-53 315 107
Telex: 861226981 AGBOT H
Dr. I. Byrne
Department of Agriculture
Agricultural House
Kildare Street
Dublin, Ireland
Tel.: 353-16 789 011
Fax: 353-16 616 263
Telex: 85225118 AGRI EI
Mr. Thorsteinn Tomasson, *Director*
Agricultural Research Institute
Keldhaholti
IS-112 Rekjavik, Iceland
Tel.: 354-1-812230
Fax: 354-1-814604
Dr. Miriam Waldman
Life Sciences Division
Ministry of Science
P.O. Box 18195
91181 Jerusalem, Israel
Tel.: 972-2-2770 062/322 399
Fax: 972-2-82 05 91
Telex: 92226188 RECO IL
Prof. Luigi Monti
Instituto di Agronomica Generale e Coltivazioni Erbacee
Cattedra di Genetica Agraria
Universita di Napoli
Via dell'Universita 100
80055 Portici - Napoli, Italy
Tel.: 81-775 20 56
Fax: 81-775 35 79
Dr. P.A.Th.J. Werry
Ministry of Agriculture, Nature Management and Fisheries
P.O. Box 59
Mansholtlaan 4
Wageningen, Netherlands
Tel.: 31-8370 986 01
Fax: 31-8370 240 60
Telex: 84475044 DLOWA NL

Dr. Even Bratberg, *National Horticultural Adviser*
Department of Agriculture
Agricultural University of Norway
Postboks 5022
N-1423 As, Norway
Tel : 47-64947804
Fax: 47-64947802
Prof. H.J. Czembor
Plant Breeding and Acclimatization Institute
IHAR
Radzikow near Warsaw
05-870 Blonie, Poland
Tel.: 48-22 552 611
Fax: 48-22 554 714
Telex: 867812914 IHAR PL
Dr. Luis Gusmão
Estação Agronomica Nacional
2789 Oeiras, Portugal
Tel.: 351-1-443 1505/0442/1510
Fax: 351-1-44 20 867
Telex: 63698 EAN P
Dr. Mihai Cristea, *Director*
Gene Bank Suceava
Bd 1 Mai, No. 17
R-5800 Suceava, Romania
Tel.: 40-87-27087/15847
Fax: 40-87-27087
Telex: 86423296
Dr. Sergey M. Alexanian, *Head, Foreign Relations*
N.I. Vavilov Institute
Bolshaya Morskaya Street 42-44
190000 St. Petersburg, Russia
Tel.: 7-812 314 4848
Fax: 7-812 311 8762
Telex: 871121414 (ALEX SU)
Dr. Alzebeta Zofajová
Výskumný ústav rastlinnej výroby
Research Institute of Plant Production
Bratislavska cesta 122
921 68 Piešťany
Slovakia
Tel.: 42-838-223 11/12
Fax: 42-838-263 06
Telex: 84993822
Dr. M. Gomez Perez
Instituto Nacional de Investigacones Agropecuarias (INIA)
Jose Abascal 56
28003 Madrid, Spain
Tel.: 34-1-347 49 30
Fax: 34-1-347 39 31
Telex: 83148989 INIA E
Prof. Roland von Bothmer
Swedish University of Agricultural Sciences
Department of Plant Breeding
Herman Ehles v 2-4
S-268 31 Svalov, Sweden
Tel.: 46-418-67200
Fax: 46-418-67081
Dr. G. Kleijer
Station Fédérale de Recherches Agronomiques de Changins
Route de Duillier
CH-1260 Nyon, Switzerland
Tel.: 41-22 363 44 44
Fax: 41-22 362 13 25
Telex: 845419975

Dr. A. Ertug Firat, *Director*
Plant Genetic Resources Research Institute
Ministry of Agriculture
P.O. Box 9
35661 Benemen
Izmir, Turkey
Tel.: (90-232) 846 13 31
Fax: (90-232) 846 11 07
Telex: 51293 AARI TR
Mr. J.C. Suich
Research Policy Coordination Division
Ministry of Agriculture, Fisheries and Food
Nobel House, 17 Smith Square
SW1P 3JR London, UK
Tel.: 44-71 23 83 000/direct: 238
Fax: 44-71 6591/5613/5597
Dr. V.R. Ryabchun
Director, Gene Bank
Ukrainian Centre for Plant Genetic Resources
Yurjev Plant Breeding Institute
Koskovsky Prospekt 142
Kharkov, Ukraine
Fax: 007-0572 478 563
Dr. M. Pencic
Federal Ministry for Science, Research & Development
Lenjinov Bulevar 2
Novi Beograd 11070, Serbia
Tel.: (3811) 199-195
Fax: (3811) 222 29 09/222 34 92
(Source: *Diversity*, Vol. 10, No. 4, 1994)

Regulatory issues

Biotechnology directive falls at Parliament hurdle

The European Parliament has finally rejected—by 240 votes to 188 with 23 abstentions—the proposed European Commission directive on legal protection of biotechnological inventions, effectively putting an end to the directive, but the Commission indicated immediately that it will return to the matter and come forward with new proposals in the future.

The parliamentary vote, which was widely expected to go the other way, was taken at a third conciliation meeting and ends nearly six years of wrangling.

In recent years, the European Council of Ministers has backed the Commission, but the Parliament has held out over several amendments to the final draft, prepared in May 1994.

The BioIndustries Association commented that the decision was "not the disaster" that some were suggesting, indicating that the final form of directive was barely acceptable to industry, as it introduced a number of measures that were problematic and ambiguous. These included extension of ethical and moral issues into the patents arena—seen as inappropriate and potentially disruptive to transgenic developments—and the compulsory licensing of genetic varieties to plant variety holders—the first time such a condition has appeared in intellectual property rights. Allowing farmers to keep genetically modified seeds for replanting was also an issue. (Source: *European Chemical News*, 6-12 March 1995)

Canadian regulatory guidelines released

The Plant Biotechnology Office of Agriculture and Agri-Food Canada has released regulatory guidelines for environmental assessments of the release of plants with novel traits. *Assessment Criteria for Determining Environmental Safety of Plants with Novel Traits* will be updated as necessary, and information requirements may vary with the availability of additional scientific knowledge. The definition of "Novel Trait", "Familiarity" and "Substantial Equivalence" may also be subject to modification.

The Plant Biotechnology Office is now in a position to accept and review applications for unconfirmed release of plants with novel traits. Once authorization for unconfirmed release is granted for specific plant materials, these plants may be grown without restrictions of reproductive isolation, post-harvest land use, and disposal of seed.

While determining the environmental safety of plants with novel traits is a critical step in the commercialization process, such requirements as food or feed safety assessments and variety registration may also be required.

In a related development, regulations to the Seeds, Feeds, Fertilizers, Health of Animals and Pest Control Products Act became law on 25 January 1995. The regulations define biotechnology and clarify that products of biotechnology will be regulated under those same acts in the same manner as traditional products. This is the first biotechnology regulation to be completed; a first for Agriculture and a first in Canada.

Still in the works are regulations governing environmental assessment. In mid January, an agreement in principle was reached between Agriculture and Agri-Food Canada and Environment Canada that the regulations under the Seeds, Feeds, Fertilizers and Health of Animals Acts (then in review by the Justice Department) were equivalent to, and therefore can be exempted from, those contained in the CEPA. The regulations will be published in the Canada Gazette near the end of February for the 60-day consultation period.

For the agbiotech industry, these developments promise one-stop regulatory service through Agriculture and Agri-Food Canada.

For further information, contact the Plant Biotechnology Office, Plant Products Division, Plant Industry Directorate, Nepean, Ontario. Canada. K1A OY9. Tel.: (613) 952-8000. Fax: (613) 941-9421. (Source: *The Agbiotech Bulletin*, Vol. 3, No. 2, February 1995)

Lighter regulation for transgenic plants coming slowly to Europe

The European agrochemical industry is attempting to foster a more lenient regulatory environment for transgenic crop plant introductions throughout the European Union (EU). Staunch public opposition and widespread bureaucratic obstacles mean that Europe has fallen behind other parts of the world in the research and development of genetically engineered agricultural products.

For a transgenic crop plant to reach the market in Europe, permission must be obtained from individual countries, a process that can take years to complete. At this stage, other EU countries can raise objections, after which another permit is required to actually market the product.

EU officials are now in the process of lightening certain permit requirements, but not all EU nations are enthusiastic. Germany, with its strong Green Party, has seen four instances of vandalism directed at genetically engineered crops, one indication of negative public opinion. Opposition in the UK was aroused following a recent field trial of a virus modified with a scorpion toxic gene to enhance death rates of target pests. (Source: *The Agbiotech Bulletin*, Vol. 3, No. 2, February 1995)

Diagnostic and predictive testing without counselling—is it ethical?

Biotechnology companies are working on a collection of predictive genetic tests that are or will be available for currently healthy patients. However, protesting organizations believe that face-to-face counselling is essential to discuss healthcare options.

Counselling associated with genetic testing is a relatively recent phenomenon in the United States of America. Trained to interpret the risks of recurrence of relatively rare inherited disease, the field of certified genetic counsellors began in the USA in 1969 with a programme started at Sarah Lawrence College in Bronxville, NY, and led to the creation of 19 other genetic counselling programmes in this country.

The total number of counsellors trained in genetics and who hold M.Ds and Ph.Ds is believed to be less than 2,000 in the USA, with much smaller numbers in other nations. They are skilled in interpreting the vagaries of testing (false-negative and false-positive results, for example) and can offer options and psychological support to those being tested.

Given the economic savings and efficiency of providing the tests without counselling, many companies throughout the world have moved forward into product R&D without planning to incorporate this medical genetics model into their plans. Indeed, some in the USA who have met resistance on this issue have simply re-targeted their sales to other parts of the world, where the technology is valued without the face-to-face counselling dimension.

One cannot leave aside all the other ethical issues that may be involved, including discrimination, based on test results, by insurance companies, employers and Governments; the confidentiality of the test results; the psychological trauma that may result in obtaining predictive test results, particularly for late-onset diseases, such as Alzheimer's and Huntington's diseases and the absence of any curative therapy for many diseases that have recently become diagnosable.

Cardiff Report

Yet, a research group in Cardiff, Wales, funded by the Commission of the European Communities, has attempted to focus solely on the question of genetic counselling and the impact of human genome analysis on clinical practice. Headed by Ruth Chadwick, of the Centre for Applied Ethics at the University of Wales College of Cardiff (P.O. Box 94, Cardiff CF1 3XB, United Kingdom), the six-member team published its report in 1993. The study is useful for understanding the global variation in values surrounding testing and the different ways in which individuals evaluate the risks of disease or birth defects. It notes that DNA technology has made possible, in a 25-year period, an almost five-fold increase in the number of fully identified genetic disorders.

Moreover, according to the report, the results of the world-wide Human Genome Project will enable not only the testing of individuals for the presence of a specific gene, but carrier screening of large populations. Since every human being is estimated to carry between four and eight deleterious recessive genes, the potential of finding millions of people with increased risks for multifactorial genetic diseases (such as cancer and heart disease) is high. "Normality" and "health" may have to be redefined if such testing and screening is introduced on a widespread basis. Yet, it may not just be the person tested who is at risk from a particular disease, but also his or her child or relatives (or, in the case of diagnostic tests for such sexually transmitted pathogens as HIV, their sexual partners).

Chadwick and her colleagues point out the wide diversity among European nations in their approach to and the availability of genetic counselling, but they conclude that such counselling is important to protect autonomy, personal integrity and privacy. The report also recommends that the traditional presumption in favour of confidentiality, while allowing a discretion to disclose information for compelling reasons (such as avoiding harm to spouses' partners and other relatives) be maintained by counsellors.

Finally, they concluded by noting that people undergoing testing have wide variations in their perceptions of risk and in the significance they put on the stakes involved in such decisions, particularly with reference to the decision to have children who may be born with birth defects. They allude to the fact that Governments also differ in the extent to which they should take steps to further efforts towards disease prevention.

While a discussion of the entire Cardiff report is not within the scope of this article, it reminds us of how complex the reactions to predictive diagnostic test results may be and why the model of face-to-face counselling has sparked such controversy. Companies involved in the diagnostic and predictive testing business need to be sensitive to such issues. (Extracted from *Genetic Engineering News*, 15 September 1994)

General

ELADA 21

The information requirements of resources managers and policy makers have increased since the adoption of Agenda 21—the action plan developed at the 1992 Earth Summit at Rio de Janeiro. The ELADA 21 software (ELectronic Atlas of Agenda 21) offers an accessible and inexpensive approach to meet these needs. A project of the International Development Research Centre (IDRC), CCRS and private industry (LMSoft and the Canadian Biodiversity Informatics Consortium) ELADA 21 uses multimedia and geomatics technology to access and disseminate Agenda 21 related information. This software will process information at regional, national and global scales and will make possible the assessment of environmental changes through the integration of various types of indicators.

The long-term objective of this project is to cover all the chapters of Agenda 21. ELADA 21 can facilitate the world-wide exchange of information generated by the Agenda 21 guidelines and support the implementation of reporting processes on sustainable development policies. Moreover, all the signatory countries to the Biodiversity

Convention could gain from a common standard for their resource monitoring activities.

Six countries, the Bahamas, Costa Rica, Canada, Kenya, Poland and Thailand and one organization, the International Plant and Genetic Research Institute (IPGRI) in Italy are associated with IDRC and CCRS in the development of a prototype ELADA 21 biodiversity chapter. The prototype will focus on selecting, collecting and integrating biodiversity data, and on producing interactive scenarios linking biodiversity with socio-economic issues. One of the key objectives of the project is to enable participating countries to meet their own biodiversity information needs through technology transfer and infrastructure development.

This CD-ROM package will be highly interactive and is being developed as a follow-on to GEOSCOPE, an interactive global change encyclopaedia produced by CCRS for the International Space Year in 1992. ELADA 21 software development began early in 1994 and the package will be released in 1996. For more information, please contact: Marc Beaudoin, ELADA 21 Project Manager, Applications Division, CCRS. Tel.: (613) 947-1257. Fax: (613) 947-1408. E-mail: beaudoin@ccrs.emr.ca. (Source: *Remote Sensing in Canada*, Vol. 23, No. 1, February 1995)

African indigenous knowledge/plants benefiting the North: awareness grows

There is a growing recognition world-wide that African indigenous plants are contributing immensely to development in the North. In particular, both genetic materials and associated local knowledge emanating from peasant farms in Africa have been benefiting industrial and research institutions in the North in the area of agriculture (particularly the seed industry), food processing and pharmaceutical industries. Very little is known in concrete or quantifiable ways about the commercial value of these resources. RAFI has compiled data from various scientific and trade journals (see table below) giving some insight into this issue.

Table: Partial list of proven or potential contributions made by Africa to the North

Country/Region to ...	Species	Discussion
Ethiopia to USA	Barley	Farmer-derived Ethiopian barley is worth $150 million in the United States each year. The annual value of the American crop is more than $670 million.
North Africa, Ethiopia, South Asia, to Denmark	Barley	Danish breeders developed barley varieties resistant to powdery mildew in the late 1960s thus preventing crop losses amounting to $200 million in the period 1967-1974. Resistant germplasm came from farmers in North Africa, Ethiopia, and Southern Asia.
Libya to Australia	Lucerne (alfalfa)	Plant collector violated his contract and pocketed lucerne (alfalfa) seed he was sent to study in North Africa and, returning to Australia, now claims the seeds are "worth millions" to his country's livestock industry.
North Africa to Canada	Oats	North African farmers saved the Canadian oat crop from disaster in the 1970s.
West Africa to USA	Maize	The only genetic resistance to Southern Corn Leaf Blight—a disease that caused $1 billion in damages in the United States in 1970, was found in a farm field in West Africa.
Ethiopia to USA	Sorghum	Sorghum from Ethiopia is worth $12 million a year to US growers. Annual value of the crop in the United States is above $1 billion.
East Africa to Australia	Bovines	Australian breeders recently introduced East African cattle breeds in order to improve the local stock.
West Africa to USA	Bovines	West-African-bred N'Dama cattle have been crossed with Britain's Red Pol breed to create Senapol, a new and hardy breed now being used in, among other places, the southern USA.
Africa to Europe, North America	Bovines	Other African breeds have made a major contribution to US and European herds through increased disease resistance and other qualities such as shorthorns.
West Africa to private companies	Cowpea	A pest-resistant cowpea variety originating in West Africa was taken from IITA in Nigeria to Durham University and the CpTi gene was ultimately patented by Agricultural Genetics Co. of the UK and licensed to seed and biotech companies.

Country/Region to ...	Species	Discussion
West Africa to private company	Cowpea	Agricultural Genetics Co. has developed a method for extracting animal vaccines from transgenic cowpea plants by infecting the Cowpea Mosaic Virus with antigenes. One leaf of a two-week-old cowpea can vaccinate 200 animals—reducing current inoculation costs substantially. The first vaccine Agricultural Genetics is developing is foot and mouth disease. World-wide patent rights have been applied for.
Ethiopia to private companies	Endod	The University of Toledo is patenting Ethiopian research related to the endod (soapberry) plant used in Africa as a shampoo and detergent. Endod also appears to be safe and effective against zebra mussels that have infested the Great Lakes and are expected to cause damages of $5 billion by the year 2000.
West Africa to US universities and private companies	Thaumatin	The University of California and Lucky Biotech have applied for patent rights over genetically-engineered thaumatin sweetener in industrialized countries and in West Africa. The plant has long been used as a sweetener in Africa.
Medicinal		
Africa to USA	Tilapia fish	Africa's Tilapia fish (sometimes known as the "aquatic chicken") have been transferred and bred for use in many parts of the world including the United States and Europe.
Zambia and Zimbabwe to Australia	Bovines	Embryos of 269 Tuli and 264 Boran cattle from Zimbabwe and Zambia were brought to Australia in 1990 to improve local Friesan herds with higher fertility levels, docility, and environmental stress resistance. Using multiple ovulation and embryo transfer techniques, the imports have been hailed as the saviours of the North American cattle industry.
Nigeria to North	Monkeys	Researchers in the Okomu Forest Reserve in Nigeria have shown that rare monkeys endemic to the forest have similar blood constitution to humans, making them valuable for medical research and drug testing.
Madagascar to North	Rosy periwinkle	Two drugs derived from Madagascar's rosy periwinkle earn pharmaceutical companies more than $100 million per annum as anti-cancer and childhood leukaemia drugs. Allelix (a Canadian biotech firm) is working with Mitsui Pharmaceutical to develop "natural" periwinkle compounds that will not need Madagascar any more. (The Leukaemia drug has turned a cancer that used to kill 8 out of 10 victims into one where 8 of 10 children survive.)

Source: RAFI, Occasional Paper Series Vol. 1, No. 1, March 1994.

(Source: *African Diversity*, Vol. 10, 1994)

Crucible Report urges UN meeting on intellectual property rights

One of the most eagerly awaited publications in the plant genetic resources (PGR) community, the report of the high-powered and diverse Crucible Group, calls for an international conference on society and innovation to be convened by the United Nations through the World Intellectual Property Organization (WIPO). This was one of the 28 recommendations contained in the 118-page study entitled *People, Plants, and Patents* that was written "to assist policy makers and opinion makers in [the] extraordinarily important, fast-changing, and politicized field [of PGR] to identify the major points and the range of policy alternatives that can reasonably be pursued".

The participants, a team of 28 multidisciplinary and politically diverse experts under the leadership of Geoff Hawtin of the International Plant Genetic Resources Institute (IPGRI), met twice since 1993 "to hammer out ideas and recommendations on [the] hotly contentious subject" of intellectual property rights (IPR) on plant genetic resources.

Many of the group had met initially during the deliberations of the 1988-1991 Keystone Dialogue on Plant Genetic Resources. Although the final Keystone Plenary

Report recommended changes and increased support for plant germplasm conservation systems world-wide, it did not tackle the difficult issue of intellectual property rights. Five veterans of the Keystone Dialogue suggested in 1992 that a similar group convene to discuss IPR.

The suggestion resulted in the formation in 1993 of the Crucible Group, whose final report would be a distillation of viewpoints and recommendations on IPR issues pertaining to crop and medicinal biomaterials, hence the group's name, *crucible*: a boiling pot used to distil diverse elements.

The group emphasized that its report "was never intended to be a consensus document", and that they had agreed only "that they would struggle together to identify trends, concerns, and opportunities on intellectual property issues relevant to plant breeding and plant genetic resources". However, the group was surprised to discover at the end of their "extended discussions and intense exchanges", that there were "many areas of shared opinion and a common sense of urgency".

The Directorate General for International Cooperation (DGIS) of The Netherlands will provide support allowing the Crucible Group to continue to monitor trends and advise on IPR matters to countries and institutions that request support. Funding for the group came from the International Development Research Centre of Canada, the Swedish Agency for Research Cooperation with Developing Countries, the Swiss Development Corporation, the Australian Centre for International Agricultural Research, and DGIS. Partner organizations were RAFI and IPGRI.

For additional information, or a copy of the report, contact: Dr. Chusa Gines, Program Officer, Environmental Policy Program, International Development Research Centre, 250 Albert Street, P.O. Box 8500, Ottawa, Canada K1G 3H9. Tel.: 1-613-236-6163. Fax: 1-613-567-7749. (Source: *Diversity*, Vol. 10, No. 2, 1994)

The Crucible Committee recommendations

1.	The United Nations, through the good offices of the World Intellectual Property Organization (WIPO), should consider convening an International Conference on Society and Innovation. This conference could be held in 1998, on the occasion of the 125th anniversary of the Vienna Conference that brought about the international patent system of today.
2.	The international community should recognize that some new technologies, and even the concept of intellectual property itself, can pose far-reaching ethical concerns for some people, as well as whole countries and cultures. These concerns must be honoured.
3.	Each country should formulate a specific national action plan for the conservation and use of plant genetic resources, within the framework of a wider strategy for the conservation of biological diversity. Such an action plan should seek out all opportunities for constructive collaboration among scientists, policy makers, and rural communities both within the country and beyond national borders, with regional and international initiatives.
4.	The Crucible Group recommends that genebanks reconsider their policies for collection, storage, and distribution to ensure that they are compatible with the FAO Code of Conduct for Germplasm Collection and Exchange. National and international genebanks can be responsible partners with the informal system when they are prepared to collaborate with farmers' organizations and indigenous communities as equals and with the same access and opportunities they afford to other institutions.
5.	To date, the international funding community has failed to recognize fully the seriousness of the loss of plant genetic resources in farmers' fields and in genebanks. The Crucible Group recommends that any new funding mechanisms arising from the Biodiversity Convention or other global fora allocate specific funds for the conservation and sustainable development of on-farm, *in situ*, and *ex situ* collections of plant genetic resources.
6.	The Crucible Group recommends that the issue of the status of *ex situ* collections obtained prior to the Convention be a major item for resolution at an early meeting of Contracting Parties.
7.	The Crucible Group cannot offer a common interpretation of Farmers' Rights or of the intellectual property aspects of the Convention. We do urge, however, that every effort be expended to resolve this issue in order to allow the international community to truly set about the task of safeguarding the world's invaluable flora and fauna.
8.	The Crucible Group commends the Fourth International Technical Conference on Plant Genetic Resources, scheduled to take place in 1996, as the most appropriate process for the resolution of all of these issues. It is essential that all concerned parties be actively involved. We especially call upon those who negotiate those important agreements to take into account the role and importance of community based efforts. The Technical Conference may prove to offer the best process for the full definition and implementation of farmers' rights.

9.	Innovation strategies should promote decentralization, diversity and democracy within local, national and international communities rather than promoting excessive centralization, uniformity, and control.
10.	Current IP systems do not provide incentives to innovations generated at the community level. Any innovation policy adopted at the national or international level should take this situation into account.
11.	The decision of whether or not to adopt some form of intellectual property protection for plant genetic resources should be taken within the framework of wider national strategies to promote science, innovation, and conservation.
12.	A national strategy in support of innovation should, as one of its primary objectives, create an environment in which community innovation systems and formal (public and private) research institutions receive mutual and fair recognition and equitable reward for their contributions. Such a strategy should nourish a climate of cooperation among all innovators.
13.	Although the Crucible Group has differing opinions on the role of international companies, there is general agreement that, along with rural innovators and universities, local entrepreneurship as expressed in the form of cooperatives, companies, and other initiatives could be broadly beneficial and is worthy of serious consideration.
14.	Sovereign States cannot be required to adopt systems of intellectual property in areas that risk the well-being of their peoples or that jeopardize the biological diversity within their borders. Neither should countries be expected to adopt unrealistic time frames to enact intellectual property provisions related to international trade agreements.
15.	Any potential conflict between intellectual property proposals and other initiatives for plant genetic resource conservation and exchange should be taken fully into account in interpreting responses to the GATT accord.
16.	The research exemption provided in intellectual property legislation ought to be clarified so that innovative research can be conducted without excessive fear of litigation.
17.	The Group wishes to advise that both government supervision and the legal enforcement of intellectual property with respect to genes requires careful consideration. IP protection for genes is made especially complex because it is sometimes impossible to control the flow of genes between plant populations.
18.	Although some members of the Crucible Group can identify circumstances where adherence to UPOV '91 might be immediately beneficial to a developing country, there is general agreement that the 1978 UPOV Convention is less demanding and would be preferable to some countries for this reason. Governments may, of course, also adopt *sui generis* national legislation that may be similar to UPOV '78 without the obligation of becoming a member State of the UPOV Convention.
19.	Countries should review the operation of national lists of recommended varieties, Common Catalogues of approved varieties, and all other regulation and policies that could constrain the availability of seeds to farmers. Particularly in combination with intellectual property laws, such rigid policies can have a devastating effect on crop diversity by limiting the freedom of farmers to grow traditional as well as new varieties.
20.	Under the principle of national sovereignty, countries should be free of externally imposed requirements to adopt any intellectual property arrangement affecting plant genetic resources. Countries are free to develop alternative (non-intellectual property) or additional approaches for the stimulation of innovation that are best suited to their particular needs, capacities and opportunities.
21.	While the Group finds an assortment of new ideas related to *sui generis* legislation—or amendments to current IP systems—interesting to explore, we cannot reach a consensus on their value. Some feel that the initiatives posed here would prove economically useless and could nevertheless lead to other forms of exclusive monopoly detrimental to the South and to farmers. Others believe that such proposals would render present IP Systems unworkable. We can only recommend that policy makers consider exploring this field.
22.	Governments and institutions responsible for plant genetic resources accessions (often held in genebanks) could explore the possibility of filing a "Defensive Publication" as is permitted in the United States. This approach could make it harder for such germplasm to be patented. It may be possible to make one filing to cover the entire contents of a genebank supported by a computer printout of the accessions list.

23.	Both bilateral and multilateral agreements have an important role to play in conservation and exchange. However, the multilateral system needs to be further developed to ensure fairness and coherence. Bilateral agreements should be considered so as not to jeopardize a strong and harmonious multilateral environment.
24.	We recommend that Material Transfer Agreements (MTAs) be studied further and be considered seriously by policy makers seeking more flexible approaches to IP Systems and compensation for their biomaterials. MTAs would operate most usefully within an international legal framework that ensures greater equity.
25.	We recommend that Governments take advantage of the several years available to them to develop the best possible strategic response to GATT Trade Related Aspects of Intellectual Property (TRIP)s.
26	The Consultative Group on International Agricultural Research (CGIAR) is strongly encouraged to quickly conclude clear policies on intellectual property, with respect to germplasm, in accordance with the Convention on Biological Diversity and taking fully into account the origins of the germplasm for which they have undertaken responsibility.
27.	The Crucible Group recommends that International Agricultural Research Centres (IARCs) conclude an agreement with the member nations of FAO placing the *ex situ* germplasm collections they hold in trust under the auspices of that intergovernmental body.
28.	We further recommend that IARCs establish MTA policies in keeping with the Convention on Biological Diversity and in accordance with their relationship to FAO that seek to ensure that benefits accrue to the donors of germplasm. IARCs should develop MTAs in consultation with the donors of the germplasm involved and with the intent of ensuring that any financial benefit arising from such agreement be distributed in keeping with the wishes of the germplasm donor. The objective of MTAs is not to support the programmes of the IARCs but to provide new funds and new technologies to developing countries. As far as is possible, MTAs should ensure that beneficial technologies are available to farmers. (Source: *Diversity*, Vol. 10, No. 2, 1994)
Source: *Diversity*, Vol. 10, No. 2, 1994.	

Focus groups reveal public attitude to biotechnology

Focus groups brought together by Public Opinion Strategies for the United States Biotechnology Industry Organization identified five key findings regarding public attitudes about the biotechnology industry:

1. **The public has a very low level of knowledge about biotechnology**. As a consequence, there is little antipathy to the industry, and people are quite willing to listen to credible information with open minds. Attempts should be made to determine an audience's level of knowledge prior to presentations.

2. **Individuals respond best to accurate, documentable, benefits-oriented information about biotechnology**. Focus groups responded positively to medical, nutritional, and environmentally-friendly aspects of biotechnology that contribute to better human health.

3. **People respond more favourably to specific anecdotes than general statements about the industry**. While people's distrust of government, industry and media is often fed by statements about "21st-century, cutting-edge science", anecdotes about actual benefits of applied biotechnology are generally well received.

4. **Biotechnology success stories from patients and consumers work, jargon doesn't**. Technical sounding names (e.g. monoclonal antibodies) quickly feeds into consumer suspicions of "mad scientists" and uncontrollable technology. Examples of consumer views and endorsements are constructive.

5. **People respond well to shared concerns and feelings, and a demonstrated sense of social responsibility**. While unfounded fears may be easily dismissed, it is vital to realize that perception itself becomes its own reality. To connect with people, it is important to acknowledge feelings and respond responsibly before attempting to convey information. (Source: *The Agbiotech Bulletin*, Vol. 3, No. 2, February 1995)

International community rallies to save germplasm of newly independent States

Five European countries and the International Plant Genetic Resources Institute (IPGRI) have stepped into the lead of efforts to save genetic resources collections in 12 newly independent States (NIS) of the former Soviet Union, according to a report released at the gathering of the International Agricultural Research Centers in Washington, DC, during the annual meeting of the Consultative Group on International Agricultural Research (CGIAR). The report by IPGRI, the CGIAR's hub for matters concerning plant genetic resources (PGR), reveals the following steps being taken to address the potential loss of valuable--and in some cases irreplaceable--cropgenetic resources in the NIS.

In the Central Asian countries of **Azerbaijan, Kazakstan, Kyrgyzstan, Turkmenistan** and **Uzbekistan**, IPGRI evaluated the PGR activities and the security of existing collections, including those maintained by three stations of the former USSR's Vavilov Institute. The most important result of the IPGRI preliminary analysis identified a range of needs including emergency action to secure existing collections, training of personnel, establishment of PGR programmes and, especially, funds to support genetic resource activities.

In the **Ukraine**, the IPGRI document reports "an urgent need" for drying equipment and packaging material in the Kharkov genebank which holds "an important crop and vegetable collection". The lack of proper drying facilities and cold storage, says the report, has meant that frequent

regeneration of the material is necessary, although this has been impossible due to lack of resources. Sweden, in combination with IPGRI, is providing support for some of this necessary equipment. Other Ukrainian germplasm locations have not been so fortunate. An IPGRI mission to evaluate the fruit collections of the Crimean Pomological Station and the Nikitsky Botanical Garden discovered that both institutions need support for maintenance and safety duplication of the collections—but so far no donors have stepped forward.

Estonia, Latvia and **Lithuania** sent representatives to a meeting on *ex situ* conservation held in Prague in December 1993 as a result of initial contacts by IPGRI. These contacts led to a joint IPGRI/UN Food and Agriculture Organization mission to the three Baltic countries in July 1994. The Nordic Council contributed US$ 260,000 to its neighbouring States across the Baltic Sea that allows development of a project, initiated in July 1994, for regional cooperation within the Baltic States in collaboration with the Nordic Genebank. The project, says IPGRI, will establish a computerized inventory of plant germplasm in the Baltic States, develop strengthened national programmes in each country, and identify existing material of Baltic origin maintained in other genebanks such as VIRs and the Institute of Plant Genetic and Crop Plant Research in Germany. Yet, IPGRI says, further funds are still needed for these projects.

The United Kingdom Government provided funds to IPGRI that allowed the rescue of the valuable Allium collection held at Olomouc, **Czech Republic**, the same IPGRI report states: "This collection was at risk due to lack of financial support and the privatization of the institute in which it was held. The material is now being duplicated for safety purposes". In addition, according to IPGRI, its intervention contributed to raising awareness of the importance of crop germplasm in the Government that has caused a reorganization of the genebank which now forms part of the National Genebank at the Research Institute of Crop Production, funded by the Czech Ministry of Agriculture.

Sweden provided funds that allowed emergency repair to the cold storage facilities of the **Hungarian** genebank at Tapioszele where malfunctioning equipment and insecure funding "were threatening a collection of more than 50,000 accessions". As in the **Czech Republic**, IPGRI reports that its intervention "contributed to raising the awareness of the importance of PGR" in the Hungarian Government. As a result, the government authorities increased funding for the nation's PGR programme.

Switzerland has approved funding of US$ 42,000 to support regeneration and evaluation at the **Bulgarian** genebank, says the IPGRI document. "The project will also include a training component and the provision of small equipment", IPGRI reports.

The Netherlands has also volunteered to aid the Eastern European countries' genetic resources. The Dutch have donated US$ 400,000 for a project designed to provide technical support to **Eastern European** genebanks that will allow importing access for plant breeders to germplasm collections. The funds will also establish an East European Germplasm Documentation System involving eight countries. The project is coordinated by the Centre for Genetic Resources in The Netherlands in collaboration with IPGRI.

The cereal germplasm in **Poland**'s national repository is not immediately threatened, according to five researchers from the Plant Breeding and Acclimatization Institute in Blonie, Poland. In a recent article they have reported that the system of seed preparation and seed storage used by the Polish Genebank resulted in suitable viability of stored cereal seeds for up to five or six years of storing.

For additional information, contact: Ms. Ruth Raymond, Public Affairs Office, International Plant Genetic Resources Institute, Via delle Sette Chiese, 142, 00145 Rome, Italy. Tel.: 39-6-518921. Fax: 39-6-5750309. E-mail:ipgri@cgnet.com. (Source: *Diversity*, Vol. 10, No. 4, 1994)

The CGIAR and the World Bank

The Consultative Group on International Agricultural Research (CGIAR) is a voluntary association of donors supporting 17 International Agricultural Research Centres (IARCs) dedicated to the promotion of sustainable agriculture for food security in the developing countries. The system is co-sponsored by three international intergovernmental institutions: the Food and Agriculture Organization (FAO), the United Nations Development Programme (UNDP), and the World Bank. It was started in 1971 around a nucleus of four centres and was initially focused on production of food crops in tropical zones. From this initial period there emerged the remarkable spread of new varieties, which, combined with extension of irrigation and other factors, led to what has been called the Green Revolution.

Over the years, the CGIAR has expanded its mandate to cover other issues (livestock, irrigation management, marine resources, and service to national research systems) and gradually introduced an ever greater concern with the environment, which today permeates its entire operations. With the passage of time it has also accumulated an impressive collection of germplasm, which collectively may be considered the largest collection of basic agricultural biodiversity maintained in trust for the international community.

This collection includes over 500,000 accessions of more than 3,000 species and was collected in agreement with national institutions dealing with each of the crops in developing countries. Although duplicate samples were left with the national programmes, many of these duplicates are no longer available owing to lack of facilities and inadequate funding for their maintenance. Much of this germplasm ceased to exist with the farmers. Landraces have been replaced with new varieties, and increasing land use for urbanization and agriculture has led to destruction of natural habitats for wild and weedy species. This unique collection of agricultural germplasm held in trust by the CGIAR remains freely available to national Governments, research and development workers, and farmers.

Recently, the CGIAR faced financial difficulties, which prompted the heads of the three co-sponsoring organizations (FAO, UNDP and the World Bank) to write a joint appeal to the ministers and agency heads represented in the CGIAR, asking them to respond to the financial needs of this long-term enterprise which remains essential to promote sustainable agriculture and food security in the face of mounting population pressure, especially in the poorest parts of the world.

But in addition to being a co-sponsor, the World Bank is also one of the largest financiers of the CGIAR. The World Bank has consistently been providing up to 15 per cent of the core funds, totally untied and distributed as a

"balancing factor" to meet the needs of the system as a whole, after the various donors have made their contributions to specific centres or programmes. In addition, the Bank funds the CGIAR secretariat and provides financial support for the work of the independent Technical Advisory Committee (TAC), which is the key instrument for the technical decisions made by the CGIAR.

It was thus natural that many supporters of the CGIAR should appeal to the Bank to make an exceptional effort to respond to the CGIAR's financial difficulties and to take on a lead role in helping to restore its finances. This was the background to the special efforts made by the World Bank and announced at the CGIAR's mid-term meeting in New Delhi.

The CGIAR supports the further development of a multilateral system governing access to plant genetic resources which is fully consistent with the Convention on Biological Diversity and will complement bilateral arrangements. Such a system would allow national and international programmes to negotiate access to genetic resources and related information (including indigenous knowledge) on terms that are consistent with the Convention, including provision for the fair and equitable sharing of benefits from their use. The CGIAR does not itself seek to gain financially from commercial use of this material and is developing mechanisms, such as material transfer agreements, to ensure the safeguarding of national interests *vis-à-vis* third parties. The benefits accruing to countries from a multilateral system may take a variety of forms, for example access to technologies and research information, capacity-building, and access to a wider range of genetic resources and enhanced germplasm, including the repatriation of duplicate samples. Benefits might also be derived from an international fund in recognition of farmers' rights and through the facilitation of negotiations between recipients and countries of origin. If requested by the Conference of the Parties, the centres stand ready to participate in the development of the clearing-house mechanisms for information on biodiversity for food, forestry, and fibre. The centres will continue to make available their scientific and technical expertise in the area of genetic sources, for example in the development of country studies and national strategies, with a view to facilitating the implementation of the Convention on Biological Diversity.

There is another set of issues that the CGIAR has been concerned about. The emerging trend is towards the patenting of genetic materials in the United States and other industrialized countries and the recognition given to patenting under the General Agreement on Tariffs and Trade (GATT) and the protection of intellectual property rights in international trade. This will require that measures be taken to protect the CGIAR collections from such patent infringement considerations which could impede the accessibility of the germplasm to the poor farmers who are the ultimate beneficiaries of the CGIAR's work in collaboration with the NARS. To protect the spirit and the letter of our current policies, and to ensure that we can effectively meet our commitments under the agreement with FAO, we have to get effective international recognition of the status of these collections, as well as recognition that the movement of germplasm samples between scientists and between the CGIAR centres and the developing countries and their poor farmers are non-commercial transactions.

The rights of farmers and indigenous people to share in the benefits from the landraces which they have developed over many generations is another issue which the convention needs to address. Equitable sharing of benefits could be achieved, for instance, through training, transfer of technologies and information, and both provision and repatriation of germplasm.

This will require more work over 1995, and possibly into 1996, with the GATT and its successor organization (the World Trade Organization), as well as with the World Intellectual Property Organization (WIPO), the International Union for the Protection of New Varieties of Plants (UPOV), and other specialized bodies, to harmonize the provisions of these various agreements with those of the biodiversity convention as they relate to plant genetic resources generally and to the CGIAR collections specifically.

For additional information on the CGIAR, contact: Mr. Heinrich von Loesch, CGIAR Secretariat, J4046, World Bank, 1818 H Street, NW, Washington, DC 20433, USA. Tel.: 1-202-473-8913. Fax: 1-202-473-8110. (Extracted from *Diversity*, Vol. 10, No. 2, 1994)

ACTIP/EWGT joint policy statement

The use of animal cell technology for the production of vaccines, therapeutics and diagnostic substances has led to the availability or development of several exciting new products with great benefit for patients and healthy individuals. In addition, the techniques used and developed in animal cell technology are being applied to develop new *in vitro* tests to screen new pharmaceutical compounds for pharmacological activity and to develop *in vitro* tests for toxicology and safety testing, thereby reducing the number of laboratory animals used in the pharmaceutical, household chemical and cosmetics industries. Animal cell technology will also accelerate the screening of useful pharmaceutical compounds and increase the safety of pharmaceutical products, since the use of possibly contaminated animal or human sources can be prevented.

Although animal cell technology has progress rapidly, the industries utilizing this technology have the conviction that much progress can still be made. This progress will result in the availability of newer, improved and safer pharmaceuticals and vaccines and will also encourage developments in other disciplines, such as pharmacology and toxicology. To realize such progress, adequate research structures and regulatory frameworks are necessary. However, public understanding of the beneficial role of this technology in improving the well-being of animals and mankind, as well as a cleaner environment, must be understood. European industries with an active involvement in animal cell technology therefore decided to establish a platform allowing them to meet on a regular basis and discuss developments in the above areas.

The initiative to establish an Animal Cell Technology Industrial Platform (ACTIP) finds its origin in the Commission of the European communities in relation to the BRIDGE T-project (T stands for "targeted") on animal cell biotechnology. This T-project is part of publicly-funded EC research programmes. The European Commission decided that T-projects should have close links to industrial end-users of the scientific results.

The formal establishment of an industrial platform, involving a representative cross-section of European companies engaged in the industrial use of animal cell

culture for production of vaccines, proteins and/or other substances, took place on 22 November 1990 in Brussels. The European Commission then formally recognized ACTIP as the industrial platform providing input for Community-funded research programmes in the area of animal cell technology.

To date, **ACTIP** comprises 28 companies representing a substantial cross-section of European industry engaged in the *in vitro* use of animal cell technology. The member companies are responsible for a significant proportion of the research, development and production efforts in this area of life sciences within Europe. The membership is composed of representatives from the following industries:

- Pharmaceuticals
- Diagnostics
- Equipment manufacturers
- Quality assurance safety testing
- Associated representatives of the European Commission and academic institutions.

ACTIP provides a forum where the members meet at regular intervals to discuss common issues relevant to animal cell technology, its application and industrial use. It acts in an advisory capacity to the European Commission on current and future publicly funded research themes and generates opinions and actions concerning industrial policies. Other major objectives are the identification of problems or obstacles to the implementation of new methodologies or technologies as applied to the commercialization of *in vitro* animal cell culture and to propose solutions. This particularly relates to responsible research, development and production, environmental and consumer protection, intellectual property and harmonization of relevant European regulations and guidelines. Also to inform the public of the beneficial effects and positive contribution that biotechnology in general, and animal cell technology in particular, can make in the prevention or treatment of human or animal ailments.

The European Working Group on Human Gene Transfer and Therapy (EWGT) was officially founded in January 1992. The group's major aim is to develop and coordinate clinical and scientific research in the field of gene transfer and gene therapy in Europe. This unique Group has achieved the federation of all major European teams working in the field. It includes around 400 members from 14 countries, including Israel.

The objective of EWGT is to maintain an interactive network for communication and collaboration. A directory of scientific forms is filled in by each team leader, these are then circulated to other members who have themselves contributed a form. The EWGT is prepared to act as a Scientific Advisory Board for the review of guidelines and clinical protocols, which it has been asked to do by the services of the European Commission DG III.

EWGT is currently creating a registry of clinical protocols in current application or planned for the future. In addition, the Board has decided to let circulate among its members primary recommendations and safety considerations, which should apply to the implementation of clinical protocols.

Gene therapy and the production of gene therapy products use molecular and cell biological methods. The techniques used for the *in vitro* cultivation of cells in the manufacture of biologics are the same, or similar to those practised to generate cell populations expressing a particular gene of interest for somatic gene therapy. When this gene has a potential therapeutic application it follows that regulatory requirement, and guidelines (together with other aspects) will be based or judged on similar issues and standards.

The emerging technique of nucleic acid vaccination (NAVAC) raises issues that are similar and often identical to those raised by somatic gene therapy: this technique also raises great hopes for the future of new vaccine development. While the work performed in this area has not gone beyond the pre-clinical stage yet, it is foreseen that clinical trials will be conducted in the near future.

The ACTIP Steering Committee and the EWGT Board are proposing to form an informal association where the view of both bodies can be expressed and discussed. Common policies can be mutually supported, and if appropriate, jointly released. This could be established by regular communication and the opportunity of exchanged visits of nominated delegates to specified meetings. (Source: *News Release*, December 1994)

Cobiotech: North-South America Conference on Biotechnology

The International Scientific Committee for Biotechnology (COBIOTECH) of the International Council of Scientific Unions (ICSU) will hold this conference in Cuernavaca, Mexico, between 27-29 November 1995, in collaboration with the Biotechnology Institute of the National Autonomous University of Mexico. The specific goals of the conference are twofold: (1) to assess the current status of biotechnology in the western hemisphere; and (2) to project biotechnological advancements into the near future in all areas that are deemed critical to the successful development of these technologies. The tentative programme includes, in the first day, the theme: **Biotechnology, Present and Potential Future**, with two symposia: (a) **Achievements in biotechnology (medicine, agriculture, food, environment, forestry, industry)**, and (b) **Needs and opportunities in different fields of biotechnology**. For the second day the theme is **Frameworks to bridge between needs and opportunities**, with three symposia: (a) **The private business sector**, (b) **University-industry relationships**, and (c) **The role of international agencies supporting biotechnology**. The last day will be dedicated to: Non-tangible barriers to success, and will include three round-table discussions: (a) **Networking**, (b) **Education and training**, and (c) **Legal and regulatory aspects, and NAFTA**. (Source: *Boletin de Biotecnologia*, Vol. 11, No. 2, December 1994)

An update on commercialization

The chart overleaf summarizes USA actions on commercialization of genetically-engineered products.

Company	Product	Altered trait	Purpose	Sources of New Genes	Agency Action[1]	On the Market
1. Calgene	Tomato	Delayed ripening	Enhance fresh market value	Tomato, bacteria, virus	USDA/Approved FDA/Approved EPA/Not required	Yes
2. Calgene	Canola (oilseed rape)	Altered oil composition – high lauric acid	Expand use in soap and food products	California bay, turnip rape, bacteria, virus	USDA/Approved FDA/Pending EPA/Not required	No
3. Calgene/ Rhone Poulenc	Cotton	Resistance to herbicide bromoxynil	Control weeds	Bacteria, virus	USDA/Approved FDA/Approved[2] EPA/Pending	No
4. DNA Plant Technology	Tomato	Delayed ripening	Enhance fresh market value	Tomato, bacteria, virus	USDA/Pending FDA/Approved[2] EPA/Not required	No
5. Monsanto	Cotton	Resistance to insects (Bt toxin)	Control insect pests	Bacteria	USDA/Pending FDA[3] EPA/Pending	No
6. Monsanto	Potato	Resistance to Colorado potato beetle (Bt toxin)	Control insect pests	Bacteria	USDA/Pending FDA/Approved[2] EPA/Pending	No
7. Monsanto	Soybean	Resistance to herbicide glyphosate	Control weeds	Petunia, soybean, bacteria, viruses	USDA/Approved FDA/Approved[2] EPA/Pending	No
8. Monsanto	Tomato	Delayed ripening	Enhance fresh market value	Bacteria	USDA[4] FDA/Approved[2] EPA/Not required	No
9. Upjohn	Squash	Virus resistance	Control virus diseases	Viruses	USDA/Approved FDA/Approved[2] EPA/Not required	No (1995)
10. Zeneca	Tomato	Thicker skin, altered pectin	Enhance processing value	Tomato, bacteria, virus	USDA/Pending FDA/Approved[2] EPA/Not required	No
11. Mycogen	Pseudomonas fluorescens[5]	Toxicity to insects (Bt toxin)	Control insect pests	Bacteria	USDA/Not required FDA/Not required EPA/Approved	Yes
12. Research Seeds	Rhizobium meliloti	Enhanced nitrogen fixation	Increase yield in alfalfa	Bacteria	USDA/Not required FDA/Not required EPA/Pending	No
13. Rhone Merieux	Vaccinia virus vaccine	Immunity to rabies	Control raccoon rabies epidemics	Rabies virus	USDA/Pending FDA/Not required EPA/Not required	No

1 Action may respond to either voluntary or required submissions from companies.
2 FDA has completed consultations with the company. Consultations are informal reviews of company safety assessments.
3 Status of consultations, if any, is unknown.
4 USDA approval is required; Monsanto has not yet applied for USDA approval.
5 The organism is killed before it is applied in the environment.

(Source: *The Gene Exchange*, December 1994)

World-wide field trials of transgenic plants: 1986-1994

The accompanying chart and map summarizing eight years of global testing of transgenic plants is adapted from a recent article by A. Krattiger in *Biosafety for Sustainable Agriculture: Sharing Biotechnology Regulatory Experiences of the Western Hemisphere.** The chart gives the number of field tests by country, while the map summarizes the information by region.

Three caveats apply. First, it is by no means certain that the chart is complete, particularly for countries where there is no regulatory oversight of the technology. It is possible that tests have been conducted in those countries without knowledge of government authorities. According to Krattiger, of the developing countries listed in the chart, only Mexico has regulations in place; Argentina and Cuba have regulations not yet incorporated into laws; and Costa Rica, Bolivia, Chile, China and Thailand have established *ad hoc* committees or are in the process of adopting regulations.**

Second, the data are uneven in quality. Data from North America and Europe were the most readily available and reliable. Information from other regions, particularly from developing countries, was more difficult both to obtain and to verify. In some cases, Krattiger was forced to obtain data through informal, unofficial contacts.

Third, the totals may be misleading and difficult to compare because the definition of a field trial differs from country to country. In general, the author considered a field trial to correspond to a field test permit, yet permits may allow a number of tests. For example, one US field trial as listed in the chart may involve several tests of the same organism at different sites. In other countries, a permit may be issued for each test site.

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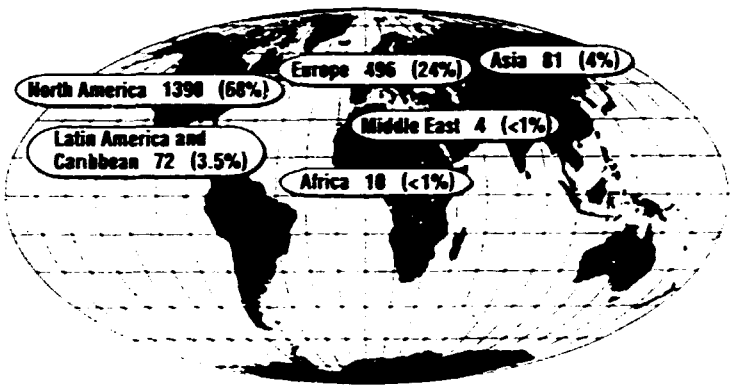
* A. Krattiger, "The field testing and commercialization of genetically engineered plants: a review of world-wide data (1986 to 1993 94)", pages 247-66 in *Biosafety for Sustainable Agriculture: Sharing Biotechnology Regulatory Experience of the Western Hemisphere*, A. Krattiger and A. Rosemarin, eds., ISAA: Ithaca and SEI: Stockholm 1994. Generally, the figures represent information collected up to July 1994. However, for the United States, data were available only to June 1994 and data for Denmark, France, Germany, Italy and Portugal were available to 15 March 1994.

** According to an article in *Science* magazine (11.11.94), China has established regulations.



Region/Country	Total
Latin America and Caribbean	
Argentina	20
Belize	4
Bolivia	4
Chile	13
Costa Rica	5
Cuba	9
Dominican Republic	1
Guatemala	1
Mexico	15
Asia	
Australia	26
China	30
Japan	8
New Zealand	15
Thailand	2
Africa	
Egypt	1
South Africa	9
Middle East	
Israel	4

Region/Country	Total
Europe	
Belgium	81
Denmark	11
Finland	10
France	168
Germany	6
Hungary	4
Italy	14
Netherlands	84
Norway	1
Portugal	4
Spain	16
Sweden	17
Switzerland	2
United Kingdom	78
North America	
Canada	359
United States	1031
WORLD TOTAL	**2053**

(Source: *The Gene Exchange*, December 1994)

International biotechnology meetings

Monterey, California, was the site of two international meetings on agricultural biotechnology, both sponsored by the United States Department of Agriculture (USDA) and other government agencies—and both notable for their exclusion of the public-interest community from the agenda.

The first meeting, a one-day workshop titled "Agricultural Biotechnology—Beyond the Laboratory: Access, Distribution and Utilization for Emerging Countries", was sponsored by USDA, the United States Agency for International Development, and the University of California. The 22 speakers, from industry, universities, and Governments around the world, discussed the opportunities and challenges facing developing countries interested in biotechnology research and commercialization programmes.

The organizers of the conference refused a request from UCS to add public-interest representatives to the programme to give a more balanced view of the technology's risks and benefits. Perhaps as a result, the meeting was remarkable in its one-sided emphasis on the benefits of biotechnology and omission of its potential downsides. There were no presentations, for example, on the environmental risks of genetically-engineered organisms, particularly the potential impacts of transgenic crops on centres of diversity, most of which are located in the developing world. No speakers addressed the possibilities of social and economic dislocations in developing countries as biotechnology products displace natural ones, an issue already raised by genetically-engineered high-laurate canola intended to replace tropical oils from a number of Asian countries.

Two days later, the USDA, in conjunction with European, Japanese, and other United States agencies, sponsored the Third International Symposium on the Biosafety Results of Field Tests of Genetically Modified Plants and Microorganisms to examine the ecological risks of genetically-engineered organisms applied in the environment. The scientists at the meeting confirmed the view that genetically-engineered organisms will present risks where they are used in agriculture, particularly at commercial scale. In addition, a consensus emerged that the small-scale field trials conducted thus far have failed to generate data needed to evaluate the risks that commercialization will bring. (Source: *The Gene Exchange*, December 1994)

The West Asia and North Africa (WANA) Plant Genetic Resources Committee held its biennial workshop from 3-7 October 1994 in Larnaca, Cyprus. In addition to discussing Phase 1 activities of the WANA Network on Plant Genetic Resources (WANANET), participants considered regional and country issues relating to genetic diversity, germplasm evaluation and utilization, and preparations for the International Conference and Programme on Plant Genetic Resources. Recommendations arising from the workshop will be the basis for WANANET's activities in Phase 2, which runs from October 1994 to October 1997. The meeting also elected a Steering Committee to coordinate Phase 2 activities with representatives from Cyprus, Egypt, Iran, Morocco, Pakistan, Syria and Yemen. For additional information, contact: Dr. Yawooz Adham, International Plant Genetic Resources Institute, Regional Director for WANA, c o International Centre for Agricultural Research in the Dry Areas, P.O. Box 5466, Aleppo, Syrian Arab Republic. Tel.: 963-21-213433 213477. Fax: 963-21-213490 225105. (Source: *Diversity*, Vol. 10, No. 3, 1994)

Prospecting for Biodiversity

The Convention on Biological Diversity establishes a framework intended to foster partnerships between technology-rich industrialized countries and gene-rich developing countries. A landmark report, entitled *Biodiversity Prospecting: Using Genetic Resources for Sustainable Development*, provides practical guidance on how those partnerships should be designed. The report, released by World Resources Institute (WRI) in 1993, argues that "biodiversity prospecting"—the search for wild species that can yield new medicines, better crops, and raw materials for industry—can help protect the plant and animal habitants on the edge of extinction if developing countries have more than a token share in the profits from commercially valuable genetic and biochemical discoveries.

Biodiversity Prospecting is a first-of-its-kind analysis of the laws, contracts, and organizations needed to promote conservation and assure that profits from biodiversity are divided fairly. The report also includes a draft contract that can help potential bioprospecting corporations and developing countries come to terms on what constitutes a fair arrangement.

"The major tenet of the biodiversity treaty is that countries and companies should pay for the use of genetic resources", said Walter V. Reid, WRI Vice President and lead author of the report. "Just as a chemical company wouldn't expect to get oil for free, the pharmaceutical and biotechnology industries should pay for their raw materials. Our report shows how these financial arrangements can benefit all parties, while at the same time contributing to conservation".

Reid believes that as Governments North and South try to come to grips with the requirements of the Convention on Biological Diversity, *Biodiversity Prospecting* can help them understand policy mechanisms by which developing countries can explore and profit from their biodiversity, and the biotechnology and pharmaceutical industries can be assured a steady supply of raw materials. Although virtually no precedent exists for national legislation to regulate wildland biodiversity prospecting, Reid said the 160 nations that signed the international biodiversity treaty must pass legislation that establishes just such a policy framework.

Since bioprospecting will not necessarily promote conservation nor fuel developing countries' economic growth, the authors recommend guidelines that would ensure that it does both. Among the report's key recommendations:

- Countries should charge for access to their biodiversity. In effect, they should establish biodiversity prospecting concessions analogous to mineral concessions.
- A significant share of the revenues generated from biodiversity prospecting should be used to strengthen conservation activities.
- Biodiversity prospectors should be required to obtain the informed consent of private landowners, local communities, and indigenous groups before gathering samples. They should return a share of the benefits from the development of commercial products to these local groups.
- Nations should inventory and protect their biodiversity. The more a country knows about what it has and where it is, the more it will benefit from the

new demand generated by the growth of biotechnology.

- Rather than just exporting raw materials, countries should seek to add value to the product by developing their own pharmaceutical research capacity.
- Contacts between pharmaceutical companies and developing countries will work only in the context of international agreements that answer such questions as who owns biodiversity, how access to it can be controlled, and how intellectual property rights and profits can be equitably divided between local communities, nations, and private companies. Thus, the Convention on Biological Diversity and other multilateral agreements are important foundations for sustainable and equitable biodiversity prospecting programmes.

Biodiversity Prospecting was published by WRI, an independent policy research centre focusing on global environmental and development issues, with Costa Rica's National Biodiversity Institute (INBio), and the African Centre for Technology Studies (Kenya). The book elaborates on the recommendations contained in the *Global Biodiversity Strategy*, a comprehensive agenda of policy reforms and conservation actions by which nations can preserve biodiversity while utilizing its benefits for food, medicines, chemicals and other necessities. The *Strategy* was developed by WRI, the United Nations Environment Programme, and the World Conservation Union in an unprecedented three-year initiative involving scientists, government officials, non-governmental organizations, business people and local leaders on nearly every continent.

For further information, contact: Shirley Green, WRI, 1709 New York Ave., NW, Washington, DC 20006, USA. Tel.: 1-202-662-2542. Copies of *Biodiversity Prospecting: Using Resources for Sustainable Development* can be obtained for US $29.95 plus $3.00 shipping and handling from: WRI Publications, P.O. Box 4852, Hampden Station, Baltimore, MD 21211, USA. (Source: *Diversity*, Vol. 10, No. 3, 1994.

The violence of the "Blue Revolution"

While international agencies and many national Governments are promoting intensive aquaculture to improve nutrition and increase exports, the ecological and economic impact of the "blue revolution" is becoming evident, even within one year of such projects being set up. Aquaculture has actually aggravated the poverty of fishing and farming families apart from negatively affecting marine fisheries and fish production, especially when diverse species, producers and consumers are fully taken into account.

Intensive shrimp farms with stocking rates of 100,000 to 300,000 prawns per hectare have to be maintained with artificial feeds, intensive water use and energy to pump the water. This becomes necessary to maintain optimal levels of oxygen, salinity, temperature, and because of the pollution caused by excessive feeds, faeces, and other organic wastes which need to be pumped out.

Sea water has to be mixed with fresh groundwater to keep the salinity within the 15-20 ppt range. Estimates show that roughly 6,000 m^3 of fresh water is needed to dilute full sea water in a one-hectare pond at one metre water depth over a cropping period of four months.

Shrimp farms, as they are set up near the coast in order to pump sea water into the ponds, have a major ecological impact on the coastal zone ecosystems as well as on communities involved in fishing and paddy cultivation. The farms are often set up in delta regions which are normally very fertile. The Thanjavur delta, known as the granary of South India, has normally phenomenal paddy yields. The "kuruwai" crop used to bring in 6.5 tons per ha. and the "samba" crop 4.5 tons per ha. before aquaculture projects were introduced. The local people now call the area a graveyard.

In India, the most rapid expansion of shrimp farming is in the districts of Nellore (named after "nellu" or rice) and Thanjavur, the rice bowl in the Cauvery delta.

The first impact of shrimp farming is on the lands and forests of the coastal region, which are destroyed to make gigantic fish farms. In the Philippines, Thailand and Indonesia, where mangroves have been destroyed for shrimp farming, the environmental impact has been particularly great, as mangroves provide nutrients to adjacent estuarine and marine ecosystems. They also contribute to offshore fisheries by acting as nurseries and providing shelter: prawn and shrimp catches at sea have been found to be directly proportional to mangrove areas. In addition, this destruction of coastal vegetation destroys the buffer zone against destructive winds and water action, increasing cyclone and flood vulnerability, which in turn create the potential for new scales of environmental disaster.

However, the greatest impact is on the availability of fresh water, both for drinking and agriculture. Shrimp farming has led to water famine in areas where it has been introduced.

The massive extraction of fresh water from underground aquifers (which are then subject to salt water intrusion) and seepage from the tanks has led to an increase in groundwater salinity. This has resulted in the destruction of paddy fields. A survey conducted by the Chittagong University Economics Department showed that the Satkhira region in Bangladesh could produce only 36 tons of rice in 1986 (after the introduction of intensive aquaculture) as compared to 40,000 metric tons of rice in 1976.

The effect of this salination is visible early.

Shrimp farms flush their effluent and wastes directly into the sea and into neighbouring mangrove and agricultural lands in the form of excess lime, organic wastes, pesticides, chemicals and disease pathogen. This waste affects estuarine and marine organisms, stifling their growth and causing water quality to deteriorate. Intensive coastal fish farming has also been linked to "red tides", an explosive growth of toxic algae that can kill fish and fatally poison people who eat contaminated sea food.

The dense stocking rate leads to overcrowding and associated stress problems, increasing susceptibility to disease, poor water quality (due to decreased oxygen levels), high level of accumulated metabolic products, excreta, rapid growth and transmission of noxious parasites and micro-organisms. The loss of fish is about 25-30 per cent.

Losses of this magnitude due to the tendency to self-pollution led to the Government of Taiwan banning the setting up of new shrimp farms.

Last, but not least, is the effect that intensive aquaculture has on marine fish stocks. Juvenile shrimp are captured from mangroves for hatcheries as they do not breed in captivity. So are egg-bearing females, which can stock one to two ponds and thus fetch high prices. This procedure involves the callous cutting off of the eyes of the

female shrimp to increase sexual activity, thus forcing captive spawning.

Aquaculture thus prevents the renewal of wild varieties of shrimp and prawn at sea, and leads to depletion of marine species.

The social impacts of "Blue Revolution"

Since coastal ecosystems where shrimp farming is being introduced are regions which support the lives and livelihoods of millions of fisherfolk and farmers, the environmental destruction caused immediately transforms into social impact. The depletion of shrimp in the sea adversely affects those whose livelihoods are dependent on shrimp. In Ramachandrapuram in India, where Rank Aqua and Siraga shrimp farms have just started to operate, the shrimp catch of fishermen has fallen from Rs. 50,000 per catamaran per month to Rs. 5,000 within one year.

While the depletion of marine fish and of agricultural lands has destroyed their resource base, the enclosure of the beaches for pumps and powerhouses has pushed fishing communities off their ancestral homes. Not only are fishermen displaced, local communities no longer can consume fish. Since intensive farms are export oriented, they do not supply local markets. The cost of fish locally has risen world-wide as a result of commercial fisheries. In Kerala, India's number one fishing state, the price of shrimp jumped from US$ 50 a ton to US$ 3,000 a ton between 1961 and 1981, leading to a fall in consumption from 19 kg per person to 9 kg per person.

While aid programmes put money into aquaculture development to boost world food production, the net result is not feed the hungry but those who can afford higher and higher prices for fish. The Indian experience with shrimp farming shows that this kind of development takes away from the poor the little they have.

Shrimp farming has led to a corresponding decrease in the livelihoods to the people. There are no livelihoods on sea or on land. Rice cultivation on 40 hectares of land needed 50 labourers, but shrimp raising in the same area needs only five workers. Each job in aquaculture needs an investment of Rs. 21 acres.

When these social costs are internalized, intensive prawn farming emerges as a highly wasteful and inefficient technology for ecological and equitable utilization of land, water and fish resources, and one that does not help in feeding the hungry.

Intrinsic to the blue revolution are value judgements that devalue nature's productivity in the sea and the productivity of fishing communities dependent on the gift of the sea. They tacitly set up a hierarchical ordering that puts the luxury consumption of shrimp by rich northern consumers and the profits of corporations above the need for drinking water, food and livelihoods of corporations above the need for drinking water, food and livelihoods of local fishing and farming communities. Shrimp farms embody an assumption of the dispensability of coastal ecosystems and the fishermen and farmers they support. (Source: *Biju*, No. 10 11, September December 1994)

Germany will be site of 1996 International Conference for Plant Genetic Resources

The United Nations Food and Agriculture Organization (FAO) has officially launched its "International Conference and Programme for Plant Genetic Resources" leading to a major international conference now scheduled for 1996. The preparatory process leading to the conference together with the revising of the FAO International Undertaking to bring it into compliance with the Convention on Biological Diversity -- will be characterized by intense dialogue and negotiations. FAO is stressing its role in the effort as facilitator of a participatory, country-driven process.

Governments will soon be asked to begin preparing country reports assessing the status of plant genetic resources and the capacity of the country to conserve and utilize them adequately in the context of national priorities and goals. Reports will be presented at a series of meetings bringing together countries grouped generally by eco-geographical and political criteria. These meetings will provide an opportunity to identify any immediate emergency needs and discuss regional problems, priorities, and opportunities for cooperation. Country reports and results from the subregional meetings will provide the foundation for FAO's first Report on the State of the World's Plant Genetic Resources. This document will present findings and analyses upon which a concrete Global Plan of Action for the Conservation and Sustainable Utilization of Plant Genetic Resources will be formulated.

According to FAO, the Global Plan of Action will set out priorities for action and contain precisely budgeted programmes. Its aim will be to promote the best use of available funds, ensure coordination of activities and programmes within a global framework, present an initial set of programmes, determine a division of responsibilities among implementing institutions, and identify emergencies and gaps in the current work. The comprehensive plan will deal with both *in situ* and *ex situ* conservation and encompass action at national, regional, and international levels. A major concern of the effort will be strengthening the link between conservation and utilization.

The international conference, to be hosted by Germany in 1996, will consider and presumably approve a revised FAO International Undertaking and the Global Plan of Action for plant genetic resources for food and agriculture.

For additional information, contact: Dr. Cary Fowler, Food and Agriculture Organization of the United Nations, Via delle Terme di Caracalla, 00100 Rome, Italy. Tel.: 39-6-5225-5925. Fax: 39-6-5225-5271. E-mail: cary.fowler *@* fao.org. (Extracted from *Diversity*, Vol. 10, No. 2, 1994.

Series of round tables on the equitable and sustainable use of biodiversity resources

The Convention on Biological Diversity has opened new perspectives on biodiversity conservation and use, and has provided many constituencies with new responsibilities and opportunities. The rapid evolution of international developments requires new initiatives to add specificity on how positive change can be facilitated. A research project of the Biodiversity Biotechnology Programme at the International Academy of the Environment led to the proposition for a facilitating mechanisms to promote the equitable and sustainable use of biodiversity.

In order for the concept of such a "Facilitator" to be tested, adapted and refined, and to develop an action agenda leading to eventual implementation, an initial round table was sponsored and organized in Mexico. Twenty senior persons from around the world were invited, representing eight countries from Latin America, as well as academia, indigenous peoples, non-governmental organizations, multilateral institutions and the private sector.

The starting point was a series of country presentations with emphasis on national goals for biodiversity and problems in achieving those goals. Based on this information, three working groups produced a coordinated objectives and procedures document. This was followed by a detailed analysis of the experiences of 10 international and regional institutional mechanisms concerning technology transfer, collaboration, information networks, training and programmes by the private sector, which served as a means to share information and experiences

The participants, despite the diversity of their backgrounds, were in broad agreement as to the content of, and strategy for executing, an action agenda towards the implementation of a "Facilitator" that would reinforce the equitable and sustainable use of biodiversity resources by:

- Brokering equitable and effective linkages among providers and recipients of biodiversity resources and biodiversity-derived products;
- Providing advice on relevant legislation and policies to ensure appropriate protection for providers and recipients;
- Developing training activities in areas related to conservation and use of biodiversity, intellectual property rights, and commercialization;
- Facilitating technology transfer;
- Assisting in information sharing through a network on scientific, local community and commercialization issues;
- Encouraging regional harmonization of legislation and policies; and
- Enhancing overall parity in biodiversity resources systems by developing programmes and projects on the equitable and sustainable use of biodiversity and on appropriate incentive systems.

The participants drafted the terms of reference for a feasibility study towards the implementation of such a "Facilitator". This study is now under way and should be completed by mid-1995. The Stockholm Environment Institute (SEI), in collaboration with the Academy, adapted this initiative for Africa and Asia where further round tables were jointly organized, one in September in Nairobi, Kenya, and another one in October in Bogor, Indonesia.

The three regional round tables were followed by a special synthesis workshop organized by SEI and the Academy, and sponsored by the Swedish Government, prior to the first Conference of the Parties to the Convention on Biological Diversity, to determine how to establish a clearing house for technical and scientific collaboration under the Convention. (Source: *International Academy of the Environment Newsletter*, January 1995)

GABA gears up for launch

Memberships are now being accepted for a new association which will serve and forward the cause of the agriculture biotechnology industry around the world.

The Global Agricultural Biotechnology Association acts as an information hub where researchers and other industry professionals can easily access resources. A database is currently being developed, devoted to such subjects as strategic alliance opportunities, public education and new developments in research and government regulations.

In addition to a quarterly newsletter, the organization is creating the GABA Online Resource Centre, a World Wide Web site on the Internet. Members will have full access to the site, including the membership directory for contacts. Non-members will also have access, but they will be limited to more general information. The site will also be linked to other sites of interest to the agbiotech industry; these links will be updated on a regular basis. GABA Online is slated to become active some time in April.

While the official launch of GABA itself has not yet been announced, preliminary information points to a mid-March or early April start date.

Contact: GABA, 230 Research Drive, Saskatoon, Saskatchewan, S7N 2R2. Tel.: (306) 975-1939, Fax: (306) 975-1966 or e-mail: gaba@lights.com. (Source: *The Agbiotech Bulletin*, Vol. 3, No. 3, March 1995)

Alzheimer's: a growing disease

A new report by *Datamonitor* examining the epidemiology of diseases of the central nervous system, reveals the high probability of the very elderly developing Alzheimer's disease. Key findings include the following:

- In the UK, 585,300 people will have Alzheimer's disease by 2010;
- In Europe, it estimated that more than 46 per cent of the population over 90 years suffers from Alzheimer's.

When such prevalence rates are applied to the United Nations population projections, they produce estimates for the future prevalence of Alzheimer's which predict a growing economic and social problem.

The large increase in the numbers of the very elderly (those aged 80 and over) predicted by the United Nations population projections, together with the high incidence rates for Alzheimer's imply that the treatment of the disease and other degenerative conditions will become a priority. This will present new opportunities in different therapeutic areas, but will also increase the pressure on health care budgets world-wide. The table below shows the proportion of the European population in each group suffering from Alzheimer's and its dramatic rise with age. This is a similar trend to that observed with Parkinson's disease.

Percentage of each group suffering from Alzheimer's in Europe

Age group	Per cent with Alzheimer's
60-64	0.4
65-69	0.9
70-74	2.0
75-79	4.4
80-84	9.6
85-89	21.2
90+	46.4

Source: Datamonitor

Details from: Sophie Smith, *Datamonitor*, 106 Baker Street, London W1M 1LA or on 0171 625 8548. Fax: 0171 625 5080. (Source: *Biotechnology Bulletin*, February 1995)

New plant programme launched

Scientists from 12 countries have launched a programme to develop new varieties of corn, rice, wheat, beans and cassava which will be able to absorb the scarce minerals in poor soils common in developing countries. These plants will need less fertilizers and water than present varieties, says the Washington-based International Food Policy Research Institute, which is coordinating the project. (Source: *Chemistry and Industry*, 6 February 1995)

World Congress of Engineering Educators and Industry Leaders, 2-5 July 1996

The World Congress to be jointly organized by the United Nations Educational, Scientific and Cultural Organization (UNESCO), the United Nations Industrial Development Organization (UNIDO), the International Union of Technical Associations and Organizations (UATI) and the World Federation of Engineering Organizations (WFEO), to be held in Paris, France, will discuss and synthesize practices and concrete projects concerning university-industry cooperation based on recommendations made during the congresses held at UNESCO Headquarters in June 1993 and the results of international and regional congresses organized in 1994, 1995 and 1996 in different regions of the world. The Congress will emphasize actions to strengthen education and training as well as research and development. The particular problems and needs of developing countries and those evolving towards a market economy will be highlighted.

The Congress is to be held within the framework of the commemoration of the 50th anniversary of UNESCO to show the contribution of the engineering community to the fulfilment of the UNESCO UNISPAR (University-Industry-Science Partnership) Programme.

This Congress is intended to interest and involve the leaders of institutions as well as industry dealing with the training of engineers and R&D activities. It also concerns representatives of public authorities and of intergovernmental and financial organizations.

The proposed themes are as follows:

Theme 1: Initial training of engineers adapted to the needs of national and international economies.

- Practices and case studies of cooperation with industry;
- Examples of cooperative training between university and industry;
- New projects.

Theme 2: Continuing training of engineers and researchers for updating knowledge and advancing development of companies and national and international economies.

- Practices and experiments carried out;
- New projects.

Theme 3: Research and development cooperation between training organizations and industries. Concrete examples and perspectives.

Theme 4: Cooperation between training organizations and industries at national, regional and international levels for the implementation of sustainable development programmes, taking into account their environmental impact. Concrete examples and perspectives. Management, financing and follow-up of projects.

Panels will discuss the general organization of training and research. Discussions by these panels will cover specific subjects but not limited to: energy, communication, public works, transport, natural resources, chemical, agricultural and food industries, biotechnology, etc.

One panel will be devoted to the presentation of the state-of-the-art of the university-industry cooperation in several countries at different stages of development.

It is expected that student engineers as well as those recently professionally employed, will respond to proposals and conclusions of panels in which they participate. A special panel will be devoted to this purpose at the conclusion of the Congress.

All correspondence and inquiries concerning the Congress should be sent to the Secretariat of the Congress: UATI, Maison de l'UNESCO, 1, rue Miollis, F-75732 Paris Cedex 15 (France). Tel.: +33 (1) 43 06 20 29. Fax: +33 (1) 43 06 29 27. E-mail: UNISPAR@UNESCO.ORG.

C. COUNTRY NEWS

Argentina

Forum of biotechnology

The Argentinian Forum of Biotechnology (abbreviated FAB in Spanish) was founded as a private entity at the end of 1986 on the inspiration of Argentinian Nobel Laureate Luis Federico Leloir and a group of Argentinian entrepreneurs. FAB intends to promote awareness about the significance of the challenge of the new biotechnology to the country, and to serve as an instrument for bridging the entrepreneurial, scientific and governmental sectors in using biotechnology as a vehicle for development and well-being.

In its structure, FAB includes an Administration Council, a Managerial and Advisory Committee, plus about 25 associated entities. Among its activities are: maintenance of a database of Argentinian biotechnological firms; organization of meetings, seminars, workshops and courses, for entrepreneurs and other interested persons; collaboration with government authorities in aspects of biotechnology policies; and maintenance of permanent contacts with similar foreign entities for exchange of information on related activities. The address of FAB is: Callao 215-P 5° "F", 1002, Buenos Aires, Argentina. Tel.: (54)40 64 13, Fax: (54) 40 99 12. (Source: *Boletin de Biotecnologia*, Vol. 11, No. 2, December 1994)

Belgium

Belgian Coordinated Collections of Micro-organisms

Since August 1993, the Belgium Coordinated Collections of Micro-organisms (BCCM) is the third European centre to be recognized as an international authority for the deposit of animal cell lines, including human cell lines, genetically modified cell lines and hybridomas, within the framework of the international patent legislation (Budapest Treaty).

The scope for deposits of genetic material has been broadened to any kind of plasmid or genetic material, including, for example, RNA and oncogenes. The material, recombinant or natural, may be presented either within a host or a purified form, as long as its preservation does not cause any major technical or biosafety problem.

Details on the practical procedures can be obtained from the LMBP Collection, Laboratory of Molecular Biology, University of Ghent. Tel.: +32/9/264 51 45, Fax: +32/9/264 53 48.

Canada

New Canadian plant breeders' rights

On 28 December 1994, Canada introduced 16 new categories of plants available for protection under its *Plant Breeders' Rights Act*, bringing to 39 the categories of plants protected under the Act.

The newcomers include: Begonia, Blueberry, Clematis, Creeping Red Fescue, Impatiens, Kentucky Bluegrass, Lentil, Maple, Mustard, Peach, Pelargonium, Plum, Raspberry, Spirea, Timothy and Viburnum.

With the adoption of these new categories, plant breeders have until 28 December 1995 to file for protection of new varieties if the sale of that variety had occurred *inside Canada* since 1 August 1990; *outside of Canada* since 1 August 1984 for woody plants and slow growing species; and 1 August 1986 for everything else.

Contact: Marusyk Bourassa Milton, MBM & Co., Box 809, Sation B, Ottawa, Ontario, K1P 5P9. Tel.: (613) 567-0762 or (613) 563-7671.

Patent information searches available

Technological information from patents can be a rich source of expertise, licensing opportunities and competitive intelligence for the agbiotech industry. Several sources offer search programmes for business and research institutions.

Among its many functions, the Canadian Intellectual Property Office (CIPO) disseminates information from its data bank on Canadian and foreign patents. CIPO's Patent Information Exploitation Programme is intended to stimulate technology transfer, promote industrial innovation and provide support to R&D through the use of technological information contained in patents.

The Industrial Research Assistance Programme (IRAP) of the National Research Council (NRC) operates its own pilot programme with CIPO. The Extended Search Programme assists business clients to extract information from patents covering: solutions to technical problems, sources of know-how and licensing opportunities, activity of competitors, and an in-depth look at the "state-of-the-art".

The Canada Institute for Scientific and Technical Information (CISTI), another branch of NRC, also provides a Patent Search Service. CISTI searches provide lists of patent titles with summaries and sources for obtaining patent documentation.

Access: Coordinator, Technology Search Service, Canadian Intellectual Property Office, 50 Victoria Street, Hull, Quebec K1A 0C9. Tel.: (819) 997-2996, Fax: (819) 953 7620 or CISTI Patent Search Service Coordinator, (613) 993-2013, Fax: (613) 952-8239, Internet: Refmail@cisti.lan.nrc.ca. (Source: *The Agbiotech Bulletin*, Vol. 3, No. 3, March 1993)

China

First medicinal genebank

The Chinese Medicinal Research Institute of Zhejiang has founded the first genebank for conserving medicinal plant germplasm, an organization that will play an extremely significant role in collecting, conserving, and utilizing medicinal plant genetic resources in China. The genebank facilities will include a management room (for coding and recording the seeds in the computer), seed check room for examining insect infestation and seed purity, cleaning room, germination room, drying room, preparation room (where the dried seeds are weighed and packed), and machinery room. Overall, the cold storage will have enough space for approximately 50,000 accessions. For more information, contact Dr. Ramanatha Rao, GD/Conservation, IPGRI Regional Office for Asia, and Pacific and Oceania, 30 Orange Grove Road, 7th Floor, REI.C Bldg., Singapore, 1025. Tel.: 65-738-9611, Fax: 65-738-9636. (Source: *Diversity*, Vol. 10, No. 2, 1994)

Trademark association established

China moved to implement recent government decisions to further develop the country's intellectual property system by establishing the China Trademark Association (CTA) in September of 1994. The CTA is comprised of 157 key profit-making enterprises and 22 experts and legal advisers.

Trademark registrations in China have increased from 32,000 in force in the late 1970s to a current level of 440,000, a 14-fold increase. China is now a member of major international treaties on trademarks, according to the World Intellectual Property Organization. (Source: *The Agbiotech Bulletin*, Vol. 3, No. 2, February 1995)

China conducts the world's largest tests of transgenic organisms

Chinese scientists are field testing genetically engineered crops and micro-organisms on a scale far exceeding anything in the West. According to a recent article in *Science*, field trials in the People's Republic cover hundreds and thousands of acres.* Two groups in Beijing, for example, have planted over 100,000 acres of transgenic plants, primarily tobacco. Much of the work is directed at developing virus-resistant crops through genetic engineering. Transgenic tobacco is already marketed in Chinese cigarettes.**

Regulations governing genetic engineering work in China are lax, even by US standards. Under rules developed just a year ago, Chinese scientists are subject to relatively little oversight—they typically proceed with research if they decide for themselves that their work is safe. Similarly, oversight of commercialization essentially relies on producers to decide whether their products are safe. (Source: *The Gene Exchange*, December 1994)

First biotech safety rules

Chinese authorities are laying the foundation for regulating agricultural biotechnology experiments, in part to retain control over the burgeoning biotechnology enterprise and also in response to suggestions from Chinese scientists to bring their country's practices in line with those used elsewhere. The clearest indication of this new philosophy came when China's highest scientific policy-making body, the State Science and Technology Commission (SSTC), issued the country's first rules for research on genetically modified organisms and formed a commission to oversee their implementation.

The rules are, however, relatively benign compared with those in the West. They establish four levels of risk for work involving genetic engineering: non-dangerous, slightly dangerous, moderately dangerous and highly dangerous. Laboratories are permitted to proceed on their own authority with work in the first two categories, while work deemed moderately or highly dangerous must receive permission from higher authorities.

The regulations mandate the establishment of a National Genetic Engineering Safety Commission to "be in charge of the coordination and supervision of genetic engineering safety", but it is not clear how the commission will exercise its authority.

Indeed, the new rules allow each government department to retain control of genetic engineering safety "within its own scope of responsibility". The practical result will be to leave scientists, or their superiors in the relevant ministry or university, to determine the degree of danger of any proposed research and whether it should be reported to the new commission.

In addition to giving scientists a relatively free hand to carry out their work, the SSTC regulations are also somewhat lax with regard to commercial use of genetically engineered products. They require only that scientists and producers undergo a self-administered safety evaluation and "determine the potential effects" before they proceed. The Science and Technology Department of the Chinese Ministry of Agriculture, according to a ministry spokesperson, is in the process of implementing more thorough rules, involving biosafety, to supplement the SSTC regulations. Existing rules only require data from three years of field tests showing the agronomic advantages of the new variety.

Among research of interest to western scientists is work on the coat protein genes of several plant viruses. Chen Zhangliang, director of the National Laboratory of Protein Engineering and Plant Genetic Engineering at Beijing University and his team has 35,000 hectares of transgenic plants, mainly tobacco but also tomato, under cultivation at 11 locations throughout China. His laboratory has also screened more than 1,100 strains of bacteria from throughout China and found several that secrete proteins inhibiting the growth of some plant pathogens such as rice blast, wheat blast and rice bacteria blight. He plans large-scale field tests of both wheat and rice implanted with genes encoding those proteins.

Extensive field testing of transgenic plants is also being conducted by the Beijing Institute of Microbiology under the Chinese Academy of Sciences. Several tens of thousands of hectares of tobacco, potato and oilseed rape, all genetically modified for resistance to viral parasites, are now under cultivation in test fields, according to plant geneticist Tian Bo.

Chinese officials say there have been no adverse effects from the widespread field testing of genetically modified organisms, and knowledgeable western scientists say they have not heard of any problems. Still, there is concern. (Extracted from *Science*, Vol. 266, pp. 966-967, from article by T. Plafker)

Costa Rica

Strategy for species survey proposed

World renowned ecologist Dr. Daniel Janzen has proposed a strategy for an unprecedented species survey in the richly bio-diverse Costa Rica. Janzen described the ambitious All Taxa Biodiversity Inventory (ATBI)—carrying a price tag of US$ 90 million - in a keynote lecture sponsored by the Department of Interior's National Biological Survey. ATBI would train civilians to collect and survey every species from tree to jaguar in a 100,000 hectare tropical wildland that contains roughly 65 per cent of Costa Rica's diversity. The end result of this "exercise

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* T. Plafker, "First biotech safety rules don't deter Chinese efforts", *Science* 266:966-67, 1994.

** A. Krattiger, "The field testing and commercialization of genetically engineered plants: a review of worldwide data (1986 to 1993/94)", Pages 247-66 in *Biosafety for Sustainable Agriculture: Sharing Biotechnology Regulatory Experiences of the Western Hemisphere*, A. Krattiger and A. Rosemarin, eds., ISAA: Ithaca and SEI: Stockholm, 1994.

in conservation for all biodiversity", says Janzen, would be an extensive catalogue of species that could hold enormous potential for agricultural crops, eco-tourism, and biodiversity theories. For additional information, contact: Prof. Daniel H. Janzen, Department of Biology, University of Pennsylvania, Philadelphia, PA 19104, USA. Fax: 1-215-898-8780. E-mail: djanzen@mailupenn.sas.edu. (Source: *Diversity*, Vol. 10, No. 2, 1994)

Cyprus

The Cyprus Agricultural Research Institute (ARI), Nicosia

The Cyprus Agricultural Research Institute is the sole agricultural research institution in Cyprus. It is a department of the Ministry of Agriculture, Natural Resources and the Environment, and its headquarters is at Athalassa, in the outskirts of Nicosia. It was established in 1962, shortly after Cyprus gained its independence, as a cooperative project of the Government of Cyprus and UNDP and FAO acting as the executive agency. By 1967 it was well-established and has since been run by local scientists.

ARI undertakes applied and adaptive research within the wider domains of plant and animal production, organized in six major research sections:

- Field crops
- Horticulture crops
- Plant protection
- Soil and water use
- Animal production
- Agricultural economics.

A central chemistry laboratory provides analytical backup services and also carries out work on pesticide residue analysis The Institute has well equipped and specialized laboratories, cold storage facilities, a genebank, herbarium and a library.

ARI has an experimental farm, near the headquarters, where the breeding of field crops is undertaken, and livestock (cattle, sheep, goats) is kept. Other activities are undertaken at outstations in Akhelia and Zyghi for citrus, vegetables and field crops, and is Saittas for deciduous fruits. Extensive experimentation is also performed in farmers' fields.

In a developing country such as Cyprus, ARI has to deal with the entire plant and livestock domain. To achieve sound and meaningful results, efforts should concentrate on selected target areas, according to needs and priorities. As priorities change with time, the same researchers are required to cope with the situation and deal with different aspects or different crops. This imposes additional strain on the researchers, but it also renders research more interesting.

Within the above framework, ARI started work with the most important crops, i.e. citrus, potatoes, cereals and even carobs. Work in animal production has been, and still is, confined to ruminants.

ARI has been cooperating with United Nations and CGIAR organizations, particularly with FAO, IAEA and ICARDA.

The results of ARI work are published in international journals, conference proceedings and in its own publications series. Copies of all papers are available free-of-charge, from: Agricultural Research Institute, Ministry of Agriculture, Natural Resources and the Environment, P.O. Box 2016, Nicosia, Cyprus. Tel.: 3572305101, Telex: 4660 MINAGRI CY, Cables: ARI, Fax: 3572316770.

Summary of ongoing research at ARI:

Field crops: Breeding of barley, durum wheat, food legumes and forage and pasture crops using local and introduced germplasm. Also, materials of other field crops are introduced and evaluated. Work is also carried out on cereal technology, cultural practices and crop rotations in drylands.

Horticulture: The bulk of the work concerns testing of new varieties and rootstocks for citrus, deciduous fruit trees, tropical trees, and varieties of potatoes and other vegetables grown in the open or in greenhouses. A collection of local clones of olive is under evaluation. Propagation through tissue culture of a number of crops is pursued.

Plant protection: Biological control of citrus pests continues. The biology and control of a number of recently introduced insect pests is studied, particularly of *Liriomyza huidobrensis* which devastated 1994's potato crop. A project on tristeza virus and grapevine viruses is under way. ELISA technique and biological indexing are used. Work continues on citrus, potato and grape nematodes, and on chemical weed control in cereals, citrus, tobacco and grapevines.

Soil and water use: Activities focus on nitrogen and phosphorus fertilization of barley and grapevine, as the two major rainfed crops of Cyprus, and fertigation of citrus and potato. In all irrigation work, evaporation from the class A pan is correlated with water requirements of crops. Water is solely applied with permanent irrigation systems (drip, mini-sprinkler, sprinkler). A programme on the use of treated sewage effluent for irrigation is nearing completion.

Animal production: Emphasis is given to the use of locally produced feedingstuffs and agro-industrial by-products in ruminant rations, management breeding and reproductive physiology of sheep and goats.

Agricultural economics: Studies concentrate on collection of input-output and time series data for the main crop and livestock enterprises. (Source: *AARINENA Newsletter*, 1994)

European Union

Europe opts for five-year BST ban

The European Union's agriculture ministers have decided to extend their ban on bovine somatotropin (BST), the controversial hormone that boosts milk yield, until the end of 1999, although animal rights campaigners had pushed for an indefinite ban.

The EU imposed a three-year moratorium on BST in 1990, then a further 12-month ban in 1994. With the expiry date rapidly approaching, farm ministers struggled to reach a compromise between proposals from the European Parliament and Commission for a six-year extension, and their own preferred two-year option.

The final decision was to extend the ban for five years, although states may use limited trials to establish more safety data. The Commission will report on these trials to the Farm Council by July 1998. (Extracted from *Chemistry & Industry*, 2 January 1995)

EMEA/biotechnology firms clash on fees

Biotechnology companies could face authorization delays following a conflict over funding of the new European Agency for the Assessment of Medicinal Products (EMEA).

The London-based agency, which was supposed to come into operation on 1 January, cannot accept applications for product evaluation from pharmaceutical companies without the appropriate fee. The European Commission and the European Parliament have both failed to reach agreement on exactly how these should be levied.

An EMEA spokeswoman said that most companies can still access national authorities for their evaluation—the only problem arises for biotechnology companies, who by law are required to submit their applications only to EMEA.

No applications had been submitted since 1 January, when the biotechnology law came into force. (Extracted from *European Chemical News*, 16-22 January 1995)

France

Biotechnology programme fulfils promise

BioAvenir, France's five-year collaborative biotechnology programme, is "fulfilling its promise and initial ambitions", according to a midway milestone assessment by leading company Rhône-Poulenc, who indicated that a number of research contracts are in the process of being signed between itself and other undisclosed industrialists. Most of these relate to methodology, including projects in metabolic and genomic targeting, structural biology, transgenics, bioavailability, ion channels and genome organization.

To date, five joint laboratories have been set up or bolstered, associating Rhône-Poulenc with its public body partners, CNRS, INSERM, INRA and CEA. The initial aim of involving 500 research personnel within BioAvenir has been exceeded.

Amon the most notable results, Rhône-Poulenc cites examples in the medical field where researchers have detected that a protein known as Grb2, which controls the activity of the RAS oncogene, also exists in Grb3-3 form. The latter appears to trigger programmed cell death. Researchers suggest it is possible that an imbalance between the two forms of the protein is the cause of a variety of pathologies other than cancer.

In a second example, transgenic mice, engineered to over-express the apolipoproteins involved in reverse cholesterol transport, have been shown to be protected against atherosclerosis. The programme has also produced the first transgenic rabbit, opening up new avenues of research.

In metabolic targeting, genes encoding five forms of cytochrome P450, a family of human liver enzymes, have been transferred into yeast. This enables the enzymes to be produced in sufficient quantities to allow the *in vitro* study of the metabolism of new drug candidates.

In the plant field, new biochemical targets have been identified, such as the biosynthetic pathways of amino acids or lipids essential to the survival of targeted plant or parasite, providing specific targets for crop protection products. (Source: *European Chemical News*, 5-11 December 1994)

Germany

Biotechnology safety code relaxed

The German government has amended its biotechnology safety code to provide flexibility in dealing with technological developments in the field. A hazard classification listing of organisms will no longer be a part of the code but will be published separately by the health ministry—allowing the list to be changed and updated quickly. Disposal of organisms will now also be subject to a two-tiered hazard classification system, allowing harmless genetically altered material to be disposed of under looser safety strictures. Previously, all organisms were classed as hazardous and were bound by disposal rules. (Source: *Chemical Week*, 25 January 1995)

Japan

Japanese Guidelines for Gene Therapy Clinical Research

The following provides excerpts from the Guidelines for Gene Therapy Clinical Research published in February 1994 by the Ministry of Health and Welfare. At the same time, the Ministry of Education published the Guidelines for Gene Therapy Clinical Research at Universities. The contents of "Guidelines for Gene Therapy Clinical Research at Universities" are essentially the same as "Guidelines for Gene Therapy Clinical Research" prepared by the Ministry of Health and Welfare in order to retain consistency across all relevant agencies.

The Ministry of Education examines gene therapy clinical research proposals submitted by the heads of university medical institutions on the basis of scientific value and need.

1. Purpose

The purpose of these guidelines is to specify the matters to be followed, to ensure scientific validity and ethics, and promote the proper conduct of gene therapy clinical research.

2. Definition of gene therapy

(a) Introducing genes or gene-transferred cells into the human body for the purpose of treating diseases.

(b) Introducing genes or gene-transferred cells as a marker into the human body for the purpose of developing treatment methods of diseases.

3. Target diseases

Diseases targeted by gene therapy clinical research should be limited to those which meet all of the following requirements:

(a) They are fatal hereditary diseases or life threatening diseases such as cancer and AIDS;

(b) The effectiveness of treatment is sufficiently predicted to be better than currently available alternative methods; and

(c) The benefits which subjects of gene therapy clinical research receive from treatment are deemed to be greater than any adverse effects on them.

4. Assuring effectiveness and safety

Gene therapy clinical research should be limited to those types of research whose effectiveness and safety can be predicted based on sufficient scientific knowledge.

5. Prohibition of genetic modification of germ cells

Gene therapy clinical research for the purpose of genetically altering human germ cells and gene therapy clinical research in which there is a possibility of genetic alteration of human germ cells, is prohibited.

6. Protection of subjects' human rights

Informed consent should be ensured in conducting gene therapy clinical research. Subjects of gene therapy clinical research should be selected carefully with consideration of health status, age, psychological ability to give consent and so on in order to protect human rights.

7. System of research and review

(a) The Director has general control over gene therapy clinical research, prepares research protocols, and gives necessary directions to researchers.

(b) The Review Committee set up in the facility which conducts gene therapy clinical research examines the planned gene therapy clinical research.

(c) The Institution Head, in response to requests from the Director, seeks the opinions of the Review Committee and the Minister of Health and Welfare concerning the planned gene therapy clinical research, gives instructions to the Director about points to consider, and approves the research plan.

8. Opinion of the Minister of Health and Welfare

The Minister of Health and Welfare, in response to requests from the Institution Head, asks for advice from experts, provides an opinion, and conducts investigations concerning the planned gene therapy clinical research.

9. Miscellaneous

The guidelines also provide for record keeping, confidentiality protection, information disclosure, and education and promotion.

(Taken from *Guidelines for Gene Therapy Clinical Research* published on 8 February 1994 by the Ministry of Health and Welfare, with acknowledgement to *Japan Bio-industry Letters* by JBA) (Source: *Australasian Biotechnology*, Vol. 4, No. 5, October 1994)

MITI looks to bioremediation

Japan's Ministry of International Trade and Industry expects to begin a five-year programme in 1995 to commercially establish bioremediation techniques for cleaning up organic chlorine compounds such as trichloroethylene. The project will include research to find micro-organisms capable of breaking down chlorinated compounds in soils. The researchers also plan to develop a method for evaluating the activities of the micro-organisms and proper conditions for their activation. The goal is feasible bioremediation technology by 1999. (Source: *Chemical Week*, 16 November 1994)

Republic of Korea

Biotechnology industry to be promoted

The government has produced a promotion package for the biotechnology industry which is aimed at laying the ground for the fledgling domestic biotechnology industry.

According to officials at the Ministry of Trade, Industry and Energy (MOTIE), the growth potential of the industry is immense.

According to a MOTIE analysis, the world biotechnology industry is expected to grow 22.1 per cent a year between 1994 and 2005 (the highest growth rate amid the existing leading-edge industries. The domestic market for the industry is expected to grow at an even higher rate of 30 per cent a year, reaching around $4 billion in 2000, about 20 times more than the $210 million in 1993.

Despite this high growth potential of the industry, domestic investments into research and development and commercialization have been far from satisfactory. This underinvestment, according to MOTIE officials, is a result of the high risks accompanying commitment to leading-edge industrial sectors, coupled with the lack of infrastructure.

In 1992, Korea's R&D investment in this field was about $35.8 million, less than 1 per cent of the $3.76 billion of the USA.

As a result, the domestic industry has failed to secure international competitiveness. To cope with this situation, the ministry intends to adopt a system to promote the development of new materials. In the first place, it plans to encourage the development of application technology that can turn basic technologies into viable commercial projects. The ministry will focus on the development of those technologies that separate and purify cells, proteins and enzymes; those that stabilize them against heat or other external environments; the biomaterial modification technologies; those related to the measurement of the vitality of micro-organisms and their evaluation; and massive cultivation of animal cells.

A total of 600 billion won (about $750 million) will be spent on R&D of these technologies from 1995, according to the ministry's plan.

In addition to the systematic support of private R&D efforts, the ministry will create a new department in charge of the industry.

At the same time, it will set up a safety and effectiveness evaluation centre near Seoul between 1996 and 2000. According to ministry officials, because of the lack of such a testing institute, domestic firms which develop new materials or new products now have to rely on foreign testing centres, wasting time and money.

To raise the international recognition of the safety of new domestically developed materials, they said, it is essential to improve safety testing standards. At the testing centre, the ministry plans to build a pilot plant which can be used to develop the optimum processes for the commercialization of newly developed materials or products.

The plant will be equipped with a fermentation facility which can ferment materials using plant, animal and micro-organism cells; a purification facility; and others needed to develop the biological processes.

The cost for building the testing centre and the pilot plant will amount to 280 billion won (about $350 million), according to the ministry's estimate.

The ministry will also provide R&D facilities to universities to build a network of technology development linking the industry and academia.

These universities will address common technological problems facing private firms and offer programmes for the retraining of their engineers.

These and other support measures are to be carried out in the hopes of creating an industrial base for the biotechnology industry by the year 2000. By then, the ministry expects domestic firms to be able to mass produce new products. (Source: *Newsreview*, 10 December 1994)

Nigeria

Workshop on Biotechnology and Food

Organized by the Foundation for African Development through International Biotechnology (FADIB) at the Department of Medical Biochemistry, University of Nigeria, Enugu Campus, Nigeria, on 11-24 April 1994, the workshop aimed to follow the modern aspects of food from the field to the table. The organizers were fortunate to have gathered a crop of teachers who, according to the assess-

ment of the students, achieved the aim of the workshop in the available time.

The leader of the teaching group, Dr. Prabhakara Choudary, Director of the Antibody Engineering Laboratory at the University of California, Davis, USA, handled the introductory aspect of the course which dealt with basic molecular biology and genetic engineering and included protein synthesis, basic tools and techniques in gene cloning and expression, cloning and expression strategies, PCR, mutations, nucleotide sequencing and ethics and safety. Plant biotechnology was taught by Drs. Herta Steinkellner and Irina Korschineck, both of the University of Agriculture, Vienna, Austria; they covered, *inter alia*, genetically engineered plant-resistance breeding, and genetically engineered antibodies in *E. coli* and plants. Prof. George Onuora of the Faculty of Veterinary Medicine, University of Nigeria, looked at modern methods of farm animal improvement, including such areas as embryo transfer, chimeric animals, shortening of oestrus period, etc. Prof. S. N. C. Okonkwo of Nnamdi Azikiwe University, Awka (UNIZIK) examined the role of plant tissue cultures in improved agricultural production. Biotechnological means of achieving crop protection through the use of entomopathogenic micro-organisms was discussed by Dr. Tony Ejiofor, also of UNIZIK, while Dr. Daniel Olukoya of the National Institute for Medical Research, Lagos, Nigeria discussed the place of lactic acid bacteria in the processing of African foods. Lectures were held in the morning hours while laboratory work was in the afternoon. In spite of the busy schedule, the participants were able to visit sites of erosion and to see Enugu at night-time.

Nigerians naturally formed the bulk of the students with a scattering of students from Benin, Ethiopia, Ghana, Kenya and Sudan.

FADIB is an independent NGO formed and registered in Nigeria in 1992 with the aim of training young Africans in biotechnology, especially genetic engineering, because of the important role it can play in the sustainable development of African countries through improvements in agriculture, health, industry and the environment. FADIB also carries out research in biotechnology. Although independent, it has strong links with neighbouring universities. It obtains its funds from the international community and for the time being, organizes short-term courses lasting about a fortnight twice a year. Its long-term aim is to have courses lasting for at least six weeks. It hopefully complements establishments such as the International Centre for Genetic Engineering and Biotechnology (ICGEB), the Rockefeller Institute, etc., because many of FADIB's trainees are new to genetic engineering and hopefully would be stimulated to work in these establishments after the courses. The workshop on Biotechnology and Food is the first FADIB has organized by itself; it jointly with the African Regional Network for Microbiology, ran one on Fermentation Technology in 1992.

IITA receives award

The International Institute for Tropical Agriculture (IITA) in Nigeria has received the Consultative Group on International Agricultural Research (CGIAR) 1994 King Baudouin Award. IITA was recognized for its pioneering research on breeding hybrid plantains resistant to black sigatoka, a devastating disease of plantain and bananas in Africa. The CGIAR began giving biennial awards, named after the late Belgian monarch, for outstanding achievements by one or more of its centres after it was the recipient of the King Baudouin International Development Prize in 1980. For additional information, contact: Ms. Stewart M. Lawani, International Institute of Tropical Agriculture, PMB 5320, Ibadan, Nigeria. Tel.: 234-22-400300, Fax: 874-1772276 via INMARSAT Satellite, E-mail: IITA@cgnet.com. (Source: *Diversity*, Vol. 10, No. 14, 1994)

Russian Federation

Yablokov looks set to win Russian crack-down on genetic engineering

Environmental scientist Alexei Yablokov, who chairs a Russian National Security Council commission on ecological security, called on the government late last year to take steps to regulate genetic engineering experiments. Pointing to the anthrax outbreak in Sverdlovsk in 1979 that killed 66 people, he warned that genetic engineering could pose a greater threat to Russians than radioactivity.

Now the Russian parliament is expected to debate a draft law that would mandate strict regulation of all genetic experiments, from basic research involving recombinant DNA to industrial projects designed to engineer transgenic plants and environmental clean-up microbes. (Source: *Biotechnology Bulletin*, January 1995)

Singapore

Singapore seeks biotechnology cooperation

Under a national biotechnology master plan established in 1990, Singapore is aiming to develop a viable biotechnology industry to contribute significantly to its economy by the year 2000. The country offers a high level of technical competence, well equipped research institutes and organized infrastructure. In addition, it provides enthusiastic government assistance and access to South-East Asia's money markets.

However, biotechnology R&D in Singapore is very much in its infancy and local manpower is limited. Most R&D researchers employed in Singapore's institutes are expatriate and the reliance on imported scientists is expected to continue for some time as Singaporeans find more prosperous employment in commerce.

There are relatively few biotechnology companies currently operating in Singapore. Most activity is in the academic institutions, where the bias is towards fundamental rather than applied R&D.

With high commitment from the Singapore government, incentive packages are generous. Singapore BioInnovations (SBI), the biotechnology arm of the Singapore Economic Development Board, is dedicated to making biotechnology related investments. Such investments can be in both indigenous and overseas companies, though the strategy of promoting a viable domestic industry is always paramount.

SBI also acts to promote strategic alliances and joint ventures and to develop and spin-off biotechnology companies to commercialization. A typical investment ranges from $200,000 to $2 million.

In terms of sector R&D, the country is involved to varying degrees with pharmaceuticals, diagnostics, agribiotechnology and food biotechnology.

Pharmaceutical development is limited, and almost exclusively associated with vaccine development, however,

Singapore could be a good centre for the administration and management of clinical trials in the region.

Research is almost entirely located in the academic institutions—the National University of Singapore, the WHO Immunology Centre and the Institute of Molecular and Cell Biology (IMCB). The IMCB collaborates with local and overseas companies, including Glaxo Research, Pfizer, Amylin and Genzyme, and is seeking other link-ups, in the form of joint ventures, licensing of technology, commercial spin-offs or contract research.

Scientific achievements include genes (p21 targets) that determine nerve cell shape, receptor-like tyrosine phosphatase, which activates cancer genes, the development of novel mosquito toxins, phylogenetics of the human papilloma virus and transgenic rat technology.

Preliminary plans are already in hand for the creation of two new institutes covering cardiovascular and cancer R&D which will be able to fully support applied pharmaceutical research.

Singapore is further advanced in developing its diagnostics sector, not surprisingly, given diagnostics' relatively shorter research-to-market times than pharmaceuticals, its requirement for fewer manufacturing skills and facilities, and less regulatory interference. The companies involved are small by international standards, and most commonly offshoots of overseas corporations. The largest is Genelabs Diagnostics, the headquarters for Genelabs Technologies' diagnostics business in the region.

With little agriculture to speak of in Singapore, agribiotechnology does not feature very strongly in the national biotechnology plan. The main commercial focus in the orchids industry, worth £90 million ($140 million). Work is also ongoing on nematode and insect resistance on micropropagated crops, including potato, banana, ginger and various vegetables. Singapore companies are also actively looking to in-license technologies in these areas, in particular genes for insect or nematode resistance.

Despite the country's long history of working with fermentation-based products, the food sector is weakest in terms of biotechnology development. (Extracted from *European Chemical News*, 2-15 January 1995)

Building a biotechnology industry step by step

In the mid-1980s, Singapore's government targeted biotechnology as a key industry in developing the country's economy, according to a recent article in *Australasian Biotechnology*.

The National Biotechnology Programme (NBP) of the country's Economic Development Board (EDB) has a mission to develop Singapore into a business centre in the Asia Pacific region with a viable biotechnology industry.

The NBP, established in 1988, is guided by the National Biotechnology Committee, a body which includes members from local governments as well as an international panel of scientists. The committee provided the basis for the NBP's master plan of five main strategies. These include promotion of biotechnology research, building the supporting infrastructure and developing the manpower needed by all levels of the biotechnology industry.

On the economic side, the strategy is to put together policies that encourage biotechnology development and send missions overseas to entice biotechnology firms to set themselves up in Singapore. Public education is also part of the mission, with a particular focus on venture capitalists and entrepreneurs.

The next step is investment. The Singapore Bio-Innovations arm of the EDB has a mandate to commercialize local inventions and make investments in viable biotechnology ventures at home and abroad. With the now established local base and links to other Asia Pacific nations, they are now able to actively foster strategic alliances, joint ventures and business and technology collaborations between foreign and local entities. (Source: *The AGBiotech Bulletin*, Vol. 2, Issue 5, September 1994)

Sweden

Sweden approves r-hFSH

The Swedish Health Authorities (Medical Product Agency) approved the marketing of Gonal-F®, AresSerono Group's (Geneva, Switzerland and Norwell, MA) recombinant human follicle stimulating hormone preparation. Marketing approval was also granted in Finland in August.

Gonal-F (r-hFSH) is the first recombinant drug used in the treatment of infertility to receive marketing approval in the world, according to the company. The product is indicated in the treatment of female infertility to stimulate the development of ovarian follicles in women suffering from ovulatory disorders as well as in women undergoing *in vitro* fertilization and embryo transfer (IVF-ET). Company officials say Gonal-F should be introduced in Sweden and Finland in early 1995. (Source: *Genetic Engineering News*, 1 January 1995)

United Kingdom

Genetically modified oilseed rape: the UK position

With the Belgian company Plant Genetic Systems (PGS) planning to first market its genetically modified oilseed rape in the UK, the temperature of the environmental debate around deliberate release could well intensify. A useful overview of the position and issues can be found in *ENDS Report 239*, pp. 15-18. Details from: Environmental Data Services Ltd., The Finsbury Business Centre, 40 Bowling Green Lane, London EC1R 0NE or on 0171 278 4745, Fax: 0171 415 0106.

Funding for biotechnology work

Phase II of the LINK Biochemical Engineering Programme, jointly funded by the UK Department of Trade and Industry (£1.5 million) and the Biotechnology and Biological Sciences Research Council (£2.5 million) has been approved.

The programme will run for the next three years and fund projects in the areas of bioreactor technology, processing and bioseparations, process control and containment and sterile engineering.

Details: Biotechnology Unit, DTI, Queens Road, Teddington, Middlesex, TW11 0LY; Tel.: 0181 9437347. (Source: *Manufacturing Chemist*, January 1995)

UK Advisory Committee calls for removal of antibiotic resistance markers from food

In a new report, the United Kingdom Advisory Committee on Novel Foods and Processes has recommended to health and agriculture ministers that those genetically

engineered micro-organisms intended to be consumed live in food should be free of antibiotic resistance genes.* The recommendation would apply, for example, to yoghurt and baker's yeast. The Committee did not recommend a similar prohibition on antibiotic resistance genes in plant and animal foods, but did urge researchers to find ways to remove antibiotic resistance markers from all genetically engineered food organisms or develop alternative markers. (Extracted from *The Gene Exchange*, December 1994)

United States of America

USDA research committee adopts voluntary fish standards

At its November meeting, the USDA Agricultural Biotechnology Research Advisory Committee (ABRAC) unanimously approved voluntary performance standards for research with genetically modified fish and shellfish. Developed by an ABRAC subcommittee chaired by Dr. Anne Kapuscinski of the University of Minnesota, the standards provide a framework within which fisheries scientists can assess the environmental risks of research that might result in the release of genetically modified organisms. The standards are purely voluntary; they contain no penalties for researchers who choose not to follow them. The ABRAC-approved performance standards will be sent to the Under-Secretary of Agriculture for Research, Education and Economics for a final decision on adoption. (Source: *The Gene Exchange*, December 1994)

Embryo research

During the first four years of clinical tests involving human gene therapy, the technology has steadily gained acceptance. Yet more recent efforts at the National Institutes of Health (NIH, Bethesda, MD) to seek acceptance for proposals involving preclinical research on human embryos seem far less assured of success, as federal support of such research has been banned for a full 15 years. Although an ad hoc Human Embryo Research Panel (HERP) recently recommended an advisory process for embryo research similar to the one being followed for gene therapy—which is overseen by the National Institutes of Health Recombinant DNA Advisory Committee (NIHRAC)—the question remains whether HERP's recommendations for open review and stringent guidelines will adequately address critics' concerns about embryo ethics.

At its recent meeting, HERP unveiled a report that it had completed by convening a half dozen times, conferring often between meetings. Three key principles undergirding a recent HERP report are that embryo research could bring significant benefits; that preimplantation embryos "warrant serious moral consideration, though not the same consideration as infants and children"; and that federal funding "will bring about consistent, public review" of embryo research.

Indeed, HERP recommends a review process for embryo research that parallels the NIHRAC's oversight of gene therapy.

Currently, limited research on embryos is being done in the private sector, with most of it under the auspices of *in vitro* fertilization clinics. At least in some cases, however, such clinics are becoming increasingly involved in diagnostic technologies and other biotechnologies, including bone-marrow-transplant procedures. Yet the Biotechnology Industry Organization (Washington, DC), for its part, claims that embryo research—perhaps because it is so controversial—is not really a discipline of biotechnology.

According to the HERP report, other areas, besides human fertilization, in which embryo research could bring benefits include:

- Early human development and the origin of certain birth defects;
- The preimplantation diagnosis of genetic abnormalities that cause inherited diseases;
- How oocytes mature and how eggs are affected by environmental agents;
- The development of cell lines for generating differentiated cells for transplantation and tissue repair.

(Extracted from *Bio/Technology*, Vol. 12, November 1994)

EPA proposes broader policy on plant pesticides

Responding to concerns over plants genetically engineered to resist pests, in November 1994 the Environmental Protection Agency (EPA) proposed an expansion of its current pesticide policy to include genetic material and pesticidal substances engineered into plants. Currently, the agency has no programme in place to regulate these substances. While the proposal was generally well-received, scientists are concerned that it exempts virus-resistant crops and ignores herbicide-tolerant crops. Scientists have urged EPA to develop a policy to regulate viral and herbicide-resistant genes introduced into plants, because these genes could flow from herbicide-resistant crops to wild relatives, creating problem weeds. (Source: *Biotech Bulletin*, 14 December 1994)

Alliance provides new libraries of chemicals

The US contract research organization Panlabs and software house Tripos have announced a two-year strategic collaboration through which they aim to provide pharmaceutical and biotechnology researchers with new libraries of chemicals and improved methods of searching out new product leads. The companies aim to optimize the chemical libraries used by researchers in drug discovery, offer joint services to clients to augment their internal research efforts and produce new methodologies to maximize the effectiveness of the screening process in the search for new products. (Source: *European Chemical News*, 6-12 February 1995)

National biodiversity information centre

The Smithsonian Institution, the National Biological Survey, and the Environmental Protection Agency are organizing a proposed US National Biodiversity Information Center. Ecologists, systematicists and users from states, agencies, NGOs, businesses and academia meeting in March 1994 agreed that an organization was needed to coordinate access and information between different groups. The centre's function will include connecting users to data sources, coordinating and promoting data and metadata standards, facilitating electronic data check-lists and

* Advisory Committee on Novel Foods and Processes, *Report on the Use of Antibiotic Resistance Markers in Genetically Modified Food Organisms*, Ministry of Agriculture, Fisheries and Food, London, UK, July 1994.

catalysing information federations. For more information contact: Bruce Umminger, Senior Adviser on Biodiversity, or Steve Young, Adviser on Biodiversity Information, National Museum of Natural History, 10th and Constitution Avenues, NW, Room W316, MRC 180, Washington, DC 20560, USA; Tel.: 1-202-786-2944. (Source: *Diversity*, Vol. 10, No. 2, 1994)

Viet Nam

Plant genetic resources system to be strengthened

Viet Nam's national plant genetic resources system will be strengthened by funding from the International Development Research Centre (IDRC) of Canada. A team of Vietnamese scientists, an internationally recruited expert, and an NGO-based ethnobotanist will assess forest, crop and medicinal plant genetic resources and develop a draft national plan for undertaking and coordinating this work. The final plan will be developed following consultation with a number of countries, including Japan and France, and international organizations such as the Food and Agriculture Organization of the United Nations. For additional information, contact Ruth Raymond, International Plant Genetic Resources Institute, Via delle Sette Chiese 142, 00145 Rome, Italy; Tel.: 39-6-518921, Fax: 39-6-5750309; E-mail: IPGRI@CGNET.COM. (Source: *Diversity*, Vol. 10, No. 4, 1994)

D. RESEARCH

Research on human genes

Cancer vaccines

A new round of prototype cancer vaccines will enter preliminary clinical trials in the next two to three years. Some will take a broad-based approach, others will be directed at specific parts of the system. The most popular targets for this directed approach are helper T-cells. When they find "antigens" they consider untoward—that is to say, fragments of proteins not normally found in the body—the helper T-cells call in teams of killer cells, draw their attention to the interloper, and encourage them to deal with it appropriately.

Researchers want to involve the T-cells because of this powerful cellular response. For years they were stuck because T-cells do not necessarily see the proteins on cancer cells as untoward.

The answer is that T-cells can "see" tumour antigens only when they are presented to them by another group of surface molecules, HLA molecules. These HLA molecules differ from person to person, presenting different antigens in different ways. This seems to be why melanoma cells from one person do not provoke an antigen-specific immune response when used as a vaccine in another.

Dr. Thierry Boon of the Ludwig Institute for Cancer Research in Brussels and his colleagues are busy seeking forms of antigens that can be recognized no matter which HLA molecules present them. For the melanoma antigens that he has identified, Dr. Boon says he is already able to include more than half of all candidate patients in an upcoming European vaccine trial, on the basis that the message sent by the vaccine will be similar enough to what their bodies would send for the vaccine to get a response.

A second problem the directed approach faces is "escape": the immune system may aim its weapons only at tumours that carry the exact antigen presented in the vaccine. To combat this, Dr. Boon and many others elsewhere are trying to design vaccines that carry several antigens in order to give them a bigger chance of wiping out all the tumour cells.

Many of those using the directed approach also plan to try to improve the T-cell response using immune-signalling molecules known as cytokines. Whereas many of these molecules have been found to affect the immune response in general, just a few seem to have a potent effect on tumours. Human trials are under way in America to test some of the most promising of these, such as interleukin-12.

The next large vaccine trial, which will involve 450 patients is scheduled to begin in March 1995. The vaccine designers, led by Philip Livingstone of Memorial Sloan-Kettering Cancer Center in New York, have linked sugars, known as glangliosides, found on the surface of many melanoma cells, to a carrier derived from a mollusc known as the keyhole limpet. They will deliver the vaccine with a powerful adjuvant, a general immune stimulant, known as QS-21, made from the bark of a South American tree. The idea is to wake up any or all parts of the immune system. It certainly seems to work on antibody-producing cells. In a preliminary trial, this vaccine elicited some kind of antibody response in every melanoma patient.

Although this is the least high-tech method of the lot, it is the first to be ready for a large trial. (Source: *The Economist*, 17 December 1994)

"Immortalizing enzyme": Ideal cancer drug target

Canadian biomedical researchers have confirmed the presence of an "immortalizing enzyme" in tumour cells, necessary for malignant runaway cell division. They believe it could offer an ideal target for new specific anti-cancer substances. Most conventional chemotherapy has been cytotoxic, that is, it destroys rapidly dividing cells, often indiscriminately killing healthy cells as well, and causing side effects.

Substances that inhibit telomerase activity could be an effective antitumour strategy by causing malignant cells to revert to a normal life cycle characterized by a limited number of divisions.

Dr. Calvin B. Harley's team from McMaster University, Hamilton (Ontario, Canada), reported the first direct evidence of telomerase activity in human tumoural tissue. They compared enzyme activity in tumour cells and non-malignant cells from late-stage ovarian cancer patients and detected telomerase activity only in tumour cells.

Telomeres that are synthesized by telomerase, appear to stabilize the ends of chromosomes in human cells. Each telomere tip contains identical repetitive gene sequences—extra DNA—that protect the rest of the gene structure. Telomeres normally shorten with each cell division. Telomere length may act as a mitotic "clock": as they shrink, these might offer the cell a measure of the number of divisions effectuated, and how many remain until the cell's programmed life-span will be terminated, normally 50 to 100 divisions, scientists suggest. Telomerase may play an important role in cell proliferation and immortalization. In cancer cells, telomerase becomes reactivated and apparently stabilizes telomere length; this prevents a critical destabilization of chromosomes and cell proliferation continues even when telomeres are short.

The researchers conclude that "progression of malignancy is ultimately dependent upon activation of telomerase".

This work is a stunning example of how basic research can be made relevant to disease in a very short period of time. *Health Horizons* has been told that researchers working with industry hope to have telomerase inhibitor in laboratory tests next year and, if promising, in clinical trials in several years. Such an approach would have limited side effects since telomerase is absent or minimally expressed in normal tissues and so healthy cells would be unaffected. (Source: *Health Horizons*, No. 23, Autumn 1994)

Made to measure proteins open doors to leukaemia treatment

Scientists at the Medical Research Council's Laboratory of Molecular Biology in Cambridge have developed a new technique which may provide a route to tackling some forms of human leukaemia and other cancers. A paper published in *Nature*, vol. 372, shows how a tailor-made protein was produced which stops uncontrolled cell growth

when introduced into cultured mouse cells made cancerous by the insertion of a human leukaemia gene.

The oncogene, is in this case responsible for acute lymphoblastic leukaemia, which, together with a related conditior called chronic myelogenous leukaemia.

The protein has been designed to act selectively on the cancer-causing gene, blocking its expression. The protein is constructed out of a combination of small structural units, called "zinc fingers". Zinc fingers are structures shown to be a key element of a class of proteins responsible for regulating gene expression. Groups of zinc fingers protruding from the surface of protein enable it to bind to very specific sequences of base pairs on the DNA double helix. These fingers have been selected to bind to very specific sites on the DNA of the oncogene, preventing the reading of the message contained in the gene. As a result, cells treated with the protein revert to being under the control of normal growth factors. Details from: Prof. Aaron Klug, MRC Laboratory of Molecular Biology, on 0223 248011. (Source: *Biotechnology Bulletin*, January 1995)

Dermatology off the beach

Skin cancers are now among the most common forms of the disease, and the incidence of malignant melanoma, the most dangerous skin cancer, is rising the fastest. However, recent research on the way in which damaged DNA is repaired may help those who spend a lot of time out of doors.

Of the several ways in which ultraviolet (UV) light can damage DNA, the most common is by causing the formation of thymine dimers. Thymine is one of the four bases that form the links of DNA chains. When two thymine groups are neighbours in DNA, UV radiation can weld them together abnormally into entities called dimers, whose presence makes it impossible for DNA to replicate. The build-up of even a few thymine dimers can kill cells and trigger subsequent cancers. Assemblies of enzymes continually patrol the lengths of genes, seeking out thymine dimers and the like, cutting out the defective bits of DNA and splicing in the correct versions.

Researchers at Boston University's School of Medicine, have shown that the excised dimers in the skin stimulate neighbouring melanocytes, cells that produce the dark pigment melanin. The extra melanin that the melanocytes start to produce finds its way to other skin cells, where it absorbs UV, protecting the cells from further damage, and in the process lending skin that desirable brown colour. The researchers decided to try to produce a tan without exposure to UV and the consequent risk of DNA damage, by finding another way to sound the alarm bell that triggers extra melanin production. Their plan was to introduce man-made thymine dimers to the skin and see if they stimulated melanin production in the same way as the left-overs from DNA repair. It appeared to work in dishes of cultured skin cells, so the next step was to try it on skin still attached to a living animal. A number of guinea pigs were partially shaved in order to expose their skin, which is said to resemble that of humans, and lotions containing thymine dimers were rubbed on. After two weeks or so the animals' skin darkened noticeably where the lotion had been applied, a "tan" that lasted for at least 60 days.

The group has been granted a patent for the use of DNA fragments in tanning creams, and there is already commercial interest. Demand could be considerable. A pre-sun tan would protect people who work outdoors from a risk of skin cancer that may be increasing as the thinning of the ozone layer admits more of the most harmful UV wavelengths. (Source: *The Economist*, 10 December 1994)

Alzheimer's disease

Research into Alzheimer's disease (AD) has received two boosts. One group has developed a technique which appears to delay—and even reverse—the damage the disease causes, while another team has devised a simple diagnostic eye test.

Researchers from the Rush Presbyterian- St. Luke's Medical Center in Chicago, Chicago Medical School and CytoTherapeutics, designed porous capsules containing baby hamster kidney cells which had been engineered to secrete human nerve growth factor (NGF). These were implanted into the brains of 25 to 29-year-old rhesus monkeys (75 to 87 years old in human terms).

The capsules were embedded in the basal forebrain, a region rich in cholinergic nerve cells. These produce acetylcholine, a neurotransmitter whose activity is reduced in AD sufferers. The capsules fed a constant trickle of NGF directly into the brain, by-passing the notoriously impermeable blood-brain barrier. Encapsulating the engineered hamster cells ensured that the monkeys' immune systems could not attack them.

According to the researchers, the monkeys with the NGF-producing implants lost 20 per cent of their existing cholinergic cells during the four-week experiment; 40 per cent less than a control group. The NGF also triggered a "robust sprouting" of new cholinergic fibres in the forebrain.

The technique, which would require only a local anaesthetic, is still a long way from human trials. The team still needs to establish how long the engineered cells can survive, and how long their effect lasts.

Meanwhile, researchers from Boston and Chicago have developed a simple eye test for AD based on the disease's similarities with the chromosomal disorder Down's syndrome. There is currently no foolproof way of diagnosing AD: as many as 25-40 per cent of diagnoses may be inaccurate. A reliable test that could detect the disease in its early stages would allow sufferers the full benefit of treatments to slow the disease's progression.

Down's syndrome sufferers who survive past the age of 30 tend to develop protein plaques and tangles in their brains which are very similar to those in AD patients. The Down's sufferers also become extremely sensitive to compounds which inhibit acetylcholine.

The researchers examined tropicamide, a compound which blocks acetylcholine receptors and is often used, at concentrations of 0.5-1 per cent, to dilute the pupils before eye examinations. For their experiments, the team used a 0.01 per cent solution, which would normally have no effect.

The researchers studied patients with clinically-diagnosed AD and those with a few, but not all, of AD's symptoms, demential sufferers (often confused with AD), and a control group. The test not only successfully differentiated all the AD sufferers from those without the disease, the team notes, but gave a positive result with one subject. The patient exhibited extremely mild symptoms but later developed AD. (Source: *Chemistry & Industry*, 21 November 1994 and *Biotechnology Bulletin*, December 1994)

Meanwhile, research by scientists at the Quadrant Research Foundation could ultimately lead to novel treatments for Alzheimer's disease and many other neurodegenerative disorders with a similar pathology. The finding, made during studies of trehalose-based drying technology, also has implications for the prevention of atherosclerosis, a major complication of diabetes and the principal cause of heart attack and stroke.

The discovery is the result of a fundamental jump in logic, whereby Dr. Camilo Colaco connected the pathology of certain diseases to a basic spontaneous chemical reaction between sugars and proteins, the Maillard reaction—that has been known since 1912. The importance of the Maillard reaction is widely recognized in the food industry in the production of colours and flavours in cooked food, as well as in the spoilage of food in storage. However, the reaction has never before been implicated in the cause of disease, and its role is only now being appreciated as a result of the hypothesis put forward by Quadrant scientists.

In the body, the Maillard reaction leads to the formation of glycated protein, resulting in the formation of "amyloid plaques" which typify a number of diseases, including type II diabetes and Alzheimer's. Strategies are therefore being developed by Quadrant and others to discover inhibitors to the Maillard reaction. Details from: Quadrant Holdings, Maris Lane, Trumpington, Cambridge CB2 2SY or on 01223 845779. Fax: 01223 842614. (Source: *Chemistry & Industry*, 21 November 1994 and *Biotechnology Bulletin*, December 1994)

May not be junk after all

Science magazine recently reported new work on the function of genetic material (F. Flam, "Hints of a language in junk DNA", *Science* 266:1320, 1994). Scientists have long been puzzled by the fact that fully 97 per cent of the DNA in human cells does not code for proteins and appears to consist of meaningless sequences. The possibility that this apparently useless DNA has some as yet unknown function continues to tantalize scientists.

The article reports on a paper suggesting that the non-coding 97 per cent of the DNA, commonly referred to as "junk" DNA, might have a function. The authors of the paper employed linguistic tests to analyse junk DNA and discovered striking similarities to ordinary language. The scientists interpret those similarities as suggestions that there might be messages in the junk sequences, although it is anyone's guess as to how the language might work. (Source: *The Gene Exchange*, December 1994)

Renewed optimism about another interleukin

Scientists are reporting evidence that still another interleukin, IL-12, is the most potent antitumour agent in the immune system's repertoire, at least in the laboratory. It is said to strengthen and stimulate proliferation of natural killer cells and T-cells and their release of gamma interferon. Some scientists hope it might even be able to restore lost immunity in AIDS. Attending a conference on the cytokines, scientists of Hoffman-La Roche, Basel (Switzerland), recalled the enthusiasm that was generated ten years ago for another interleukin, IL-2, that they helped to develop for medicine. It showed limited efficacy in clinical trials but has been authorized for use in renal cell cancer. Maurice K. Gately, who directed that work as well as current work with IL-12, believes that the toxicity is manageable. The biotechnology company Genetics Institute of Cambridge (Massachusetts) also has found it and is preparing to test IL-12 against HIV. Gene Shearer of the National Cancer Institute reported that IL-12 prevented cell deaths or apoptosis in T-cells, which could be important in AIDS. His team also finds that in symptomless HIV-positive people, a particular shift due to less IL-12 predicts AIDS. IL-12 might restore cell-mediated immunity or prevent development of AIDS, scientists hope. Interleukins are crucial for communication among immune cells and act early to govern the system's response to injection or injury. (*Science* 263: 1685-85, 1994)

UC San Francisco researchers have also found that interleukin-12 (IL-12) can boost the immune function of human foetal cells in the test tube, reinforcing the protein's potential value as a treatment for AIDS. The protein was able to stimulate natural killer cells in foetal cells taken from umbilical cord blood. "When we put IL-12 back into the system, the immune system became normal", according to Allan Lau, M.D. "So if AIDS patients are deficient in natural killer cells, we may be able to do the same for them."

Dr. Lau and co-workers also found very low levels of gamma interferon in the foetal cells. Following treatment with IL-12, the researchers observed an increase in gamma interferon levels as well. The scientists also found that foetal cells treated with IL-12 became activated in the presence of HIV-infected cells, similar to the way in which treated adult cells are stimulated to fight off the virus. (Source: *Health Horizons*, No. 23, Autumn 1994 and *Genetic Engineering News*, 15 June 1994)

Breast-cancer gene: no test near

Lest anybody nurse hopes that the wildly publicized discovery of the breast cancer gene will offer up new screening techniques or treatments any time soon, scientists caution that the gene is proving to be as frustrating and recalcitrant as the disease.

In the journal *Nature Genetics*, three teams of scientists reported on their studies of the gene, called BRCA1, which in its mutant form is thought to be responsible for about half the instances of hereditary breast cancer, or up to 5 per cent of all breast cancer cases.

The new reports only confirm and extend the initial observations that this is a long, unwieldy gene prone to many different mutations—factors greatly complicating the task of designing a test to reveal a woman's inherited risk.

In the three reports, researchers confirmed the identity of the gene that Dr. Mark Skolnick, at the University of Utah, and his colleagues had said was a "strong candidate" for BRCA1, and they added 31 mutations to the original five.

But the true number will prove to be much higher, Dr. David Goldgar, also at Utah, is completing a report in which he summarizes all mutations detected to date, and the list has reached about 80. As researchers continue their analysis they expect the number to climb into the hundreds.

Equally confounding, the scientists found that they could detect mutations in only about half the women whom they expected, from previous chromosomal or medical studies, to carry a defect in the gene.

They attribute much of the problem to the insensitivity of the techniques they used to screen for mutations, as well as to the possibility that the defects in gene performance lie not in the chemical structure of the gene, but in genetic switches that are in regions of the chromosome

outside the scope of their search. In addition, some of the women may turn out to have mutations in genes entirely unrelated to BRCA1. (Extracted from *International Herald Tribune*, 1 December 1994)

New type of measuring technique using firefly luminescence

Pola R&D Laboratories and Prof. Shibahara have developed a new luciferase assay technology that enables the genetic expression of pigment cells, transfected with the fusion gene containing the firefly luciferase gene, to be captured on photographic images, as a method of elucidating the functions of the genes inside the pigment cell that largely influences the skin colour.

Firefly luminescence is a means of communications for promoting the smooth mating of male and female fireflies. The luminescence is generated when a substance called luciferin undergoes an oxidation reaction with a luminescent enzyme known as luciferase, by an enzymic reaction. The light discharged by this reaction has a yellowish green colour and can be quantified by chemical luminescence measurement.

Up till now, the general method to investigate the functions of target genes had been to measure the light quantity generated in a test tube, but with this method the measurements have to be made with disrupted cells, requiring the use of numerous cells. In addition, ascertaining the exact reaction spots was quite difficult.

The colour of the human skin is generally determined by melanin pigment produced in melanocytes, and the pigment transfected into keratinocytes in epidermis is basic to the skin colour. The new measuring technology is a method of introducing a "fusion gene" into the pigment cells that contains the promoter region of the tyrosinase gene concerning the melanin pigment production and the protein coding region of the luciferase gene. The luciferase gene is used as the marker and the tyrosinase gene expression is assayed.

In the new technology, the melanocytes were transfected with the fusion gene containing the tyrosinase gene upstream from the firefly luciferase gene but the research team observed that the probability of the pigment cell incorporating the fusion gene is at best about 20 per cent, so a more effective transfection technology has to be developed.

The expression of the fusion gene transfected into the pigment cell generates luciferase protein. Adding luciferin, magnesium ion, and adenosine triphosphate (ATP) to the cell in this state activates the luciferase and the manifestation area becomes luminous. This feeble light quantity is captured by the photocounting camera method. Applying this technology enables the fusion of the genes of each cell to be assessed directly as a light quantity and to enable the states of cells expressing the genes to be captured directly as images. Since it is also possible to identify the specific areas where reactions are occurring, it will be possible to investigate the manner of protein transportation inside these cells.

Further details are available from Pola R&D Laboratories, Dermal Research Department, 560, Kashio-cho, Totsuka-ku, Yokohama, Kanagawa Pref. 241, Tel.: +81-3-45-826-7231, Fax: +81-3-45-826-7249. (Source: *JETRO*, November 1994)

Cancer gene linked to ageing

Researchers at the University of Southern California Medical School (Los Angeles) have provided evidence that cancer is a gradual accumulation of genetic errors leading to uncontrolled tumour growth. Gino Cortopassi and colleagues counted the mutations in an oncogene called BCL-2, which is known to be involved in non-Hodgkin's lymphoma, and found that there was a dramatic increase in cancer risk that correlated directly with age. They found that mutations occur frequently in the BCL-2 gene, and suggested that they may be a "common prerequisite for lymphoma".

The scientists studied gene damage in which chromosomes 14 and 18 break and rearrange themselves, causing the BCL-2 gene to get "turned on" full time; thus, the mutant cells stay in the blood for a year or more instead of dying after their normal two-week life-span. Cortopassi explains that the added life-span is expected to allow for even more mutations to occur inside the cells, eventually increasing the likelihood of tumour growth and malignancy. (Source: *Genetic Engineering News*, 1 October 1993)

Industry-university team discovers gene for breast and ovarian cancer

Scientists from a consortium of five research teams have discovered and isolated BRCA1, a novel tumour suppressor gene located on chromosome 17 that produces susceptibility to breast and ovarian cancer. The discovery of BRCA1 may facilitate early diagnosis of such susceptibilities as well as provide a better understanding of the biochemical events involved in tumour progression, and may eventually lead to the development of therapies.

The research was conducted by a total of 45 scientists from Myriad Genetics (Salt Lake City, UT), University of Utah (Salt Lake City), National Institute of Environmental Health Sciences, Eli Lilly and Co. (Indianapolis, IN) and McGill University (Montreal, Canada). Lilly, in addition to being a research collaborator, funded a portion of the basic research. Genesis Inc. has formed ECM Pharma™, a wholly owned subsidiary, to develop medical devices and pharmaceutically active compounds based on natural components of the extracellular matrix. The company plans to supply cell-produced human collagen to medical product and pharmaceutical companies for evaluation, testing and ultimate use in medical devices, drug delivery, and research and manufacturing processes. With their new understanding of the biological interactions of the extracellular matrix, the company also hopes to develop lead candidate agents to regulate the production or degradation of tissues. Organogenesis will provide the initial funding for ECM Pharma, which is occupying laboratory and manufacturing space at Organogenesis' facility in Canton, MA. (Source: *Genetic Engineering News*, October 1994)

Human lactoferrin gene

Karol Wrage, writing in *Biotech Reporter*, July 1994, reports that the company Agennix of Houston, Texas, has succeeded in genetically engineering the gene for human lactoferrin into a fungal species and that the resulting fermentation process is able to produce one gram of lactoferrin per litre. This should result in a lower cost for pharmaceutical grade lactoferrin. Lactoferrin has a number of antimicrobial and other therapeutic properties. The new

process will provide competition for the transgenic cow processes being developed currently.

Agennix is looking for strategic alliances with food and pharmaceutical manufacturers in this project. Contact Dr. Roger Wyatt of Agennix on Fax No.:1-713-796-1044. (Source: *Australasian Biotechnology*, Vol. 4, No. 5, October 1994)

Genentech-patented VEGF may be main cause of diabetic retinopathy

A growth factor that has been patented by Genentech appears to be the main cause of diabetic retinopathy, opening the door to potential new therapies for the leading cause of blindness in young adults, according to recent animal studies.

The appearance of the factor, a protein called vascular endothelial growth factor (VEGF), has been tightly correlated to the abnormal growth of new blood vessels in the eyes of monkeys, according to a team of Boston researchers.

In diabetic retinopathy and retinopathy of prematurity, new blood vessels appear in the retina. The vessels tend to leak and form scar tissue, which gradually leads to the detachment of the retina off the back of the eye, and blindness.

The new findings may pave the way to new treatments for other types of eye diseases that arise mainly from abnormal blood vessel growth, including the "wet form" of macular degeneration, a common cause of blindness in the elderly and neovascular glaucoma. Joan Miller, an associate professor of ophthalmology at Harvard University, led the multi-centre team of 12 researchers.

The new research is the first time that a specific growth factor has been so tightly correlated with proliferative retinopathy. Diabetic retinopathy occurs when the blood vessels in the retina are starved of oxygen, which acts as a stimulus for new growth of tiny capillaries. The tiny vessels tend to break and bleed, forming scar tissue that eventually leads to a detached retina. In macular degeneration, the blood vessels tend to leak under the retina, but the same overall disease process of scar formation occurs that gradually destroys part of the retina.

The Boston team's research showed that VEGF was secreted from oxygen-starved retinas in monkeys to spur capillary growth. The extent and timing of new blood vessels growth was closely correlated with the amount of VEGF present

Several research groups have found elevated levels of VEGF in the vitreous of patients with diabetic retinopathy. The finding raises the possibility that a way could be found to block VEGF and thus prevent retinopathy. However, so far, no VEGF inhibitors have been identified, but monoclonal antibodies aimed at blocking VEGF have been successfully used in animal studies to block tumour growth in experiments.

VEGF may be used in other diseases where it is desirable to spur new growth of blood vessels. The protein, for example, could be used to increase collateral circulation to the feet in diabetic patients with impaired circulation, a common problem.

Boston researchers led by Jeffrey Isner, a cardiologist at St. Elizabeth's Medical Center, will soon conduct the first human tests with VEGF in patients who have a blockage in one or two major arteries that supply blood to the leg. An advisory committee to the National Institutes of Health approved the experiments in September 1994. The team plan to use an angioplasty balloon coated with VEGF genes near arteries adjacent to the blockages. It is the first gene therapy to be attempted for the treatment of cardiovascular disease. (Source: *McGraw Hill's Biotechnology Newswatch*, 17 October 1994)

Tuberous sclerosis gene identified

Scientists have announced that they have identified a gene for tuberous sclerosis, an inherited disease which affects around 10,000 people in the UK alone. The research, published in the scientific journal *Cell* on 31 December 1993, was carried out by a consortium of research groups at the MRC Molecular Haematology Unit in Oxford, the Institute of Medical Genetics in Cardiff and by two groups in the Netherlands.

Tuberous sclerosis is an inherited disease, although many cases are due to new mutations in the gene responsible in previously unaffected families. The condition is dominantly inherited and children with one affected parent stand a 50 per cent chance of inheriting it, although the degree of severity is variable. Tuberous sclerosis is characterized by learning difficulties, epilepsy and a wide spectrum of other medical problems, including tumours (usually benign) which develop in different organs. The gene, which the scientists have isolated on chromosome 16, accounts for about half the families affected by this disorder.

Working together with patients with tuberous sclerosis and their families, the team used an approach known as "positional cloning" to identify the gene. Inherited variations in the proteins and DNA which make up genes can be tracked in families carrying genetic disease and act as "genetic markers". Disease genes can be linked to these markers through studies of families with the disorder.

The discovery marks a major step forward in understanding tuberous sclerosis, previous research having failed to identify the specific cause of the condition. The gene may be involved in regulation of cell growth and it may play a more general role in the development of tumours.

For further information, contact Dr. Peter Harris, MRC Molecular Haematology Unit, Oxford. (Extracted from *The Genetic Engineer and Biotechnologist*, Vol. 14, No. 2, 1994)

Research on animal genes

Mouse model for Alzheimer's disease

Researchers took a major leap towards finding a treatment for Alzheimer's disease with the announcement that Athena Neurosciences and Eli Lilly had developed transgenic mice that exhibit key features of the brain disorder. They took a mutated human gene known to be a cause of the disease and inserted it into mouse embryos. Within a year of birth, the mice developed Alzheimer's-like brain conditions—including protein deposits known as amyloid plaque, damage to nerve endings and thinning of the synapses. Despite the optimistic statements made at the time, however, it is unlikely that a drug will reach the market until early in the next century. (Source: *Biotechnology Bulletin*, February 1995)

Spider venom goes against the grain

Life is left-handed. The peptides and proteins that make up all creatures are built out of the left-handed enantiomers of amino acids. Researchers from Utah have

now found an interesting exception from a source which is both dexterous and sinister—the funnel-web spider. Their research may improve our understanding of how the brain works and could help peptide drug research.

The researchers from NPS Pharmaceuticals in Salt Lake City, the University of Utah and Pfizer, found that funnel-web venom contains two peptides (ω-Aga-IVC and ω-Aga-IVB) which have identical amino acid sequences, but different properties. IVB is three to five times as potent as IVC. Investigating further, they found that IVB has one amino acid—a serine—which is right-handed rather than left (*Science*, 1994, 266, 1066).

Such peptides, although rare, are known in nature, and are almost always poisonous. However, these are built from scratch, using an already inverted amino acid. In contrast, the antagonistic arachnid makes an enzyme which converts IVC into IVB by inverting the amino acid when it is already in the chain. This is unknown in nature, says Nick Saccomano of NPS.

IVB's potency is connected with its stability. The D-serine occurs near the acid end of the peptide, which appears responsible for its potency. Most of the enzymes which normally cleave peptide bonds cannot break down the bonds on either side of the inverted unit so the "tail" of the peptide is protected.

This property could be exploited to increase the stability—and the effectiveness—of peptide drugs, or to change their properties without going back to the DNA which encoded the peptide, says Saccomano.

The toxins in funnel-web venom are extremely specific for one calcium channel. Studying their effects can shed light on each channel's function, explains Saccomano. The research could also be useful in developing new drugs for strokes, some psychiatric disorders, and Alzheimer's and Parkinson's diseases, all of which involve calcium channels, he adds. (Source: *Chemistry & Industry*, 21 November 1994)

Intramuscular fat control gene

Evidence of a major gene in Meishan pigs that control intramuscular fat is one of several areas of progress reported on recently in the newsletter *Pig Genome Update*. Others include identification of new microsatellite markers, demonstrations of new physical mapping techniques, and identifying a gene that affects production of Paris Hams and evidence for a major gene for litter size in pigs. For additional information, contact: Dr. Max F. Rothschild, National Pig Genome Coordinator, 225 Kildee Hall, Department of Animal Science, Iowa State University, Ames, IA 50011 USA; Tel.: 1-515-294-6202, Fax: 1-515-294-2401. (Source: *Diversity*, Vol. 10, No. 4, 1994)

Research group isolates cells responsible for oral tolerance development

Harvard Medical School scientists (Boston, MA) working with mice have isolated cells responsible for the generation of oral tolerance, the mechanism that enables the body to accept ingested foreign proteins as food by suppressing potential immune reactions.

Autolmmune Inc. (Lexington, MA), which owns an exclusive licence on the Harvard technology, is exploiting oral tolerance for the treatment and control of autoimmune diseases, including relapsing remitting multiple sclerosis (MS) and rheumatoid arthritis (RA). The company's therapeutic strategy consists of administering oral formulations of antigen from the tissue under attack in an autoimmune disorder.

While this approach to therapy has proven efficacious in Phase I II clinical trials, Autolmmune has pursued isolation and characterization of the group of regulatory T-cells mediating active suppression. In this most recent work, Drs. Youhai Chen, Howard Weiner and their associates at the Brigham and Women's Hospital in Boston, fed and immunized SJL mice with myelin basic protein (MBP). Cells from these animals were isolated, and a specific group of CD4+ clones secreted the inhibitory cytokines TGF-Beta, IL-4 and IL-10, which are thought to mediate immunosuppressive effects operating in oral tolerance.

The investigators further examined whether these MBP-specific cells could affect autoimmune encephalitis induced by MBP or proteolipid protein (PLP), another antigen. Both MBP- and PLP-induced disease were suppressed by the MBP-specific regulatory T-cell clones in animals treated with the cells.

In the discovery that forms the core of the company's patent position, Dr. Weiner and his colleagues found that oral administration of antigens capable of provoking autoimmune attacks in patients suffering from MS and RA diseases alleviated the severity, frequency and duration of the attacks. So encouraging were the results of its first Phase II clinical trial, which used Colloral™ (the company's oral antigen for RA) in 60 patients, that the company initiated a Phase II double-blind placebo-controlled trial to assess the impact of four different doses of the treatment in about 280 patients. (Source: *Genetic Engineering News*, 15 September 1994)

Molecular and biochemical studies on the mechanism of intercellular signal transduction with specific protein

Animals are composed of various kinds of cells with different morphology and functions, and their functions are regulated by cyto-signalling factors mediating intercellular signal transduction. The cyto-signalling factors are secreted by certain cells, which we call "effector cells", in response to some stimuli. Intercellular signals, by which biological functions are regulated, are transferred from effector cells to various functional cells, which we call "target cells", with cyto-signalling factors. Among such cyto-signalling factors, proteinous ones are vital, and elucidation of the functional mechanism is essential for cell biology as well as for the application to medicine.

In this research by Japan's National Institute of Bioscience and Human Technology (Cellular Biochemistry Laboratory), new cyto-signalling factors, especially proteinous ones, will be identified, and their characteristics and structures will be elucidated by applying molecular biological methods such as gene cloning. At the same time, the mechanism of intercellular signal transduction, such as how effector cells secrete cyto-signalling factors in response to stimuli and how target cells receive and respond to the factors, will be analysed on the molecular level with the aim of developing technologies for utilizing the newly identified specific proteins.

Research will focus on blood cells, and mast cells as effector cells, and bone marrow-derived stem cells and mast cells as target cells. The new cyto-signalling factors relating to the proliferation and differentiation of blood cells and such factors relating to DNA transcriptional

activity of mast cells will be identified. Their characteristics and structures will be clarified mainly by applying molecular biological methods such as gene cloning. Furthermore, the mechanisms of cellular signal transduction with those factors will be analysed, and technologies for utilizing those factors will be developed. Memory-controlling factors in animal brains will be also be studied and their structure and functions will be analysed. (Source: *JETRO*, December 1994)

Research on plant genes

Seeds made resistant to insects

A team of researchers from the USA and Australia report producing seeds genetically engineered to be resistant to insects. The work involves inserting a gene that prevents attacks from weevils on certain beans into garden peas, which normally lack resistance to the pest. The gene is active only when the pea is a seed, becoming dormant as the seed begins to germinate. The scientists say if the gene can be transferred into other crops, such as corn, rice and other beans, it might prevent pest damage to the crops while in storage. Members of the research team include scientists from Purdue University, the University of California at San Diego and Australia's Commonwealth Scientific and Industrial Research Organization. (Source: *Chemical Week*, 4/11 January 1995)

Potato research

Researchers at Iowa State University in Ames, USA, are attempting to genetically engineer potatoes in order to increase protein levels. Potatoes are the fourth largest world crop, so any effort to improve protein qualities would benefit protein-poor areas. The research team is looking for tuber-specific genes that trigger the plant to start forming potatoes.

Meanwhile, Monsanto Corporation has applied for deregulation of seven Russet Burbank lines of potato genetically-engineered to express *Bacillus thuringiensis* var. *tenbrionis* endotoxins for the control of Colorado potato beetles, a major pest of the crop.

Finally, in Fredricton, New Brunswick, a team of scientists at the Agriculture and Agri-Food Canada Research Station used a transfer of germplasm from a wild potato species to successfully establish genetic resistance to common scab, a disease of potato. The validity of resistance has been confirmed over a two-year trial period. (Source: *The Agbiotech Bulletin*, Vol. 3, No. 3, March 1995)

Maize transformation: a new, simple and inexpensive method

The problem of genetically engineering maize has occupied researchers for more than a decade. The first report of the successful introduction of genes into the germline of maize appeared in 1990, when researchers at DeKalb, using particle bombardment, introduced the *bar* and *uidA* (gus) genes. Subsequently, other methods, including PEG-mediated DNA uptake into protoplasts and electroporation of immature zygotic embryos have been tried with success, although particle bombardment remains the method of choice for most commercial and university laboratories.

Recently, ICI Seeds announced the development of a new method to effect maize transformation. The process is simple: cells from embryogenic suspension cultures are mixed with a suspension of fibres (5 per cent w/v, Silar SC-9 whiskers) and plasmid DNA (1 ug/ul) and then placed either upright in a multiple sample head on a Vortex Genie II vortex mixer (Scientific Industries, Inc., Bohemia, NY, USA) or horizontally in the holder of a Mixomat dental amalgam mixer (Degussa Canada Ltd., Burlington, Ontario, Canada). Transformation is then carried out by mixing at full speed for 60 seconds (Vortex Genie II) or shaking at fixed speed for 1 second (Mixomat).

This process results in the production of cell populations out of which stable transformants can be selected. Plants are regenerated from the stably transformed calluses and these plants and their progeny can be shown by Southern hybridization analysis to be transgenic.

Other researchers have described the generation of stable clones of non-regenerable maize cell lines, but this is the first report of transgenic plant production, in any species, with a silicon carbide fibre-mediated transformation approach.

The principal advantages of the new approach are its simplicity and low cost. Unlike particle bombardment, expensive equipment and supplies are not required. Currently, ICI Seeds is working to improve the efficiency of the process, but even at its current efficiency the method can be considered as a practical alternative transformation method for maize. (Source: *BioLink*, Vol. 2, No. 1, 1994)

Tobacco plant produces prototype vaccine

The potential to produce low-cost, high-volume vaccines is suggested by recent research by Biosource Technologies Inc., based in Vacaville, California, and the US Naval Medical Research Institute in Bethesda, Maryland.

The research, which involved the production of a prototype malaria vaccine in tobacco plant, suggests that less developed countries that find it difficult to afford high-tech vaccines could begin to use tobacco and similar plants to make vaccines almost literally in their backyards. In the experiment, the researchers genetically engineered tobacco mosaic viruses to carry and display proteins taken from the surface coat of the malaria parasite. They then injected the viruses into the leaves of a tobacco plant grown in a greenhouse. The tobacco mosaic virus is well known for its ability to convert a tobacco plant into an effective factory for making more virus. A month after the injection of the viruses, the leaves were harvested and the new viruses extracted. For each gram of tobacco leaf, the researchers were able to extract 0.4 to 1.2 milligrams of viruses. These yields suggest that a kilogram of tobacco-leaf protein could provide thousands of doses of vaccine. (Source: *Biotechnology Bulletin*, January 1995)

Biotechnological approaches to sweet potato improvement at Tuskegee University

Sweet potato (*Ipomoea batatas*) is a crop with tremendous potential. It is well-suited to address the growing world concerns for food availability, nutrition and sustainable agricultural systems. An important staple crop in many tropical countries, it has been ranked fourth in importance in the developing world after rice, wheat and corn. It is also a significant source of feed for livestock and raw material for industry. Sweet potato is tolerant to a wide range of agro-ecological conditions and is easily adapted to varied farming systems. It is a crop especially suited to

low-input farming which makes it very popular among farmers with limited resources.

Tuskegee University has a rich tradition of sweet potato research. The primary focus of the Plant Molecular and Cellular Genetics Laboratory at Tuskegee University is to utilize molecular genetic approaches to gain a better understanding of the sweet potato genome biology and contribute towards its productivity. Unlike other crops, sweet potato is relatively intractable to conventional breeding and poses many challenges to sexual hybridization. It is an hexaploid with 90 chromosomes (2n) and has problems such as pollen sterility, incompatibility and poor seed germination. Biotechnological tools including gene transfer and gene mapping have become especially relevant to sweet potato as these techniques enable rapid incorporation of specific traits into pre-adapted cultivars and complement conventional approaches to crop improvement.

To develop transgenic plants, it is essential to have a reliable method for efficient production of plants in tissue culture. Initially, none of the published protocols for sweet potato tissue culture satisfactorily produced plantlets in a high-frequency manner. Researchers at Tuskegee University aimed toward developing a better method for rapid production of adventitious plants *in vitro*. After a systematic study that examined many factors such as explants, genotypes, combinations of auxins and cytokinins, developmental stages of the explants and culture conditions, an adventitious shoot regeneration system was developed that produces shoots at almost 100 per cent frequency. The method relies on the use of petiole explants from apical portions of the *in vitro* grown plants of responsive genotypes and culturing them on a two-stage medium. The first stage consists of Murashige-Skoog salts and vitamins with 2,4-D (0.2 mg/l) while the second stage medium consists of thidiazuron (0.2 mg/l) instead of 2,4-D. In parallel, research at Tuskegee has resulted in the development of a very efficient and rapid system of producing somatic embryos from sweet potato explants.

There are several areas in sweet potato improvement where transgenic technology will be useful. Many fungal, bacterial and viral diseases infect sweet potato world-wide causing substantial economic damage, making the development of cultivars with improved disease resistance very useful. In a collaborative effort that includes Demeter Technologies, Louisiana State University, USDA/ARS and researchers at Tuskegee, attempts are being made to introduce synthetic lytic peptide genes, *Shiva-1* and *SB-37*, into elite sweet potato cultivars. These genes encode for peptides that are highly antimicrobial and have shown promise against bacterial and fungal diseases in potato and tobacco.

Among virus diseases, sweet potato feathery mottle virus is the most destructive, especially in Africa and Asia. It is an RNA virus and belongs to the Potyvirus group. Impressive resistant to many viral diseases in other crop plants such as tomato and potato recently has been achieved by introducing viral genome components into the plants. In collaboration with Scripps Institute, Tuskegee researchers are introducing coat protein and anti-sense RNA genes of the sweet potato feathery mottle virus into sweet potato cultivars. Several putative transgenic plants with the SpFMV coat protein gene have been developed and will be tested for resistance by challenge inoculation with the virus.

By far the most destructive agent on sweet potato, especially in the tropics, is the sweet potato weevil (*Cylas* and *Euscepes* spp). Production losses due to weevils often reach 60 to 100 per cent in certain areas. Feeding by the sweet potato weevil considerably reduces the quality and marketable yield of storage roots; secondary compounds such as terpenoids produced in response to weevil feeding make even slightly damaged roots unpalatable. Unfortunately, little or no resistance to this pest is available in the sweet potato germplasm.

Availability of gene transfer technologies may aid in the development of transgenic sweet potato plants that are resistant to weevils. Introduction of the cowpea trypsin inhibitor gene is already being pursued at Agricultural Genetics Company in England. Use of coleopteran-specific endotoxin genes from *Bacillus thuringiensis* (*B.t.*) is another option which Tuskegee researchers are exploring. Several *B.t.* strains have been assembled with the assistance of the International Potato Center.

When compared to animal proteins, plant proteins are deficient in essential amino acids, and sweet potato is no exception. Many young children around the world depend on sweet potato as a source of valuable protein. An improvement in the protein quality of this crop would have significant ramifications in the diet of many people.

Sweet potato is one of the crops chosen by NASA to be grown under hydroponic conditions in the proposed space station and to be used as a food by astronauts. In a project funded by NASA, Tuskegee researchers are trying to introduce a synthetic gene (*Asp-1*) into sweet potato and thus improve its protein quality. The *Asp-1* gene, developed by Dr. Jesse Jaynes, while similar in structure to other plant storage proteins, encodes many essential amino acids such as isoleucine, lysine, methionine, threonine and tryptophan. The Tuskegee laboratory is targeting the expression of this gene specifically into the edible storage roots of sweet potato by fusing the coding region of the gene with the sporamin promoter. To achieve high expression of this gene, researchers are also using translation enhancer sequences and introns in the vector construction.

Sweet potato is a relatively new entrant to the biotechnology scene. Unlike crops such as rice and corn, where intensive efforts are being focused by hundreds of laboratories around the world, only a handful are pursuing biotechnology research in sweet potato. Because of the adaptability and high nutritive values of this crop, it has high potential in meeting the nutritional demands of an increasing population in the developing world. Efforts to understand and improve this valuable resource by biotechnological and other means may prove to be a wise investment.

For more information, contact: C. S. Prakash, Assistant Professor, Plant Molecular and Cellular Genetics Lab, School of Agriculture and Home Economics, Tuskegee University, Tuskegee, AL 36088-1614 USA; Tel.: (205) 727-8023, Fax: (205) 727-8067; E-mail: Prakash@Acd.Tusk.Edu. (Source: *BioLink*, Vol. 2, No. 1)

Sweet potato fact file

- Member of the morning glory family.
- Sweet potato is grown in more than 100 countries.
- The estimated world production of sweet potato is around 115 million tons.
- China is the largest producer with about 80 per cent of world production.
- Sweet potato is one of the first crops to be domesticated. Archaeological evidence from Peru shows that sweet potato may have been domesticated 8,000 years ago.

•Sweet potato produces more edible energy protein and dry matter on a per hectare per day basis than any other crop.

•Among the food crops, sweet potato has the highest recorded net protein utilization (based on percentage of food nitrogen retained in the body).

•A serving of sweet potato provides 121 per cent of the recommended dietary allowance of vitamin A; orange-fleshed varieties of sweet potato contain higher beta carotene than carrots.

•Sweet potato is also a good source of ascorbic acid, thiamine, iron, calcium and B vitamins.

•Sweet potato is a versatile food consumed regularly in many countries.

•Food items prepared around the world from sweet potato include chips, curry, candy, noodles, tempura, soup, vermicelli, chapathi, pie, muffins, bread, cookies and doughnuts. Recipes are available from the author. (Source: CIP, FAO and *Sweet Potato Technology for the 21st Century* (1992) published by Tuskegee University (Eds. W.A. Hill, C.K. Bonsi and P.A. Loretan)

Applications for ice nucleating Zymomonas mobilis cells

Certain aerobic, Gram negative bacteria possess a membrane protein that enables them to nucleate crystallization in supercooled water. These ice-nucleating bacteria are generally members of plant epiphytic communities, particularly certain species of *Erwinia*, *Xanthomonas* and *Pseudomonas*. The phenotype is encoded by a single gene named *ina* or *ice* that has been cloned. *Pseudomonas syringae* possess the *inaZ* gene and currently is used in artificial snow manufacture under the name Snowmax. In addition, ice-nucleating bacteria have potential applications in the production and texturing of frozen foods.

However, for practical reasons such as regulatory and safety constraints, the use of ice-nucleating genes in food-based applications would be more straightforward in a GRAS (generally regarded as safe) organism such as *Zymomonas mobilis*. For this reason, European researchers have transferred and expressed the *P. syringae* ice-nucleating gene *inaZ* in *Z. mobilis*. The research, which promises new applications of ice-nucleating genes as reporters in extremophilic micro-organisms, is seen as of potential interest to the bioprocessing industry and to academic researchers. Details from: Phil O'Leary, BioResearch Ireland, Forbairt, Glasnevin, Dublin 9, Ireland or on +353 1 8370177. (Source: *Biotechnology Bulletin*, February 1995)

Research on viral genes

Gene swap vexes vaccine makers

Just as light began to dawn on how the human immunodeficiency virus (HIV) subverts the body's defence system, another problem has clouded the view. British and American researchers have found that different strains of the virus can swap genes, creating hybrids that could be immune to any vaccine or drug.

So far, eight different strains of the most prevalent type of HIV have been identified. Only one of these has been found in the US and UK, but Africa and South America have all eight of these "sub-types". The researchers, led by Paul Sharp of Nottingham University, studied all 114 published gene sequences for HIV, and found that 10 of them had genes which could have only come from a different sub-type.

Several viruses have been known to do this trick (called recombination), but until recently HIV was not thought to be one of them. Sharp explains that recombination can only occur if two strains of the same virus are in the body.

The most worrying detail for vaccine designers is that there is no way to predict which genes will cross between viruses. Vaccines are targeted at the protein coat which surrounds the viral RNA. Drug researchers hope to avoid HIV's phenomenal ability to mutate by finding a section of this protein which never changes: this would then be the target.

However, if the virus can swap the genes for these proteins with those from another strain, that section could be deleted from the gene sequence. (Source: *Chemistry & Industry*, 20 March 1995)

Epstein-Barr virus vaccine candidates and alternative vaccine adjuvants

The Epstein-Barr Virus (EBV) is an important human viral pathogen. More than 95 per cent of the global human population becomes infected at some stage, although in the West infection is often delayed until adolescence. The viral infection gives rise to clinical symptoms only in a limited number of cases, normally in the Third World.

The main diseases with which EBV is associated are Burkitt's Lymphoma (BL) and Nasopharyngeal Carcinoma (NPC). The virus is also associated with tumours in immunosuppressed patients and with Hodgkin's disease. Subunit vaccines based on EBV envelope glycoprotein have been developed. These vaccines have been expressed in cell systems at very high levels. This EBV glycoprotein (gp340) has been shown to be a protective immunogen in a primate model of lymphoma induced by EBV. The immune protection was provided by cell-mediated immune responses.

Subunit vaccines require adjuvants. Currently, the only adjuvants licensed for human use are based on aluminium salts, which are only effective in a limited number of conventional vaccines. Furthermore, they are not as effective when used with the new experimental recombinant viral subunit vaccines as they only induce weak cell-mediated immune responses. Therefore they probably will not be as effective in inducing protective immunity.

Now immuno-stimulating complexes (ISCOMs) are being investigated as alternative adjuvants, with possibilities for human use, since ISCOMs of chemically defined composition have negligible toxicity. A recombinant-derived subunit vaccine based on gp340 will shortly enter human clinical trials. The parties involved are interested in finding joint venture partners or licensees. Details from: Phil O'Leary, BioResearch Ireland, Forbairt, Glasnevin, Dublin 9, Ireland or on +353 1 8370177. (Source: *Biotechnology Bulletin*, February 1995)

Clue to a new type of hepatitis

A US Government scientist reports that his team has found preliminary evidence of a new virus that is believed to cause a new type of hepatitis.

The newly reported virus can apparently be transmitted through blood transfusions, said the scientist, Dr. Harvey J. Alter of the National Institutes of Health in Bethesda.

It would be the second new type of hepatitis virus reported in recent months. Late last year, a team of researchers in France reported finding a virus that they say causes a sixth type of hepatitis. But the finding of a hepatitis F virus, as they called it, has not been confirmed.

Particles of what may be a new virus were detected from one of the unexplained cases of transfusion hepatitis in the institutes' collection, Dr. Alter said. His team is trying to identify the virus further by using the latest molecular biology techniques on blood and other tissues from other cases. (Extracted from *International Herald Tribune*, 12 January 1995)

bDNA assay allows monitoring of virus load in HIV and HCV

Chiron Corp. (Emeryville, CA) has developed a quantitative DNA probe-based assay that directly measures viral RNA or DNA in serum and plasma samples from patients infected with HIV, hepatitis C virus (HCV) and hepatitis B virus (HBV).

Key to the assay's ability to detect and quantify relatively low titers of viral nucleic acids is the company's patented "branched" DNA (bDNA) technology. The assay uses bDNA probes to create an amplified signal that correlates to the quantity of target nucleic acid and, thus, the virus load in the blood.

Chiron's bDNA assay represents one of an emerging breed of probe-based amplification assays that, unlike other nucleic acid assays, not only detect but also quantify viral nucleic acid. Roche Molecular Systems (Somerville, NJ) and Cangene/Organon Teknika (Mississauga, Ontario, Canada) have developed quantitative versions of their PCR and NASBA nucleic acid detection assays, respectively, which are based on amplification of the target as opposed to the signal.

The ability to precisely monitor virus load in HIV- and HCV-infected patients is becoming increasingly critical, especially given a number of recent reports suggesting a relationship between antiviral drug efficacy and viremia. Currently, physicians must rely on indirect markers, which they consider imprecise, for monitoring the course of the infection and for making treatment decisions. (Extracted from *Genetic Engineering News*, October 1994)

Research on yeast and fungus genes

Summary of research at University of Malaya

The following are details of some relevant research being carried out at the Institute of Advanced Studies, University of Malaya.

Utilization of Sago Hampas by Microfungi by Shim Yok Lam (awarded in 1993; Supervisors: Drs. S. Vikineswary and J. J. Thambirajah).

This study investigated the possible strategies for microbial utilization of sago pith residue, "hampas". A survey of several sago processing factories in Sarawak has led to the estimation that 7-10 tons (dry weight basis) of sago hampas are produced by each factory daily. Proximate analyses of sago hampas revealed about 66 per cent starch, 15 per cent crude fibres and about 1 per cent crude protein.

Isolation of fungi from sago-related sources yielded 35 thermophilous isolates. Preliminary screening, based mainly on amylolytic activities yielded seven promising isolates capable of utilizing raw sago starch. Further screening for sago hampas utilization led to the selection of *Myceliophthora thermophila*. This study was able to produce an activity of 1,300 U/kg of sago hampas against carboxymethylcellulose and 1,800 U/kg of activity against raw sago starch after 72 hours of solid-state fermentation.

It was found that the amylase activity against raw sago starch was growth-related and fluctuated during fermentation of sago hampas. *Myceliophthora thermophila* was found to prefer a moisture content of about 80 per cent (v/w) or less and 1.0 per cent (w/w) equivalent mineral nitrogen (sodium nitrate) for the fermentation of sago hampas, based on its amylase production. Raw starch amylase activity was insignificant between culture filtrates of sodium nitrate-supplemented and urea-supplemented fermentations. Weight loss achieved in this study reached 21.5 per cent after 60 hours of fermentation. The loss was mainly from the fibrous portion of the substrate.

Bioconversion of Oil Palm Frond Parenchyma Tissue and Palm Oil Sludge Solids by Selected Fungi by Dinesh Nadaraj (awarded in 1994; Supervisors: Dr. S. Vikineswary and Prof. T. K. Mukherjee)

Bioconversion of oil palm fronds parenchyma tissue (OPFPT) with the grey oyster mushroom, *Pleurotus sajor-caju*, into a protein-enriched animal feed was carried out by solid substrate fermentation (SSF). The optimal conditions determined for upgrading OPFPT at shake flask level was 73 per cent moisture (v/w), supplemented with 20 per cent w/w with palm oil sludge solids (POSS) and 1 per cent $CaCO_3$ and incubated at room temperature for seven days. The increase in crude protein obtained was 41.7 per cent while the crude fibre decreased by 21.1 per cent. This resulted in a favourable improvement in *in vitro* dry matter digestibility (IVDMD) of the substrate to 49.5 per cent. Although there was an overall improvement in the amino acid profile of the upgraded OPFPT, the low amounts of histidine, methionine and tryptophan may require appropriate supplementation. Upgraded OPFPT was free from contamination with *Aspergillus flavus*, *Aspergillus parasiticus*, aflatoxins B_1, B_2, G_1 and G_2, as well as excessive amounts of heavy metals. OPFPT has been demonstrated to have good potential to be upgraded with *P. sajor-caju* into a protein-enriched feedstuff. Further upscaling experiments with more replicates is envisaged to verify these results. The feed produced may be utilized as a roughage by ruminants *in situ* within the oil palm plantation.

Biochemical Changes Associated with Growth of *Pleurotus sajor-caju* on Oil Palm Frond Parenchyma Tissue by Ling Sui Kiong (to be awarded in 1995; Supervisors: Dr. S. Vikineswary and Prof. S. Balabaskaran)

The growth of *Pleurotus sajor-caju* on oil palm frond parenchyma tissue (OPFPT) was improved by supplementing the substrate with 20 per cent palm oil sludge solids (POSS) and urea at 0.23 per cent N and 0.46 per cent N. The increase in crude protein content was 39 per cent, 40 per cent and 46 per cent respectively. The highest percentage loss in lignin of 19 per cent was observed in urea-supplemented cultures at 0.46 per cent N during a 10-day fermentation period.

Exocellulase, endocellulase, β-glucosidase, xylanase, laccase and protease activities were detected in *P. sajor-caju* cultures. Higher levels of enzyme activities were observed in cultures supplemented with urea at 0.46 per cent N. The maximum activities of endocellulase, xylanase

and laccase were 4,300, 6,600 and 16,930 U/kg substrate which occurred on day 10, 5 and 10, respectively.

Further investigation showed that the laccase activity was influenced by the inoculum age, inoculum size and the supplementary nitrogen source. The laccase of *P. sajor-caju* was 100 per cent thermostable at temperatures of 30 to 50° C for two hours. The pH for optimal laccase stability was found to be at pH 6. Based on these results, the degradation of OPFPT by *P. sajor-caju* was inferred. The possible utilization strategies of this bioprocess were proposed and discussed.

Solid-state Fermentation of Starch Processing Residues using *Pleurotus sajor-caju* (Sanar Kumaran K., Master of Philosophy project; Supervisors: Prof. C. A. Sastry and Dr. S. Vikineswary)

Large quantities of lignocellulose is generated as a residual by-product, especially in the agricultural sector. One such residual waste produced from sago starch processing is "hampas". Modern sago factories in Malaysia produce about 10 tons or more of hampas daily, which is sold locally as an animal feed supplement or channelled into waterways with little or no treatment. Sago hampas, which contains about 66 per cent starch and 15 per cent lignocellulose, can be used by white rot fungi in solid-state fermentation (SSF).

In this study, enzyme production by *Pleurotus sajor-caju* (grey oyster mushroom) and the optimization of substrate utilization for increased enzyme production is investigated. Initial studies show that the *Pleurotus sajor-caju* colonized hampas has appreciable amounts of enzyme activities of endocellulase (CMCase). Filter paper activity (FPase), β-glucosidase, xylanase and laccase during a 21-day SSF. Further investigations on fungal inoculum size, age and fermentation time is on the way to enhancing the SSF for selected enzymes.

Spent Mushroom Compost as Biofertilizer for Crop Production on Marginal Soils (Vimala P., Ph.D. project; Supervisors: Drs. S. Vikineswary, Sayed Sahar and Ahmad Barakbah)

Spent mushroom compost is available in large quantities from the commercial production of *Pleurotus* sp. (black and white oyster mushroom) in Malaysia. For every 200 g of mushroom production about 600-800 g of spent compost is produced. At present this spent compost is discarded by mushroom farms. One such farm discards about 1,000 bags daily or 21 tons of compost each month.

The mushroom compost consists of 90 per cent rubber wood dust, 10 per cent rice bran and $CaCO_3$. Preliminary studies have shown that in its natural state the mushroom compost cannot sustain crop growth although germination was not affected.

Studies on bioconversion of the spent mushroom compost using natural inoculants like chicken dung and cow dung as well as inoculation with *Trichoderma* sp. would be conducted with the objective of converting the spent mushroom compost into a biofertilizer, for the amelioration of marginal soils for food crop production. (Source: *Institute of Advanced Studies*, University of Malaya)

Research on bacterial genes

Sub-sea research opens whole new world of bacteria

Marine microbiologists have discovered unique bacteria thriving in the Pacific Ocean at depths of more than 1,000 m.

Microscopic analysis revealed divided and dividing bacteria in core samples of sediments taken at depths of up to 900 m from five sites in the Pacific Ocean. The research team reports in s letter to *Nature* [371, 410–413 (1994)] that they found whole bacterial cells in even the deepest samples, taken from 518 m below the seabed.

Culturing the bacteria, rapid growth in enrichment slurries, and the presence of high molecular weight DNA confirmed the viability of the bacteria even in the deepest sediments.

At least some of the bacteria are species of *Desulfovibrio*. However, although they are closely homologous with *D. salexigens* in 16S rRNA sequence analysis, other characteristics are very different.

The team says the bacteria have a broad and high range of growth temperatures "completely unlike those of known sulphate-reducing bacteria". They also have a different metabolism and salt and temperature tolerance, and are barophilic—they are active at pressures of more than 27 MPa. (Source: *Microbiology Europe*, Vol. 2, No. 6, November/December 1994)

Study describes structural characteristics of key enzyme from resistant bacteria

Scientists at Penn State (University Park, PA) have described some structural characteristics of an enzyme that can turn a common gut bacteria into a drug-resistant source of serious infection. Dr. Michael Crowder and co-researchers combined spectroscopic and kinetics studies to characterize metallo-beta-lactamase, which contains amino acids that bind the metal zinc in several specific locations in its framework.

Addition of zinc to certain strains of the bacteria group *Bacteroides fragilis* make the pathogen resistant to virtually all known drugs derived from the antibiotics penicillin and cephalosporin. These bacteria do not usually harm healthy people, but a break in the internal surface of organs found below the diaphragm, such as the stomach or liver, can lead to serious infection from the bacteria.

By substituting another metal, cobalt, for the zinc, the researchers showed that each metal ion is bound by six ligands. Spectroscopy confirmed the presence of at least two different amino acids, histidines and a cysteine, that bind the metal. The next step for the researchers is to describe the kinetics of metallo-beta-lactamase. (Source: *Genetic Engineering News*, September 1994)

Tooth decay bacteria

Much of the research into how bacteria cause tooth decay could be invalid. That is the striking implication of new research from scientists in Canada.

A team at the University of Manitoba, Winnipeg, have found that subculturing dramatically and rapidly alters the biochemistry of *Streptococcus mutans*, which is found in plaque and is one of the main causes of dental caries.

They revealed statistically significant change in the biochemical properties of the bacterium over daily subculturing for 225 days. In particular, glycolytic activity increased and hydrophobicity and synthesis of extracellular polysaccharide decreased in the *S. mutans* strains.

Most research with oral streptococci has used established laboratory strains, and results are often extrapolated to explain microbiological activity *in vivo*. (Source: *Microbiology Europe*, Vol. 2, No. 5, September/October 1994)

Research instrumentation

High-sensitivity measurement of blood immunity globulins

Prof. Ujidaira M. Umemoto and their research team of the University of Tokyo's Research Centre for Advanced Science and Technology, have jointly developed a new technique for very accurately measuring the immunity globulins (Igs) in the blood by using magnetic particles which are attracted by magnets and a liquid crystal oscillation sensor.

Quantitative measurement of immunity globulin G (IgG) could detect IgG at 0.001 mg/cm^3, which was made possible by first adhering IgG antibodies on the magnetic particles. The quantity of the magnetic particles which reacted with IgG and antigen antibodies was measured with a crystal oscillator sensor, from which the IgG quantity was measured.

The immunity sensor electrode was coated with antibodies, and the quantity of antigen complexes generated through bonding with antigens in the blood is measured. The crystal oscillation sensor is based on the phenomenon of a vibration generated when an AC voltage is impressed on a crystal plate sandwiched with electrodes. This super high-sensitivity sensor is based on the change in the oscillator frequency with the adhesion of even a small quantity of foreign substances. An odour sensor has already been commercialized that uses an oscillator with a resonance frequency of 9 MHz and by remodelling the oscillator surface with a resonant bimolecular film.

The sensor has been applied to IgG measurements, but the process of fixing a substance (protein A) that adsorbs IgG selectively on the surface of the crystal oscillator is quite difficult, and when the sensor is used repeatedly, biological substances other than IgG adhere to the protein A, which deteriorates the measurement reproducibility.

The new measurement technique eliminates these problems and uses a protein A remodelling plate and a magnetic antibody. The oscillator actually measures the quantity of magnetic particles. Firstly, the IgG is bonded with the inspection samples inside a glass plate separate from the sensor, and IgG antibodies with magnetic particles are further reacted to form complexes. After washing off excess antibodies, the complexes are decomposed, and only antibodies with magnetic particles are collected selectively with a magnet and concentrated. Immersing the crystal oscillator sensor in this solution and observing the changes which occur will ultimately enable the quantity of IgG to be measured.

In IgG measurement experiments, magnetic particles available on the market and adhered with IgG antibodies were used, but if the magnetic particles were adhered with other types of antibodies, it will become possible to apply the new technique to the measurement of the quantities of other molecules. Since the magnetic force can be utilized to recover the magnetic particles, the technique is advantageous in that valuable antibodies can be recovered for reutilization.

Further details from: The University of Tokyo, Research Centre for Advanced Science and Technology, 4-6-1, Komaba, Meguro-ku, Tokyo 153; Tel.: +81-3-3481-4423, Fax: +81-3-3481-4571. (Source: *JETRO*, November 1994)

New DNA synthesis system

Beckman Instruments says its new UltraFAST DNA system can significantly reduce the time required for two steps in the synthesis of oligonucleotides.

The synthesis of these short DNA segments, about 20 nucleotides in length, is now one of the most widely utilized techniques in biotechnology research and production. The technology is central to the development of an enormous number of products covering the entire range of genetic engineering. These include antisense oligonucleotides, which are expected to provide a new generation of designer drugs in the treatment of genetic and viral disease, diagnostic probes, primers for PCR and probes for the Human Genome Project.

Chemical synthesis of oligonucleotides is accomplished in three distinct steps. First, individual nucleotides are sequentially assembled on a solid support where they form a oligonucleotide chain. Next, the chain of the "protected" oligonucleotides is cleaved from the support, and finally, "deprotection" of the oligonucleotide converts it to a biologically active molecule.

According to the Beckman scientist, rapid advances in coupling chemistry and automation of the process with commercial synthesizers have compressed the time for the synthesis of a typical oligonucleotide down to an hour, which is currently acceptable.

From scrutiny of the protective process emerged Beckman's proprietary protective nucleotide block and their methylamine/ammonia cleavage system. With this technology, the cleavage takes place in five minutes, as contrasted with the hour of conventional methods, and the deprotection is complete in five minutes, as compared with the usual three hours.

No less important than speed is the quality of the final product. This was achieved through the use of a protected derivative of deoxycytidine, known as C^{Ac} phosphoramidite.

This compound requires the standard benzoyl protection of the dC monomer to be replaced with acetyl. This seemingly minor change in the protecting group led to an oligonucleotide which can be cleaved and deprotected in 10 minutes using the methylamine/ammonia reagent. The use of this phosphoramidite completely eliminates undesirable transamination side product formation during the deprotection.

For the three other monomers, the protective strategy is conventional, employing well-established nucleotide derivatives. Thus, there is no need for changes in the synthesis programme already in place or in other reagents used on the DNA synthesizer. Moreover, the system can be used on any commercial DNA synthesizer. (Extracted from *Genetic Engineering News*, 1 October 1994)

Tools for selecting stem cells show clinical trial promise

Two novel instruments are showing promise in clinical trials for the large-scale selection of stem cells for reconsti-

tuting bone marrow that has been destroyed by chemicals or radiation in the treatment of cancer or autoimmune disease.

The stem cells, which can be harvested from bone marrow, peripheral blood, cord blood or foetal haematopoietic organs and then transplanted, are capable of rapidly regenerating leukocytes and platelets whose dearth, following marrow destruction, places the patient at high risk for life-threatening infection and bleeding.

The Ceprate®-SC Stem Cell Concentrator, a device that selects stem progenitor cells using a bifunctional monoclonal antibody (Mab)-based separation technique, has been developed by CellPro Inc. (Bothell, WA). The Isolex™-300 Magnetic Cell Separator, which selects stem progenitor cells using Mab-coated magnetic beads, is being developed by Baxter Healthcare Corp. (Santa Ana, CA). Ronald J. Berenson, M.D., executive vice-president and chief medical and scientific officer of CellPro, said that Ceprate consists of (1) a biotinylated (biotin-conjugated) murine anti-CD34 Mab; (2) a disposable set of solutions, plastic bags and—importantly—a column the size of a teacup filled with several million plastic beads covalently linked with avidin; (3) a programmable computer that controls a system that automates and regulates the flow of the cell suspension through the column. Briefly, said Dr. Berenson, bone marrow or blood cells are reacted with the biotinylated Mab, washed with saline to remove unbound Mab, suspended in 300 ml of saline and placed in a plastic bag hooked up to the disposable plastic unit and passed through the column. He explained that biotin·CD34+ cells will stick to the column through biotin-avidin interaction, one of the strongest known chemical interactions in nature.

A number of American and European groups have achieved promising results in lymphoma and breast cancer patients transplanted with autologous CD34+ bone marrow and blood cells selected with the CellPro device. Dr. Berenson said that a Phase III trial of CD34+-selected marrow transplantation for breast cancer has been completed, and the data has been submitted to the FDA in support of a request for FDA approval of the Ceprate for clinical use.

Baxter's Isolex kit consists of three components: (1) a disposable plastic mixing chamber with inlet and outlet tubing; (2) two magnet systems controlled by a microprocessor-driven motor; and (3) a reagent kit containing Dynal paramagnetic microbeads, two antibodies (a bifunctional monoclonal murine anti-human-CD34+ antibody; a monoclonal sheep anti-mouse antibody) and chymopapain (an FDA-approved enzyme that can digest the antibody linkage between the cells and microbeads).

The device uses a so-called indirect selection method, said Ping Law, Ph.D., assistant director of technical affairs in the immunology division at Baxter. First, bone marrow or mobilized peripheral blood cells are reacted with anti-CD34+ antibody (0.5 g/10⁶ cells). Unbound antibody is removed by centrifugation washing. The cells are then rosetted with sheep-anti-mouse antibody-coated Dynal beads (0.5 beads/cell). The primary magnet system is used to trap the rosetted beads, and saline washes are used to free the non-target cells that are trapped by the cell bead rosettes. Finally, the CD34+ cells are released from the beads by chymopapain digestion of the antibody-antibody linkage. The secondary magnet system is used to remove the beads, and the CD34+ cells are concentrated by centrifugation washing. The procedure yields an 80 per cent or greater concentration of CD34+ cells, regardless of the cell source (bone marrow, peripheral blood or cord blood), according to Dr. Law. (Extracted from *Genetic Engineering News*, 1 September 1994)

Collaboration to offer access to DNA sequence data

Researchers who are part of a gene-sequencing collaboration say they have completed the initial technical work required to give academic scientists access to the largest human-gene database in the world.

The information and materials that make up the Human cDNA Database resulted from a two-year joint research project between the Institute for Genomic Research (TIGR, Gaithersburg, MD) and Human Genome Sciences, Inc. (HGS, Rockville, MD). The database includes partial and complete DNA sequences characterizing between 30,000 and 35,000 human genes. It also provides information about where in the body and how frequently individual genes are expressed.

This information includes more than 150,000 partial human gene sequences; in a number of cases, several gene fragments relate to a single gene. In elucidating the structure of these fragments, the exact sequence of more than 50 million nucleotides was determined.

The Human cDNA Database is managed and operated by TIGR. It is supported financially by HGS and SmithKline Beecham (SB, Philadelphia, PA), a corporate partner of HGS. HGS and SB have committed more than $100 million to DNA sequencing, bioinformatics and gene-function analysis. (Source: *Genetic Engineering News*, 15 October 1994)

General

Osaka University captures four kinds of DNA bases by scanning tunnel microscope

Tomoji Kawai *et al* of the Institute of Scientific and Industrial Research, Osaka University have successfully captured the shapes of the four bases that form DNA using a scanning tunnel microscope (STM). The width of adenine and guanine are 1 1,000,000 mm (ten Angstroms), and adenine is heart-shaped; thymine and cytosine are six Angstroms wide and are round, and it was ascertained that all of them have flat, rice cake-like shapes. After this, effort will be put into capturing the chains. Since, if this is possible, it will open the path for selectively rearranging bases, these results are attracting attention as something that will make for great progress in gene manipulation.

Using the property that a tunnel current flows when a small metal probe approaches the surface of substance, Kawai *et al* produced an STM in their laboratory, and they have been working on capturing the structure of the bases.

The strontium titanate substrate on which the samples were placed this time was heat treated to increase the flatness of the surface after it had been mechanically polished, and along with this, the resolution of the STM itself was increased, so they were able to capture the four bases. Tungsten was used for the probe.

The laboratory was successful under conditions of two bases being included, and it plans to work on capturing a mixture of all four bases on the one hand and viewing them in DNA without breaking it down on the other. (Source: *Kikkan Kogyo Shimbun*, 20 March 1995)

Genetically engineered "fluorinated" polypeptide

Genetic engineering offers the potential for creating new proteins with novel materials properties. D. A. Tirrell and co-workers reported an example of an *in vivo* synthesis of a structurally homogene non-natural polypeptide. An *Escherichia coli* strain was mutated so that the bacteria produced periodic polypeptides of sequence $[(Ala\text{-}Gly)_n\text{-}Phe\text{-}Gly]_m$ and that they were no longer capable to biosynthesize phenylalanine but became completely dependent on phenylalanine in the growth medium. Fed with a mixture of natural amino acids (except phenylalanine) and non-natural *p*-fluorophenylalanine (pfF), the bacteria were stimulated to synthesize the desired genetically engineered "fluorinated" polypeptide $[(Ala\text{-}Gly)_2\text{-}pfF\text{-}Gly]_{15}$, which was isolated from the cell culture and showed near-perfect replacement of phenylalanine by *p*-fluorophenylalanine. (Source: *Chemistry & Industry*, 5 December 1994)

Insecticidal genes isolated

Scientists at Monsanto say they have isolated a new class of insecticidal proteins and genes from soil microbes that could prove valuable in controlling a range of insects. Monsanto says the proteins, including cholesterol oxidase, appear to be effective against a broader spectrum of insects than those from *Bacillus thuringiensis* (Bt). A number of chemical producers, including Monsanto, are developing insect-resistant plants genetically modified with Bt genes. The company says the new genes could be used in commercially available insect-resistant crops in five to six years. (Source: *Chemical Week*, 1 March 1995)

IGT develops biomass fuel cell

The Institute of Gas Technology (IGT) says it has successfully operated a bench-scale molten carbonate fuel cell on low-calorific value fuel gas using sugar cane residue. IGT says this is the first time a fuel cell produced electricity from a fuel gas that was thermochemically derived from biomass. The gasifier uses renewable biomass to produce either an industrial fuel gas or a chemical synthesis gas, depending on air- or oxygen-blown operation. The Pacific International Center for High Technology Research is testing a 100 tons day demonstration unit of this technology in Maui, Hawaii, USA. (Source: *Chemical Week*, 22 March 1995)

Tissue engineering

Although new bioengineered materials are beginning to enter the medical marketplace, it appears that the next generation of tissue engineering technology will usher in revolutionary changes. Tissue scaffolding, the use of bioabsorbable materials and the introduction of cell-based techniques will forever change the medical care landscape, according to Harold Alexander, Ph.D., from the department of bioengineering, Hospital for Joint Diseases (New York, NY).

Dr. Alexander predicts that emphasis will be placed on therapeutic prevention, repair and regeneration rather than on reconstruction and replacement. Medical practitioners will displace surgeons because of the minimally invasive nature of the treatment. Allied health professionals will play a greater role because of the resulting simpler procedures and a greater reliance on automation.

While such new technology may involve high start-up costs, it is expected to lower the total bill for health care in the long run, said Dr. Alexander.

Tissue loss and end-stage organ failure result in health care costs of more than $400 billion annually in the USA alone. According Robert Langer, Sc.D., of MIT, each year over one million patients need new cartilage, over four million patients in America require new skin and hundreds of thousands of patients need new urological structures.

Tissue engineering is defined as the application of the principles and techniques of traditional biomedical engineering to products and processes involving living cells. Although the technology only emerged in the 1980s there are already many companies and universities devoted to tissue engineering product R&D.

New types of polymers with specific cell sequences attached are now being designed to expand the range of biomedical applications for tissue engineering.

Companies may make biomaterials useful for modifying a local tissue response by designing controlled release systems for growth factors. Applying such an approach, new blood vessels can be directed to grow towards specific tissue and cell structures. Another example involves the localized release of gene therapy agents such as antisense oligonucleotides to prevent restenosis, following balloon angioplasty.

Critical to any success of a tissue engineered product is its *in vivo* performance. It is important to conduct experimental studies early on to accurately simulate the totality of the environment the implanted construct will face.

In the USA, the FDA has established the InterCenter Tissue Engineering Initiative to help evaluate tissue engineering applications and to identify areas for further study. The FDA InterCenter Tissue Engineering Working Group, with members from the Center for Biologics Evaluation and Research (CBER), Center for Drug Evaluation and Research (CDER), Center for Devices and Radiological Health (CDRH) and Center for Veterinary Medicine (CVM), has also been formed.

The Working Group has developed a draft report examining recent developments in tissue engineering and scientific and regulatory issues in a number of tissue product application areas. These product areas range from biosynthetic skin covering, collagen, bone, blood substitutes, cardiovascular devices and dura mater, to *in vitro* and *ex vivo* use of encapsulated cells and human tissue products.

The Working Group has identified generic safety and effectiveness issues for the development of products. Some of these include:

- Material sourcing (cells and tissues);
- Cell and tissue characterization (structural and functional activity);
- Adventitious agents (testing and process validation);
- Characterization of biomaterials;
- Sterilization and sterilization by-products;
- Product consistency; and
- Product stability and shelf-life.

According to Dr. Hellman, coordinator for biotechnology of CDRM, FDA Centers will continue to use different approaches in the evaluation of tissue engineered products. These include: (1) research (bioeffects analysis and test method development); (2) data and information monitoring (databases); (3) regulatory guidance (generic product-specific and points to consider); (4) training and education (FDA Staff Colleges; workshops conferences); and (5) cooperation with public and private groups.

Tissue Engineering's Potential for US Economic Benefit

Tissue	*Indications*	*Patients per year*
Skin	Burns, ulcers	4,700,000
Nerve	Spinal cord, neuromuscular, nerves	240,000
Bone	Joint replacement, bone graft, fixation	1,310,000
Cartilage	Knee, arthritis, ligaments, tendons	1,200,000
Heart		754,000
Blood Vessels	Large and small replacements	606,000
Liver	Metabolic disorders, cirrhosis, cancer	205,000
Pancreas	Diabetes	12,800,000
Kidney		600,000
Dental	Tooth implants, gingival tissue	10,000,000
Blood	Haemophilia	20,000

Source: Advanced Technology Program - Focused Program Recommendation, Stanley Abramowitz, Ph.D., and Edith R. Schwartz, Ph.D., 28 October 1994

(Source: *Genetic Engineering News*, 1 January 1995)

Gene pharming

New processes of "gene-pharming" may prove to be cheaper than the more conventional methods of gene production that produce tissue cultures yielding little protein, according to Genzyme Transgenics, which recently purchased a 166-acre farm in Massachusetts, USA that could support 1,000 host goats. The company, exploring gene-pharming with pigs and sheep, may soon begin breeding genetically altered goats that produce medically valuable proteins in their milk. Biotechnologists transfer foreign genes to dairy animal embryos and, if the genes integrate properly in the DNA of the host, become constituents of the animal's milk. For more information, contact: Harry Meade, Genzyme Transgenics Corporation, 1 Mountain Rd., Framingham, MA 01701-9322 USA; Tel.: 1-508-872-8400, ext. 2256, Fax: 1-508-872-9080. (Source: *Diversity*, Vol 10, No. 2, 1994)

VAPOR enzymes

Many micro-organisms possess enzymes which can reversibly transfer electrons between artificial 1-electron mediators and pyridine nucleotides. The term VAPOR was coined for these enzymes as they are viologen accepting pyridine nucleotide oxido reductases. These VAPOR enzymes have been studied because they are catalysts for pyridine nucleotide regeneration and because they have interesting mechanisms of action between their 1-electron and 2-electron transfer steps. This work has led to the preparation of chiral compounds and three, as yet non-commercially available, viologens have been synthesized.

For more information, contact: Phil O'Leary, Bio-Research Ireland, Forbairt, Glasnevin, Dublin 9, Ireland; Fax: 353 1 837 0176. (Source: *Australasian Biotechnology*, Vol. 4, No. 5, October 1994)

Integrated circuit

A discovery about the physical properties of DNA made by Thomas Meade of the California Institute of Technology could revolutionize the business of genetic testing. When he tested a double strand of DNA, he found that electrons could move along it with ease. The difference seems to be that the core of a double helix is not a chain of molecules bound together, but a stack of molecules held apart. Electrons appear to rush through the core with alacrity.

The implications are obvious to a molecular biologist. DNA strands do not wrap themselves around each other at random; their binding is controlled by the genetic sequence they carry. So a single-stranded piece of DNA attached to an electrode could be used as a probe to look for any genetic sequence of the same length. When the right sequence came along, e.g. in a properly treated blood sample and stuck to the probe, electrons that were previously stuck in the single strand could charge down the double strand. The genetic information could be turned into an electrical signal.

The technology for wiring up molecules already exists; it is used to take advantage of the properties of proteins in biosensors. Affymetrix, a company in Silicon Valley, has taken the technology used to print microchips and made it into a way of producing arrays of single-stranded DNA for tests.

At present, however, the arrays are on glass, and the presence of double strands is revealed only by the use of an optical scanner. If the DNA sequences on the chip could be read directly by circuitry, the procedure would become a lot easier and, in the end, cheaper. A single chip in a machine the size of a pocket calculator could in principle carry out a wide variety of tests, removing the need for laboratory analysis except in rare cases. (Source: *The Economist*, 25 February 1995)

E. APPLICATIONS

Pharmaceutical and Medical Applications

Biological and man-made designs converge to create DNA chips

Hewlett-Packard recently joined forces with Affymetrix to co-develop and market systems that will use so-called "DNA chips" to perform sophisticated analysis of DNA samples.

These DNA chips represent a new direction in extremely sensitive medical analysis equipment, which could quickly detect genetic diseases for example, and in computing where synthetic DNA molecules could be used as a type of microprocessor, capable of performing calculations much faster than today's high-end silicon chips.

DNA chips are essentially microscopic, high-density arrays of DNA probes built on a glass substrate. Each DNA probe consists of a synthetic strand composed of different combinations of four different nucleotides—the basic building blocks of DNA.

Each DNA strand can be constructed differently, through a process Affymetrix describes as Very Large Scale Immobilized Polymer Synthesis (VLSIPS) technology.

To test a DNA sample to determine whether it contains a specific gene or sequence of genes, the sample is tagged with fluorescent markers, and then the DNA chip is immersed in the sample solution. DNA probes on the chip will combine with like segments of DNA in the sample. The chip is washed to remove the non-bound DNA and a laser scanner determines which probes have combined with the sample DNA. From this information the sample can be analysed—much more quickly than with conventional techniques.

Building a DNA chip combines micro-lithography with DNA synthesis chemistry. Photolithographic masks are used to build the array and DNA synthesis methods create the probes. An Affymetrix DNA chip can hold more than one million DNA probes on a 1.28 cm^2 area.

The first DNA chip-based analytical equipment using Affymetrix's Gene chip technology is expected in 1996 and initial products will be focused on research into Human Immunodeficiency Virus (HIV). Scientists will be able to use the analytical systems to test out new drugs that will target specific gene characteristics found in HIV and also use the equipment to detect resistant mutations.

Affymetrix says that variants of its technology could also be used in mapping the human DNA in the global Human Genome project, which is attempting to decode all 100,000 genes that make up the human DNA molecule. The Human Genome project involves about 350 laboratories around the world and is expected to cost $3 billion and take until the year 2005 to complete. DNA chips from Affymetrix and others, could significantly speed this project and dramatically cut the costs of the project.

A different kind of DNA chip technology has also been developed by the United States Government funded Argonne National Laboratory. The commercial rights to the technology have been acquired by California-based Hyseq which will develop analytical instruments that it will market to laboratories involved in the Human Genome project and also to other research centres investigating the role of genetic influences on common diseases.

The Argonne developed technology is for a different kind of DNA chip that can analyse the individual base pairs that make up a gene rather than detect specific genes as in the Affymetrix approach. The commercial benefits from distinguishing genes can be staggering since, once identified, the genes can be used to not only treat human diseases, a large market in itself, but can be applied to genetic engineering in animals, plants and microbes.

Key to commercial exploitation are DNA chips that can perform the complex analysis at a rate 1,000 faster and ten times cheaper than with current methods. The Argonne DNA chip technology, for example, will be able to analyse one million DNA base pairs per day. It would take a laboratory at least a year to perform the same analysis. A similar approach is being taken by Californian firm Nanotronics but there are still few pioneers in this area despite the potential benefits. (Source: *Electronics Weekly*, 11 January 1995)

Cautious welcome for malaria vaccine outcome

The results of the most severe test yet of the efficacy of a new malaria vaccine have been greeted with caution.

The trial found that the *Plasmodium* polypeptide, SPf66, was 31 per cent effective in protecting children in southern Tanzania against the disease, which researchers defined as a parasite density of at least 20 000 μL^{-1} blood, plus measured fever. The research team had hoped for a protective efficacy of 50 per cent.

The researchers chose children (almost 500 of them) aged between one and five years for the trial for two reasons: along with the very old, they are the group most at risk of dying of the disease; and previous studies had shown that SPf66 was best at protecting the very young and the very old.

The vaccine is against the blood stage of *Plasmodium falciparum*, and induces an immune response in the host to prevent the parasite from multiplying. It is made up of three asexual blood-stage antigens linked by a sporozoite antigen to form a β-pleated sheet polypeptide.

Similar tests are being done in Gambia and Thailand, and results are expected in a year's time. (Source: *Microbiology Europe*, Vol. 3, No. 1, January/February 1995)

Chemical cocktail - Extra Dry

Quadrant Holdings, a bioscience company in Cambridge, UK, has developed a way of drying vaccines so they can be carried around in a briefcase rather than shipped in a refrigerator. The secret lies in removing the water from the sample: it is a trick with many other applications, too.

Replace water with a sugar called trehalose and you can dry things out without damaging them. Quite how it works is not clear; its ability to form hydrogen bonds, which hold water to surfaces, is probably part of the answer, but it works. Various living things could not survive without it. These organisms cryptobionts can lose up to 99 per cent of their body water. They enter an inert,

brittle state in which even the most sensitive tests fail to detect any metabolic activity, but from which they can emerge later.

Trehalose's role in all this was discovered in the 1980s. Bruce Roser, Quadrant's founder, then working at a government research station, was the first to apply it to the preservation of unstable biological samples. The company has world-wide patents on the use of trehalose to stabilize pharmaceuticals, laboratory reagents, human blood and foodstuffs. Quadrant has been collaborating with the WHO on applying the technique to polio vaccine. The company is also on the point of signing licensing deals with vaccine producers to manufacture heat-stable vaccines against other diseases.

Quadrant has also worked on live vaccines. The current measles vaccine is preserved by freeze-drying. Once out of the fridge it loses 90 per cent of its activity in a week at tropical temperatures—an enormous problem in developing countries. Dr. Jaap Kampinga, who heads Quadrant's research department, says his dried measles vaccine is stable for eight weeks, though the drying process causes some loss of activity. Polio vaccine has turned out to be more of a problem, in that it loses 99 per cent of activity and increasing doses a hundredfold to compensate would be too pricey. Dr. Kampinga is looking at ways to change the manufacturing process that may make drying more effective.

The technique might also help in the development of oral vaccines—which have huge advantages. Drying allows vaccines to withstand the rigours of industrial coating techniques, so they can also be protected against the stomach. To be effective the vaccine must get from the gut to the lymphoid tissues, where immunity is born. The route from the gut to the Lymphoid tissues is not yet well understood, but drying may be a good way for vaccines to reach them. (Source: *The Economist*, 4 March 1995)

AIDS test using saliva, not blood

Based in Beaverton, Oregon, Epitope Inc. has won US Food and Drug Administration (FDA) approval to begin United States marketing of the first test to use a saliva sample, rather than blood, to detect the presence of the HIV virus.

The test, which comes as a kit and takes about two minutes to administer, is also the first to be cleared by the FDA for collecting oral specimens for disease diagnosis of any type.

The test kit, called OraSure, has two components: a treated cotton pad on a stick to collect saliva and a specific test to analyse specimens for antibodies to HIV. It is expected to dramatically extend the range of HIV testing, especially among difficult-to-contact groups like the homeless and chronic drug users. (Source: *Biotechnology Bulletin*, January 1995)

Growth hormone

The Ares-Serono Group says that the US Food and Drug Administration (FDA) has approved a Treatment Investigational New Drug (TIND) programme for the use of the company's mammalian-cell derived recombinant human growth hormone (r-hGH), Serostim, in HIV-associated catabolism (AIDS-related wasting syndrome). This TIND will allow the use of Serostim in a controlled clinical setting.

AIDS-related wasting syndrome is a profound weight loss of greater than 10 per cent of usual body weight in a person with HIV infection. The Centres for Disease Control (CDC) have defined HIV-associated catabolism as one of the indicators of progression from HIV infection to AIDs. The syndrome is one of the leading causes of death in people with AIDS. The DFA has authorized the TIND with a "cost recovery" programme, which will allow Serono to charge $25 per milligram in the United States for the drug in accordance with FDA regulations. Cost recovery, as defined by the FDA, includes costs of manufacture, research, development and handling of the investigational new drug. Details from: The Ares-Serono Group, 15*bis*, chemin des Mines, CH-1202 Geneva, Switzerland or on +41 22 738 80 00. (Source: *Biotechnology Bulletin*, January 1995)

Kind to kidneys

Most anti-cancer agents have their downside: as they usually work by stopping DNA from replicating, they often affect healthy as well as tumourous cells. One of the worst culprits is also, unfortunately, one of the most useful of this class of drugs—*cis*-diamine-dichloroplatinum, usually known as cisplatin. Although effective against a wide range of cancers, the compound is also extremely toxic to the kidneys, and this factor often limits the safe dose of the drug.

Research into glutathione and other molecules carrying -SH groups by a team from Fuji Kagaku in Japan may have found a solution to these problems. These molecules "detoxicate" active oxygen and other "chemically reactive toxicants" in the body, says the team. Of particular interest is S-adenosyl-L-methionine (SAMe), a compound found in all living cells.

SAMe is very unstable, and was difficult to study until the recent discovery of stable salts. The team has found that, when administered intravenously, SAMe migrates to the kidneys, where a complex series of reactions convert it to homocysteine, cysteine and glutathione. These compounds do not seem to enter the bloodstream, but stay within the kidneys' tissues, grabbing and neutralizing toxic reactive species, including those generated by antibiotics, immunosuppressants, and anti-cancer agents. When used as an adjunct to cisplatin, it seems to enhance the drug's effects, the team claims. (Source: *Chemistry & Industry*, 7 November 1994)

Gene jabs

Merck researchers' latest patent concerns DNA-based vaccines which mimic several parts of the virus particle. The team has used several DNA fragments, encoding the nucleoprotein and matrix protein which enclose the virus' own genetic material, and the haemagglutin protein found in the viral coat. These strands are incorporated into plasmid (circular) DNA, which cannot replicate.

In animal tests, the team found that the proteins encoded by the DNA in the vaccine were expressed at cell surfaces, encouraging the subjects' immune systems to produce antibodies. The nucleoprotein fragments seem to induce the biggest response and give the most protection, they claim. (Source: *Chemistry & Industry*, 7 November 1994)

Rheumatoid arthritis drug trials look promising

The pace of development of drugs to combat rheumatoid arthritis (RA) seems to be quickening, with

UK biotechnology firm Celltech announcing results of the first small-scale trial of their genetically-engineered agent. The drug not only relieves the joint pain and tenderness, but also appears to slow the disease's progression.

The drug, CDP571, is based on a synthetic antibody. It blocks the action of tumour necrosis factor α (TNFα), the protein that attacks the joints of RA sufferers. In a trial involving 36 patients, the drug induced "statistically significant" improvements in pain and tenderness of affected joints.

More importantly, the disease's "biochemical blood markers"—proteins produced by the body in response to joint inflammation—were reduced, "in some cases to within the normal range". This indicates that the drug affects the disease's progression, even after only eight week's treatment, according to Celltech Therapeutics.

The next step is a year-long trial to determine the most beneficial dosage, to start in early 1995. (Extracted from *Chemistry & Industry*, 7 November 1994)

Pig intestines provide source of cell mimics

Researchers from the Hillenbrand Biomedical Engineering Center at Purdue University in Indiana have found that a material made from pig intestine has remarkable chameleon-like properties. "Once inserted into the body, it gets broken down and rebuilt into something that resembles the original tissue or organ", explains the centre's director, Stephen Badylak.

Pigs' small intestines have three layers: an outer, muscular section; a middle layer, only about 15 blood vessels thick; and a layer of mucus. Badylak's material is made from the middle layer, small-intestinal submucosa (SIS). Although the layer is thin, he says, it is extremely strong and can be moulded into different shapes.

The remarkable thing about SIS is that the body can adapt it to mimic its own tissues. Badylak explains that the material is a composite of connective tissues including collagen, proteins and other bioactive molecules which are not yet fully characterized.

Inside the body, the host's cells send signals telling the implant how to "perform" like the original tissues at that site. This might be similar to the process which creates distinct tissues from undifferentiated cells during foetal development, Badylak believes.

If damaged ligaments are replaced by long strands of SIS, the implant forms long bundles of cells and gradually becomes stronger, just like a natural muscle, says Badylak. This could cure the catastrophic knee ligament "blowouts" which often end athletes' careers. The material can also be used to build replacement bladders, or as a graft for severely burned skin, he adds.

The team has four patents to use the material in humans, and clinical trials are expected soon. (Source: *Chemistry & Industry*, 7 November 1994)

Second BB cancer drug promising

First clinical trials of British Biotech's second cancer product, the stem cell protector BB-10010, have revealed no adverse side-effects in healthy volunteers and have confirmed pre-clinical studies that the drug mobilizes stem cells from the bone marrow into the bloodstream.

The genetically-engineered protein is the first of a new class of drug designed to prevent damage to stem cells in patients undergoing chemotherapy. The company is targeting two potential clinical uses of BB-10010: the first, to protect the stem cells during chemotherapy; the second to allow the stem cells to be harvested from the bloodstream before chemotherapy and replaced afterwards.

If BB-10010 is confirmed to have stem cell protection activity, it could make chemotherapy more effective by permitting higher doses. The ability to mobilize stem cells into the bloodstream could offer the possibility of allowing stem cell transplantation, less invasive than bone marrow transplantation procedures.

In the study, which involved 36 healthy volunteers, subcutaneous injection of BB-10010 was found to have advantages over intravenous administration.

The first study to test safety in cancer patients is now under way, with more extensive efficacy studies scheduled to start over the next three to six months in both the UK and the US.

British Biotech's leading cancer drug, *Batimastat*, continues to show promising results in Phase I II clinical trials. (Source: *European Chemical News*, 7 November 1994)

Interferon shows positive MS results

Ares-Serono has announced "positive results" from clinical trials of its native human interferon beta drug in the treatment of relapsing-remitting multiple sclerosis (MS). Six-month interim results from a study in Malaga, Spain, are reported to show a 67 per cent reduction in the number of active lesions as measured in magnetic resonance imaging scans.

The results follow earlier positive results with recombinant interferon beta. The new data "complement the significant position of interferon beta as the first ever effective therapy for patients with relapsing-remitting multiple sclerosis", according to Ares-Serono.

Interferon beta is thought to counteract the immune dysregulation seen in MS patients, so reducing the frequency of attacks and possibly preventing the deterioration of the central nervous system. (Source: *European Chemical News*, 14 November 1994)

Mutagenicity tests

A new version of the most widely used laboratory test for determining if substances cause genetic damage has been launched in the USA. The new mutagenicity test is a refinement of the so-called Ames test, developed by biochemist Bruce Ames at the University of California at Berkeley.

Ames and colleagues at Berkeley also developed the new test, dubbed Ames II. Like its predecessor, it relies on identifying "point mutations" of single DNA bases in strains of the bacterium, *Salmonella typhimurium*, to predict possible mutagenicity in humans or other mammals.

However, the new test uses six new strains to identify the changed DNA bases, which gives a kind of mutational "footprint" for any particular chemical (*Proc. Nat. Acad. Sci.*, 1994, 91, 11,606). Furthermore, it works in liquid media in microtitre wells rather than on agar-coated plates, and hinges on a colour change. These features, say its developers, allow it to detect changes with lower doses of the test substance, and make it easier to automate mutagenicity screening with a robotic laboratory system.

One other difference: while the existing test is unpatented and the strains can be obtained free (or, for companies, with a "donation") from Ames' laboratory, the new test is for sale.

The original Ames test, developed in the 1970s, is cheap, fast, easy to use and reasonably good at predicting if a chemical will cause cancer in animals. It became part of regulatory requirements world-wide for screening new pharmaceuticals, food additives and other chemicals for potential carcinogenicity. (Source: *Chemistry & Industry*, 5 December 1994)

Mastering metastasis

Researchers from Toray Industries in Tokyo have found a new weapon for the armoury against metastasis, the often-terminal stage of cancer when tumour fragments lodge and grow in different parts of the body. There is currently no way to prevent metastasis, and there are few effective treatments.

The team has found that *Beraprost*, a synthetic derivative of a prostaglandin hormone, appears to inhibit metastasis in mice. Although not spectacularly effective—it has a 52 per cent chance of success—the treatment's side-effects are relatively mild and only seen at extremely high doses, they claim. (Source: *Chemistry & Industry*, 5 December 1994)

Inexpensive test for detection of oral cancer

A doctor and two chemists have patented what they say is a simple and inexpensive test to detect oral cancer, which strikes primarily tobacco users and heavy drinkers and is the eighth most common type of cancer in the USA. Because there is no commercially available test for oral cancer, it is usually detected through a physical examination. However, by the time the cancer is visible, it has often already spread to other parts of the body. Dr. Pier Cipriani, a dentist in Washington Crossing, Pennsylvania, and two colleagues developed a test that makes use of toluidine blue, a dye that is used to colour textiles but that has been put to medical use. (Source: *International Herald Tribune*, 12 January 1995)

Diagnostic test for myocardial infarction

BioResearch Ireland has developed an early screening test for Myocardial Infarction (MI). The assay utilizes Latex Agglutination technology for the detection of the cardiac marker Myoglobin and is suitable for hospital and emergency units or for doctor's office use. The Myoglobin assay has the potential to be particularly useful in screening out the high proportion of patients who present at clinics with chest pains but who have not had a MI. High Myoglobin has a correlation with MI of only 75-85 per cent. However, if the patient has a low Myoglobin, they have not had an infarction—this correlation is 100 per cent. Thus the assay is fast, inexpensive and can screen out non-MI patients easily.

The assay detects Myoglobin released into the blood as a result of damage to the cardiac muscle. Myoglobin gives an earlier indication of a heart attack than other markers such as creatine kinase or its isoenzyme CK-MB. Levels of these enzymes also rise after a heart attack, but more slowly.

The Myoglobin protein is normally present at levels below 90 μg/litre, but following a heart attack concentrations can increase more than tenfold within 2 to 18 hours - peak levels are between 6 to 9 hours (after the onset of chest pains). Myoglobin is removed from the serum by kidney filtration, and levels return to normal within about 24 hours. Thus, acute myocardial infarction can be ruled out if there is no increase in serum Myoglobin between initial onset and 24 hours after symptoms develop.

The BRI Myoglobin Latex test provides a *qualitative assessment* of Myoglobin levels. Polystyrene particles coated with anti-human Myoglobin interact with the Myoglobin in serum to form visible aggregates when the Myoglobin concentration is greater than the cut-off point of 90 μg/litre.

The test kit is available from January 1995.

For further details please contact Sinead Canning, Marketing Department, BioResearch Ireland, Glasnevin, Dublin 9, Ireland. Tel.: +353-1-8370177; Fax: +353-1-8370176. (Source: *News Release*, 9 January 1995)

First drug for neutropenia

Amgen's *Neupogen* (filgrastim) has been approved by the United States FDA for the treatment of severe chronic neutropenia (SCN), a life-threatening blood disorder in which the body fails to produce sufficient white blood cells to fight infection.

Neupogen, a recombinant granulocyte colony stimulating factor, is the first product licensed for the condition, previously "managed" by antibiotic use. In clinical trials, 90 per cent of patients demonstrated complete or partial recovery of normal levels of neutrophil, one type of white blood cell.

SCN is the third indication for which *Neupogen* has been approved. The first, approved in 1991, is for use in cancer patients undergoing chemotherapy; the second, approved in July 1994, is for use in bone marrow transplantation. (Source: *European Chemical News*, 2-15 January 1995.

AIDS—A seething battlefield of mutants

Inner-city riots, civil war zones and rugby club dinners might all be hostile environments, but they are nothing compared with the seething battleground in the bodies of human immunodeficiency virus sufferers. New analyses of HIV drugs reveal that millions of viruses are wiped out and replaced every day. Combination drug therapies could be the only answer.

American and British researchers joined forces to investigate how fast HIV replicates when under the onslaught of three new drugs: nevirapine, which inhibits the HIV-1 reverse transcriptase enzyme, and ABT-538 and L-735,524, both of which inhibit HIV-1 protease. They used statistical techniques to count the number of new viral particles and infected immune cells (*Nature*, 1995, 373, 117 & 123). The teams were from the Universities of Alabama and Oxford, Merck, Abbott, Californian firm Genelabs Technologies, Los Alamos and the Aaron Diamond AIDS Research Centre in New York.

The analyses revealed that, with all drugs, 30 per cent of the free viral particles in the bloodstream—between 100 million and 1 billion viruses—were destroyed every day. In the early stages of treatment, the levels of circulating immune cells rise at the same time. However, the total level of free virus does not change, the disease infects new cells, which churn out new viral particles as fast as the drugs clear away existing ones.

Worse, the viral particles produced by the newly-infected cells are mutants, and usually drug-resistant. In less than a month, all the "wild-type" virus in the body was replaced by drug-resistant mutants, the teams found.

Commenting on the results in *Nature*, Simon Wain-Hobson of the Institut Pasteur in Paris says that this work proves single-drug therapies for AIDS are doomed to failure: "Only combinations of drugs have the potential to outgun the virus". But he adds that the research shows the immune system can recover if the virus can be stopped from replicating. "HIV is behaving more and more like a virus, without frills or special effects. It is unique and subtle, but a virus none the less". (Source: *Chemistry & Industry*, 16 January 1995)

Plants show promise for vaccine production

Using plants to make vaccines has moved a step closer with Axis Genetics' unveiling of its first results on animal trials with an HIV vaccine produced using the company's chimaeric virus particle (CVP) technology. The results indicate that a preventative HIV vaccine can be produced by presenting a "cocktail" of specific HIV epitopes on the surface of a plant virus. Phase I clinical trials are now being planned for 1995.

Chimaeric virus particles presenting the gp41 peptide were able to produce high levels of neutralizing antibodies. Sera from laboratory mice were shown to greatly reduce the multiplication of the HIV virus in laboratory T-cells. Scientists reported a 95 per cent reduction in HIV virus multiplication and similar inhibition of three strains of HIV.

The virus is grown in the leaves of the cowpea plant. (Source: *European Chemical News*, 12-19 December 1994)

Ciba in antimalarial drug venture

Ciba-Geigy has signed an agreement with three Chinese partners to develop a novel, orally active, fixed combination antimalarial drug.

The drug will combine benflumetol, a substance invented by the Institute of Microbiology and Epidemiology, Beijing, with the antimalarial treatment artemether. The substances act synergistically to produce a treatment which is effective and can be administered over a short period of time, Ciba explained.

Several clinical trials have already taken place in China, including trials in 1993 and 1994, conducted by a Chinese clinical team in cooperation with Ciba. Further clinical trials are planned over the next few years in Africa, East Asia and Europe, with first market launches considered possible in 1997.

The venture will source the active substances in China. The finished product will be produced in Ciba's facility in Changping, near Beijing, for export markets, and in the Kunming Pharmaceutical Factory for the Chinese market.

Ciba's partners in the project are the Institute of Microbiology and Epidemiology, the Kunming Pharmaceutical Factory, and their commercial representative and coordinator, CITIC Technology of Beijing. (Source: *European Chemical News*, 12-19 December 1994)

Alpha 1 reports hepatitis trial results

Alpha 1 Biomedicals, Inc., has reported positive results in two trials to treat hepatitis using a combination of standard interferon therapy plus two injections a week of Thymosin alpha 1.

The first clinical used the combination therapy to treat hepatitis C. Patients in the ongoing double-blind, placebo controlled trial were randomized to three arms: placebo, standard interferon and the combination therapy, said an Alpha 1 official. In the combination therapy arm, eight of 21 patients showed sustained normalization of their liver enzyme (ALT) levels compared with three of 24 for those treated with interferon alone. None of the 22 patients treated with placebo had sustained normalization of their ALT by the 26th week of treatment, the official said.

In addition, the official continued, Alpha 1 conducted an open label trial for the treatment of hepatitis B on 15 patients, six of whom had not previously responded to standard interferon therapy. Nine of these treated patients lost evidence of viral DNA and normalized their liver enzyme. Of these responders, seven also lost the hepatitis e antigen and six also lost the hepatitis surface of s antigen, said the official. (Source: McGraw Hill's *Biotechnology Newswatch*, 5 December 1994)

New gene therapy for cystic fibrosis

A new method for gene therapy may lead to an effective treatment for the fatal inherited condition cystic fibrosis (CF), according to British scientists. Using microscopic fat globules as "shuttles" for DNA, the researchers have corrected the defect caused by the condition.

CF is caused by a single defect in a gene called CFTR, which encodes a protein found in the cell membranes lining the lungs, airways and intestines. Normally, this protein forms the pores which control the transport of chloride ions and water through cell membranes; defective pores are blocked. In the lungs, this leads to a build-up of thick mucus, which makes sufferers vulnerable to lung infections.

As CF is a single-defect disorder, correcting that defect should cure the condition. The difficulty is in how to replace the defective CFTR gene with a correct version. Deactivated common cold viruses have been used as "vectors" to carry the gene, but these tend to cause lung inflammation—undesirable when CF sufferers' lungs are already so vulnerable.

The new method was developed by St. Mary's and the Royal Brompton Hospitals in London, the UK Medical Research Council's Human Genetics Institute in Edinburgh, and the University of Pittsburgh. It involves surrounding the DNA fragment with liposomes, the minute spheres of fat familiar as ingredients in high-tech cosmetics. The team tested this technique by spraying the DNA-liposome complex into the noses of CF sufferers, as the membranes lining the nostrils are also affected. It is both easier and safer to test such techniques here than in the lungs themselves, they explain.

Cell membranes are made of similar fats to liposomes, so the complexes bind easily to the cell walls. The DNA can then diffuse into the cell, where it should make the proteins form normal pores and allow the cell to secrete moisture. By measuring the voltage across the membranes, before and after spraying, the team found that there was an average 20 per cent correction of the defect, lasting about four days, in five of the nine patients treated with the spray. Moreover, they add, there were no harmful side effects.

The researchers concede that the technique needs some work before it can enter use. They need to prove that it works in the lungs, and must also improve the gene transfer and expression efficiency. However, the results of their trial were hopeful enough for the UK Gene Therapy Advisory Committee to approve further trials. (Source: *Chemistry & Industry*, 16 January 1995)

Diagnostic trends

While the economics of *in vitro* diagnostics (IVD) are attractive, it has been seen as an industry in which it is difficult to succeed. The end-user market is complex, encompassing large commercial laboratories with tremendous purchasing power, several hundred large hospitals and thousands of small hospitals. Moreover, the susceptibility of the industry to capital purchasing cycles and government regulation adds additional layers of risk.

Nevertheless, the introduction of significant new clinical chemistry and immunoassay products together with the underlying growth in health care expenditures allowed the IVD industry to expand at a 15 per cent compound rate throughout the 1980s.

The advent of the molecular biology revolution in the mid-1980s provided the diagnostics industry with tools to increase the sensitivity of its tests several fold and to bolster its revenues with the addition of novel products. This second generation of tests (immunoassays) is based on monoclonal antibody technology, which opened a new frontier in diagnostics by providing highly specific and sensitive assays, which could still be run in large centralized laboratories and in some cases on the same equipment that ran the chemistry-based tests. World-wide immunoassay sales reached $3.4 billion in 1993.

The current emphasis at the large diagnostics manufacturers is on leveraging the installed base of analysers with additional assays and emphasizing automation and productivity products. Increased integration of information management systems, such as local area networks, into laboratory management as well as the increased utilization of robotics, bar code scanning and other automation techniques in the clinical laboratory is driving business expansion. Leveraging the installed base of hardware with new software products, be they immunoassays or automation programmes, is the cornerstone strategy of many IVD manufactures.

The power of genetic engineering, including our rapidly expanding understanding of the human genome, is ushering in a new era in diagnostic testing based on the ability to probe samples for characteristic sequences of DNA. The diagnostic gambit of probe technology already stretches from the ability to rapidly and accurately identify a virulent pathogen like *M. tuberculosis* to the ability to screen a foetus's DNA for genetic defects.

In addition to the infectious disease and medical genetics applications of gene probes, cancer screening and diagnostic applications are being driven by a new-found understanding of the molecular abnormalities of cancer cells.

Over the next decade, the use of gene probes will grow from its current market of about $78 million to a market of $600 million in 2000 and $2 billion in 2004, implying 35 per cent compounded annual growth. The infectious diseases (ID) testing market appears to be the most promising, followed by cancer screening and diagnosis and, finally, the genetic screening market. ID testing is currently a $2.7 billion market world-wide, with sales of hepatitis diagnostics alone accounting for $300 million. There will be 15 per cent annual growth in overall ID diagnostics over the next five years, with a rapid conversion of current ID tests to gene probe tests.

The other major trend in medical diagnostics with exceptional commercial impact is the decentralization of diagnostic testing. Technology is now providing the framework for moving more and more testing to medically convenient locations, such as the emergency room, critical care unit, and outpatient clinic. Diagnostic devices are now available for use at the patient's bedside; they can provide accurate, rapid results thereby allowing health professionals in urgent situations to treat patients with the right therapy. As important, decentralized testing plays into health care reform's emphasis on streamlining delivery and reducing utilization of services.

Some of these point-of-care (POC) diagnostics are simplified or miniaturized immunoassays. Others are novel technologies utilizing silicon chip photolithography, microfabrication and micro-electronics. So-called biosensors—electronics which can detect changes in biological constituents—are being developed by intrepid pioneers. Experience with the first point-of-care devices in the operating room and intensive care unit has demonstrated that the instruments improve patient care.

But broader acceptance has been slow, as pioneers in POC have had to deal with the battle lines drawn up within hospitals between clinical departments and laboratory personnel. And like the early days of personal computers, pricing has been an impediment to broader implementation of POC testing. But just as innovation drove down costs in the PC industry, new technologies are expected to present not only unique systems for POC testing, but also cost-effective ones. (Source: *Genetic Engineering News*, December 1994)

Non-invasive diagnosis: early markers of renal dysfunction

The human kidney consists of about 1 million functional units, called nephrons. This is one of the more vulnerable organs of the body and can be affected by a variety of diseases, drugs or chemicals. Urinary analysis is a useful diagnostic tool for the detection of kidney impairment. Traditionally total protein concentration in urine and the levels of creatinine in blood were the most important measurements taken for monitoring renal function. However these analytes are not sensitive enough to detect early renal damage and moreover do not indicate the location of altered nephron function. Now EU funded research under the STEP programme has concentrated on an approach to diagnose more subtle renal changes comprising both nephron segment specific and sensitive analytes.

Improved biochemical and immunological methods allow the detection of minute concentrations of enzymes or renal proteins in urine which can be related to the function of specific nephron segments. This collaborative EU research project has evaluated about 30 analytes with diagnostic potential on about 800 subjects at risk of developing kidney dysfunction. Groups studied were occupationally or environmentally exposed to heavy metals (lead, cadmium) or solvents (perchloroethylene).

It was shown that several nephron segments are affected in the early stages of heavy metal or solvent exposure. In these cases no changes in proteinuria or creatinine were caused yet, but several glomerular (such as urinary fibronectine) and tubular markers (such as N-acetyl-β-D-glucosaminidase) were affected, indicating functional alterations.

Now these researchers wish to work on the further development of test systems, such as the combination of different immunological assays on one microtitre plate and

are looking for the partnership of competent industrial partners. They are suggesting differential diagnostic approaches for different stages of kidney impairment using different combinations of these analytes with an emphasis on the detection of early changes in renal function.

The researchers are interested in a joint venture agreement to extend their work and to facilitate commercial exploitation. There is potential for the development of a range of diagnostic kits based on combinations of the analytes, to detect changes in renal function over different stages of kidney impairment. For information in the first instance, contact: Phil O'Leary, BioResearch Ireland, Forbairt, Glasnevin, Dublin 9, Ireland. Tel.: 353-1-8370177; Fax: 353-1-837016.

Epstein-Barr Virus vaccine candidates and alternative vaccine adjuvants

A project funded under the EU Biotechnology Programme is investigating candidate Epstein-Barr Virus vaccines for a range of applications. The Epstein-Barr Virus is an important human viral pathogen. Greater than 95 per cent of the human population world-wide becomes infected, although in the West infection is often delayed until adolescence. The viral infection gives rise to clinical symptoms only in a number of cases, normally in the third world. Namely: Burkitt's Lymphoma (BL) and Nasopharyngeal Carcinoma (NPC). The virus is also associated with tumours in immunosuppressed patients and with Hodgkin's disease.

Subunit vaccines based on the EBV envelope glycoprotein have been developed. These subunit vaccines have been expressed in cell systems at very high levels. This EBV glycoprotein gp340 has been shown to be a protective immunogen in a primate model of lymphoma induced by EBV. The immune protection was effectively provided by cell-mediated immune responses.

Subunit vaccines require adjuvants. Currently the only adjuvants licensed for human use are based on aluminium salts, which are only effective in a limited number of conventional vaccines. Furthermore they are not as effective when used with the new experimental recombinant viral subunit vaccines as they induce only weak cell-mediated immune responses. Therefore they probably will not be as effective in inducing protective immunity.

Now immunostimulating complexes (ISCOMs) are being investigated as alternative adjuvants with possibilities for potential human use, since ISCOMs of chemically defined composition have negligible toxicity.

A recombinant-derived subunit vaccine based on the EBV envelope glycoprotein gp340 molecule will shortly enter its first human trials. The parties involved are interested in finding joint venture partners or licensees. For further information in the first instance, please contact: Phil O'Leary, BioResearch Ireland, Forbairt, Glasnevin, Dublin 9, Ireland. Tel.: 353-1-8370177; Fax: 353-1-837016.

Livestock applications

Improved fish farming tank

Scientists at Norway's Veterinary Medicine Centre for Aquaculture Research, which is part of the SINTEF group based in Trondheim (Norway) have developed an aquaculture tank that can dramatically reduce the risk of disease transfer. Dr. Bjørnar Eikebrokk of SINTEF NHL, who has been at the centre of the development of the BIOFISH simplified recirculation tank, and is the head of research, says "We believe we have developed a relatively simple technology that will mean fish farming can take place without any danger of harmful discharges of nutrients and fish pathogens, which ought to make it easier to obtain permission to start small-scale farming of freshwater fish in rural districts. We believe that this technology could be the basis of a supplementary income for farmers threatened by competition but with access to water resources".

The BIOFISH tank is already in commercial production, and the investment needed is not great. The tank is a closed aquaculture system suitable for charr, salmon, trout etc., as well as for raising fry and fish for stocking. It is fitted with its own simple biological water treatment unit, which means that water consumption is extremely low, since the water is used over and over again. Air is blown into the water to ensure that the oxygen supply is adequate. Pure oxygen can also be used. The freshwater consumption of a 7 m^3 BIOFISH tank applied for the production of brown trout restocking fish, is only 7-10 litres a minute, compared to a consumption in a typical flow-through system, which is as high as 150-200 litres a minute. The low water consumption and the integrated biological water treatment system make it simple and cheap to disinfect the water against any disease-carrying micro-organisms. The tanks that have been tested are three metres in diameter and about a metre deep. The results of a three-year demonstration and test project where the fish farmer used and operated the system himself, have been very good. The self-cleansing unit functions extremely well, feed consumption and discharges are low, and the fish have grown well. The BIOFISH tanks have also turned out to be very simple to operate.

The BIOFISH system has also been tested in Trondheim and in a number of other places in Norway. The University of Trondheim, AVH has purchased the system for its research station. (Source: *Gemini*, November 1994)

BSE—First ever test available in a year

UK Biotechnology company Proteus has developed the first test for bovine spongiform encephalopathy (BSE). The company believes that the technique could make it possible to detect the disease in live cattle before symptoms develop.

Researchers at Proteus made a portion of the "prion" protein which is believed to cause BSE. They injected this into rabbits, whose immune systems generated an antibody that binds to this peptide and to the complete prion protein. The prion-antibody complex can be detected by staining, says Peter Swift, head of the animal health division.

At the moment, BSE can only be detected by examination of carefully-prepared brain tissue through a microscope. The Proteus test would make detection far simpler, says Swift. If, when the antibody is added, a brain section stains, the prion is present. This form of the test could be used on all freshly slaughtered cattle to confirm whether the animal had been infected.

But the most interesting application for the test is with live animals. The company is trying to boost the technique's sensitivity so that it will work on body fluids, allowing diagnosis from a blood sample. This would be useful, explains Swift, because most beef cattle are slaughtered before the disease's symptoms develop.

The company has tested its technique by diagnosing BSE in samples of cattle brains, only some of which were from infected cows. The test proved to be 100 per cent accurate, says Swift. The UK Ministry of Agriculture is currently checking these results.

Proteus is discussing commercialization with several major companies. (Source: *Chemistry & Industry*, 7 November 1994)

Unresolved: BGH impact on the health of cows

Debate continues on the question of whether the engineered bovine growth hormone (BGH) approved by the US Food and Drug Administration in 1993 to boost milk production harms cows. At issue is whether cows stimulated by the drug exhibit increased rates of mastitis, an inflammation of the udder that can trigger increased use of antibiotics. Monsanto says that its data reveal little difference in mastitis in injected versus non-injected cows. Other scientists, however, question Monsanto's conclusions. The controversy persists, in large measure, because the company has not fully disclosed all its data on mastitis.

In a recent *Nature* article,* for example, three British scientists have taken a new look at Monsanto's data from eight trials that counted the number of white blood cells in milk from BGH-treated and non-treated cows. The level of milk blood cells is used as an indicator of the status of inflammation in the udder. According to the *Nature* article, Monsanto's analyses were based on selected data from the trials. Monsanto analyses, which showed little difference in milk blood cells between treated and untreated cows, relied on data from weeks two and 28, not from the full 43 weeks of the trial. In their study based on an analysis of the full 43-week data and pooled data from all eight trials,** the British scientists concluded that BGH treatment produced a highly significant effect—a 19 per cent increase in white blood cells compared with milk from non-treated cows.

According to the *Nature* article, Monsanto has recently published a new paper discussing mastitis in seven trials in addition to the eight mentioned above but has refused to release the new data. (Source: *The Gene Exchange*, December 1994.

Agricultural applications

Bees recruited to kill agricultural pests

Scientists at the US Department of Agriculture in Tifton, Georgia, have worked out a way to use the honey bee to target pesticides more precisely on crop-damaging pest larvae. The bees are coated with a naturally occurring virus, *Heliothis nuclear polyhedrosis*, and deliver it to flowers in their unending search for nectar. Each bee flies some 500 miles during its 15-20 day life.

The heart of the new development is a tray attached to each hive, designed so that foraging bees pass through a talcum powder containing the virus. The approach has been tested against the corn earworm and tobacco budworm. The virus-coated bees killed between 74 per cent and 87 per cent of corn earworm larvae, compared with a natural death rate of up to 14 per cent. (Source: *Biotechnology Bulletin*, February 1995)

Simple test aids defence against cereal disease

A simple diagnostic strip test that costs only 25 cents can help farmers and researchers identify Barley Yellow Dwarf Virus (BYDV), the single worst disease of cereal crops around the world. Despite the seriousness of the disease, its impact is often underestimated because its symptoms mimic other conditions, including drought.

The breakthrough comes after 12 years of international collaboration funded by Canada's International Development Research Centre (IDRC).

The test is now being used in Canada, and will soon be applied in Morocco and Chile.

IDRC also reports that resistant cereal varieties have also been developed, and are already available in Canada. Cultivars suitable for international use are currently being tested. (Source: *The Agbiotech Bulletin*, Vol. 3, No. 2, February 1995)

Super rice

The International Rice Research Institute (IRRI) in the Philippines has developed a new breed of "super rice" that can produce 25 per cent more grain on the same amount of land as other varieties. The new rice will yield up to 12.5 tons per hectare versus 10 tons per hectare for present-day rice, translating into enough rice to feed an additional 450 million people a year. Researchers say the yield could be even further increased by developing hybrids from crosses of the new variety. IRRI breeders conceded, however, that considerable work remains to be done to build in other desirable traits before the new rice is ready for farmers and consumers. For further information, contact: International Rice Research Institute, Public Relations, P.O. Box 933, Manila 1099, Philippines. Tel.: 63-2-818-1926; Fax: 63-2-818-2087. Email: IN%"Postmaster@IRRI.CGNET.COM. (Source: *Diversity*, Vol. 10, No. 4, 1994)

Yam breeding breakthrough

Scientists at the International Institute of Tropical Agriculture (IITA) have achieved a breakthrough in conventional yam breeding by their development of new genotypes through seed hybridization. The yam-breeding problem, which had seemed impossible to solve for years, was solved because IITA had been able to accumulate a large germplasm collection of new yam genotypes with better flowering qualities which can be manipulated by crop breeders to generate new varieties. The new materials are being made available in both seed and tissue culture form to be sent to a number of African countries. For additional information, contact: Dr. Robert Asiedu, Head, Root and Tuber Improvement Programme, International Institute of Tropical Agriculture, PMB 5320, Ibadan, Nigeria. Tel.: 234-2-2410848; Fax: 874-1772276 via INMARSAT Satellite. (Source: *Diversity*, Vol. 10, No. 4, 1994)

Hope for acid soils

Scientists at an agricultural research centre in Colombia think they have found the key to unlocking a vast potential bread basket in Latin America. The 250 million hectares of

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* E. Millstone, E. Brunner and I. White, "Plagiarism or protecting public health?" *Nature* 371: 647-48, 1994.

** With pooled data, the scientists could run more powerful statistical analyses on the data from eight separate trials.

tropical lowland savannahs are so acid that farmers have been hard put to find anything that will grow here. Until now large-scale use of the savannahs has been restricted to cattle ranchers, and the fragile soils have been damaged by over-grazing. But scientists at the Centre for Tropical Agriculture (CIAT), based near the city of Cali, have come up with a two-pronged plan which could revolutionalize use of savannah grasslands all over the world.

The strategy consists of growing two recently developed crops—acid-tolerant rice and high-protein forages—side-by-side to make the most of the arid land. The rice, *Oryzica Sabana 6*, is the result of 10 years of CIAT research. It is the first high-yielding rice variety capable of surviving in difficult savannah soils, characterized not only by acidity but by high levels of toxic chemicals such as aluminium. The improved grazing crops consist of a tough species of grass (*Brachiaria humidicola*) which originated in Africa and a wild peanut plant native to Latin America. The wild peanut (*Aracus pintoi*) is extremely nutritious and can carry six times more cattle and fatten them nine times faster than normal savannah grass. Wild peanut plants also have the advantage of improving the soil by "fixing" nitrogen. Soil bacteria in nodules on their roots convert atmospheric nitrogen into nitrogenous compounds usable by the plant.

Says Professor William Scowcroft, a director of genetic research at CIAT: "The impact of these legumes is to lower the acidity of the soil to the extent that we are in a position to put in grain crops like maize, rice and soybeans".

Experiments with rice-pasture cultivation began in Colombia's Eastern Plains in 1989. The breakthrough came when *Oryzica Sabana 6* was released in 1991, making rice-pasture association possible in the savannahs for the first time. Grown together in this way, the rice can be harvested in four months and the land then used for grazing. The rice harvest covers the cost of establishing the improved pasture and even leaves a small profit. The pastures benefit from residual fertilizer applied to the rice. In turn, rice benefits from the fertility of well-managed pastures, particularly nitrogen-fixing legumes.

Trials on farms in Colombia's Llanos region and in a similar Brazilian area called the Cerrados have had promising results. The system is now being opened up to commercial farmers in both countries.

Increasing the productive capacity of the savannahs may also set off a positive cycle which will improve the land for generations to come. According to CIAT's agricultural geographer, Professor Peter Jones, the technique could be used in other tropical countries, particularly in sub-Saharan Africa. "Central and southern Africa, Zimbabwe, Zambia and Zaire are very similar in climate and in soil to central Brazil", Jones points out. "Therefore if we get something to work in the Llanos of Colombia or Brazil it could be transferred to these countries". (Source: *Development & Cooperation*, No. 3/1994)

Applications for ice nucleating Zymomonas mobilis cells

Certain aerobic, Gram negative bacteria possess a membrane protein that enables them to nucleate crystallization in supercooled water. These ice-nucleating bacteria are generally members of plant epiphytic communities, i.e. particular species of Erwinia, Xanthomonas and Pseudomonas. The phenotype is encoded by a single gene named ***ina*** or ***ice*** that has been cloned. *Pseudomonas syringae* possesses the *inaZ* gene and currently is used in artificial snow manufacture under the name Snowmax. In addition ice nucleating bacteria have potential applications in the production and texturing of frozen foods.

However for practical reasons such as regulatory and safety constraints the use of the ice nucleating gene in food based applications would be more straightforward in a GRAS (Generally-Regarded-As-Safe) organism such as *Zymomonas mobilis*. For this reason European researchers have transferred and expressed the *P. syringae* ice nucleating gene *inaZ* in *Z. mobilis*.

This research studied the use of the *inaZ* gene as a sensitive signal reporter for genetic work, i.e. this gene operates a very sensitive signal, more than 10^5 times better than β-galactosidase and it can be quantified by a straightforward droplet freezing assay.

This research also opens the possibility of use of the organism expressing the *inaZ* gene for industrial biotechnological applications. One of the applications could be freezing control. Freezing is a common step used in food processing. Bacterial ice nuclei can be used as a controlled source of nucleation sites in freeze processing.

This study will be of interest to both researchers and the bioprocessing industry. In the academic world the availability of ice nucleation reporter genes as a sensitive signal is of great importance. Regarding the industrial applications, this research is building a solid foundation from which many potential applications can be developed with time. For more information, in the first instance, please contact: Phil O'Leary, BioResearch Ireland, Forbairt, Glasnevin, Dublin 9, Ireland. Tel.: 353-1-8370177; Fax: 353-1-8370176.

French go-ahead for hybrid wheat

Hybrinova, the seeds subsidiary of Lafarge Coppée and Crédit Agricole, has been granted registration by the French authorities for its first hybrid wheat varieties. The company plans to have its first seeds on the market this autumn, ahead of its competitors Monsanto and Ciba.

The group is seeking investment partners "with a view to putting it on a profitable footing as early as possible". In Europe, the group estimates the market could be as high as FF 15 billion; in China it is potentially twice as large.

Production of hybrid wheat involves cross-fertilization between two varieties, of which one is partially sterilized by the artificial elimination of the male gametes or pollen. Hybrinova has chosen a chemical hybridizing agent, rather than a genetic route. The breakthrough follows six years of research in collaboration with Institut National de la Recherche Agronomiques, plus two years in gaining regulatory approval. (Source: *European Chemical News*, 2-15 January 1995)

UK approves three "whole foods"

Three genetically-modified foods, developed by Zeneca, Monsanto and Belgian firm Plant Genetic Sciences (PGS) are safe for human consumption, the British Government has decided. However, none will go on sale until the issue of labelling has been resolved.

Zeneca's products are tomato ketchups and purees, made from the tomatoes developed with Campbell's to resist softening and rotting. PGS has engineered oilseed rape plants whose flowers have sterile "male" parts, this stops self-fertilization and makes it easier to create

vigorous, high-yield hybrids. Extracts from Monsanto's soya beans, engineered to be resistant to the company's **Roundup** brand of pesticides, have also been approved.

However, the products will not reach the market until the Government decides how the foods should be labelled. Zeneca has already decided to label its tomato products voluntarily; the pastes and ketchups could go on sale by the end of the year. PGS's oilseed rape and Monsanto's soya beans are both still in development and are not yet available in bulk; it will be two to three years before products from either company reach the market.

The UK is the first country in Europe to approve "whole foods" produced by genetic engineering—that is, foods containing altered genes rather than those made using genetically-engineered organisms such as yeasts, or enzymes made by modified bacteria. (Source: *Chemistry & Industry*, 16 January 1995)

Transgenic squash to be marketed

The US Department of Agriculture (USDA) has approved the commercialization of the first transgenic crop engineered for virus resistance. With the USDA's approval, the crop—a transgenic virus-resistant yellow crookneck squash developed by the Asgrow Seed Company, a subsidiary of the Upjohn Company—is now cleared for entry into the market place.

The transgenic squash will be the first genetically-engineered whole food to enter the market place unlabelled. The company plans to sell seeds to farmers who will grow and market the squash. Unless the farmers choose to label the squash—an extremely unlikely possibility—they will enter the market place next year indistinguishable from normal squash. The FDA does not require that most genetically-engineered food be labelled. The first genetically-engineered whole food, a delayed ripening tomato sold directly to consumers, was labelled voluntarily by its producer.

UCS criticized the USDA approval of the squash because the Department, despite two years of deliberations, has not properly addressed the environmental risks of the transgenic squash. Those risks include the potential for engineered genes to move into wild relatives and produce new weeds or threaten a centre of diversity for squash, creating new viral strains, and enhancing the weediness of squash. (Source: *The Gene Exchange*, December 1994)

Tissue culture products

The canned and concentrate pineapple industries rely on a continuous supply of pineapple fruit as their main raw material. Though seedlings produced by conventional means cost less than those produced by innovative means of propagation, the pineapple industries cannot rely solely on conventionally produced seedlings because production cannot keep pace with demand.

In establishing new banana or ginger plantations, large numbers of seedlings with uniformity in size, age and quality are needed. To provide those seedlings of superior quality in a short time, propagation methods, other than the conventional, must be considered.

Tissue culture has many advantages over other propagation methods. Seedlings may be provided all the year round and it can be used as a tool to obtain disease-free plants. These advantages and superior seedling quality make tissue culture an obvious choice for the pineapple industries and banana and ginger plantations.

In 1994, the world's import of canned pineapple is estimated at 1.12 million tons, representing an increase of 27 per cent over only four years. This projection indicates a need for greater production capability.

At first, tissue culture is not cost competitive as a propagation method for many crops. To complete with the cost of conventional methods, tissue culture would have to be made more efficient and cost effective, by keeping equipment costs down and plantlet quality high. Entering into this highly specialized business requires great effort. To lower production cost, labour and total process time must be reduced along with an increase in the multiplication rate.

Several methods must be explored to develop an advanced system for propagating plants *in vitro*. The bioreactor micropropagation method developed by DNA Plant Technology could be the most important and promising technique employed at Fitotek in the near future in anticipation of a demand for more than 15 million plants per year. By using the bioreactor system, it may be possible to reduce costs to a level lower than conventional propagation methods, making the products commercially feasible.

Fitotek, of the Kaltimex Jaya Group, is confident that the bioreactor will be very efficient and replace a large number of conventional micropropagation systems. With the advantages of superior quality and a well-developed sales network, Fitotek will be able to sustain the production of seedlings in the coming years.

The main concern in using the bioreactor for mass propagation is the production of uniform plantlets both in size and high quality. In a search for that consistency, design, media and frequency of subculturing are among the variables that have been observed. To prevent the plantlets from suffering a lack of green-coloured leaves, enough lights must be placed around the bioreactor vessel. Suitable media to provide nutrients and a simple technique in the subculturing process have been employed in an effort to raise the consistency of the quality of the plants. Fitotek found that the total number of harvestable plantlets from one, 10 litre bioreactor vessel is 3,400 (generated from 32 initial shoots), which are graded as follows:

Grade A: 4.0 - 6.0 cm
Grade B: 1.5 - 3.9 cm
Grade C: < 1.5 cm

Disuniformity in size was observed in the results of the process and it is evident that further investigation is needed to achieve uniformity of the propagated plantlets.

One of the most important barriers to the propagation of plants using tissue culture is the genetic variability in the regenerated plants. It is important, though costly and time consuming, to conduct fidelity tests to compare the plantlets produced by the bioreactor with those produced by conventional means of propagation. It is only with the results of such a test that customers may be assured of the quality of tissue culture products.

Isoenzyme electrophoresis has been used extensively to analyse the regenerated plants genetically and has shown that the plants contain isoenzyme bands found in the mother plants. Isoenzymes can serve as a method to prove true-to-type seedlings; however, they are variable within plant tissues and zymograms should be interpreted cautiously. (Extracted from *Bio Link*, Vol. 2, No. 1, 1994)

Extraction industry applications

Bacterium living in petroleum

A joint research team of Japan's National Institute of Bioscience and Human Technology and Tonen Co. Ltd. has succeeded in creating a strain of bacteria that normally lives only in an aqueous solution, allowing the bacteria to survive in an organic solvent such as petroleum.

Biocatalysts such as microbes are normally hydrophilic, and cannot live in an organic solvent. Most chemical substances are not soluble in water but can be dissolved readily in an organic solvent. Therefore, most chemical industries involve organic solvent processes, and with a few rare exceptions, biocatalysts such as microbes are little used as catalysts in chemical industries.

Experiments were conducted on 400 million types of bacteria by mutation such as ultraviolet irradiation, then adding an organic solvent to cause mutation, from which three strains of bacteria capable of resisting organic solvents were created. Bacteria capable of living in organic solvents will free them from the limitations of utilizing microbes in aqueous solutions and enable application to efficiency improvement of various industrial processes. The research team observes that the technology is applicable to various microbes and is engaged intensively in further research for early commercialization.

The new technology is a so-called time machine biotechnology that causes artificial evolution by modifying deoxyribonucleic acid (DNA) possessing gene information. It does not induce mutation at random but with a specific function as the target, and mutations are based in that function. Ultraviolet radiation is irradiated on microbes and bacteria with the aim of creating mutants by causing mutation in special types of environments.

To create organic solvent-resisting bacteria, the joint research team used a bacterium that decomposes a sulphur compound known as dibenzothiophene (DBT). Firstly, the bacterium culture was spread on a specified agar plate, then irradiated with ultraviolet rays for about 20 s, followed with the addition of an organic solvent such as heptanol and then culturing. These processes were repeated 20 times while gradually increasing the concentration of heptanol.

Heptanol is highly toxic and ordinary bacteria will not survive, but it was possible to detect three strains of organic solvent-resisting bacteria from among roughly 400 million which were cultured. They survived even in a highly concentrated solution consisting of almost 100 per cent heptanol. The details of the mechanism of evolution are as yet unknown, but a big change has been confirmed in the fatty acid structure of the cell membrane, where the saturated fatty acids were changed to unsaturated fatty acids and the fluidity increased, which are the factors allowing resistance to organic solvents.

The capability to decompose DBT was about 80 per cent compared with before the evolution, but the technology developed by the joint research team has a broad range of applications, such as for using microbes to produce diverse chemical products. Further details available from National Institute of Bioscience and Human Technology, Agency of Industrial Science and Technology, 1-1, Higashi, Tsukuba City, Ibaraki Pref. 305, Tel.: +81-298-54-6022; Fax: +81-298-54-6005. (Source: *JETRO*, October 1994)

Chemical applications

Biopolymers

Traditionally, Mexicans used to eat just about all of the Nopal cactus plant found dotted around the country's dry and dusty deserts, but they never quite acquired a taste for Nopal "saliva"—a sticky, viscous stuff—and tried to get rid of it by throwing brass coins into the cooking pot. However, the saliva contains a mix of biopolymers which may prove to be the latest in raw materials for the paper and paint industries.

Philippe Tanguy at the Ecole Polytechnique of Montreal (Canada) is working with colleagues at the University of Mexico to develop the biopolymer for paper coatings. Currently 20 per cent of paper is coated with a fluid to improve its "printability" for colour printing. In the near future, he believes, all paper will be coated.

The industry uses a coating fluid based on water, clay and polymer additives which act as binding agents, says Tanguy. One of the most common additives is CMC, carboxymetalo-cellulose.

The attraction of the cactus biopolymer over typical additives is its stability. Also, more polymers are used now than in the past, which adds an intrinsic instability to the fluid itself.

Tanguy thinks that the saliva extract could replace most polymer additives. This would stretch to paints, food and chemicals and he believes that they will be cheaper. The raw material grows profusely in Mexico, it just depends on the costs of extraction and refining.

The Aztecs used the Nopal saliva in their paintings which can still be seen today. (Source: *Chemistry & Industry*, 19 September 1994)

Photocatalytic bactericidal tiles and sanitary ware

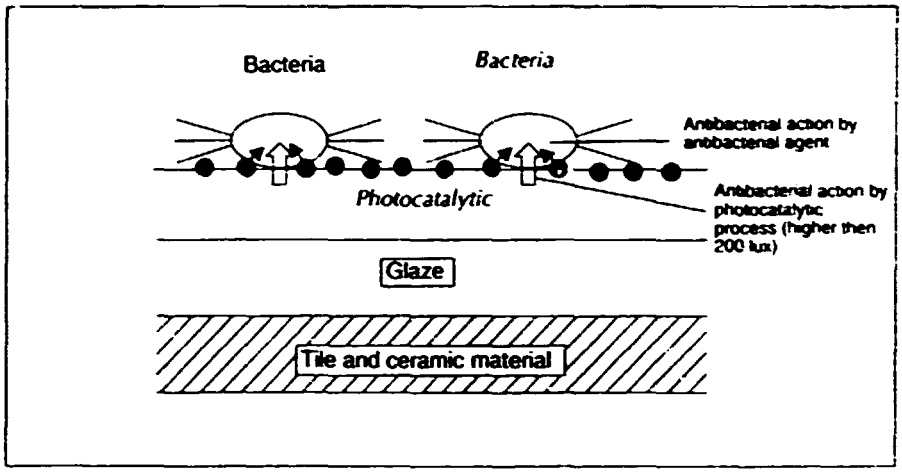
Toto Ltd. of Japan has developed the world's first bactericidal tiles and sanitary ware using photocatalysis. The ceramic surface has a film of photocatalytic titanium oxide which is then plated with a silver or copper compound by photoreduction.

In the presence of fluorescent light, 99 per cent of bacteria are killed in about one hour. Even in darkness, the same bactericidal effect can be achieved in some three hours. The photocatalytic ability of the new product also decomposes organic materials, so that stains and unpleasant odours are eradicated.

When titanium oxide is put in water and irradiated with fluorescent light or ultraviolet radiation, the decomposition of water occurs and oxygen and hydrogen are formed. Active oxygen is also formed, which is a very strong oxidant that destroys enzymes of pathogenic bacteria including *Escherichia coli*, *Pseudomonas aeruginosa*, and methicillin-resistant *Staphylococcus aureus*.

Titanium oxide film can be formed on ceramics by conventional methods, but the film is not firmly attached. When a ceramic simply coated with titanium oxide is heated, the coating peels off from the under layer. Toto invented a special solvent for titanium oxide. The solution is sprayed on workpieces to form films about 1-μm thick. The film strongly bonds to the under layer without needing adhesive.

In darkness, the photocatalytic titanium oxide does not cause a chemical reaction, and so cannot kill bacteria. The company takes advantage of the reducing power of the



Antibacterial principal chart of photocatalytic bacterial tiles and sanitary ware

photocatalysis to coat each article with bactericidal silver or copper ions. The photoreduction coating technique achieves bactericidal activity in darkness.

Potential customers include medical institutions such as hospitals and nursing homes for the aged. Food processing plants and other firms required to maintain high standards of hygiene are also potential markets.

The special treatment will make the ceramics some 30 per cent more costly than conventional interior tiles and sanitary ware. Further details from Toto Ltd., Tokyo Public Relations, 1-1-28, Toranomon, Minato-ku, Tokyo 105. Tel.: +81-3-3595-9422; Fax: +81-3-3595-9498. (Source: *JETRO*, October 1994)

Food production and processing

Fingerprinting bacteria in food

In the laboratories where bacterial cultures are told apart by means of their colour, shape, smell, texture, appetites, effluents and general vivaciousness, workers joke that Pasteur himself could still help at the bench, so long-established are the techniques they use. This could all be changed by new technologies, notably those that a team at Du Pont, a plastics maker, has incorporated into a device called a RiboPrinter. Ribosomes are vital pieces of cellular equipment that turn genetic messages into useful molecules. All living creatures have them, but always in slightly different forms. The Du Pont machine scoops out the DNA from a culture of bugs and cuts it into fragments. The sizes of the particular fragments looked for depends on the ribosome genes; by comparing the sizes with those of 10,000 bug-types stored in its memory, the RiboPrinter does to the bugs something similar to what DNA fingerprinting does to people.

This bug-printing technology, like its human analogue allows producers of food to find exactly what strain of bug is causing a problem, and so to narrow their search for the source of contamination. It allows doctors to know what is infecting someone with food poisoning, and thus to narrow down the range of sources from which the bug might have come. In both respects, the RiboPrinter is faster and more precise than older methods.

Du Pont's machines have been developed as part of a strategic attempt to make more money out of the R&D assets Du Pont has built up for its core businesses. (Extracted from: *The Economist*, 24 December 1994 - 6 January 1995)

Europeans grapple with issues surrounding biotechnology and food supply

Public acceptance of biotechnology is clearly a key issue for all companies involved in the food sector, especially those that sell directly to consumers—like the food industry.

Experience to date shows that the public is unlikely to accept all applications of new technologies. In response, Europe's food industry is increasingly recognizing that it needs information on just what consumers would accept so that it can focus on these applications.

Europe's food industry does not have a strong history of communicating with the consumer. In the recent past, inadequate communication has led to poor acceptance of "E" numbers—the safety-based system of classifying food additives in the EU, which has been a focus of consumer discontent.

A second example was consumers' rejection of irradiation to prolong the shelf-life of foods. This occurred because the industry was unable to get across the message that this is a safe technology, despite the broad scientific consensus that it poses few risks and despite legislation that would have allowed its use.

The food industry is eager not to repeat the same mistakes with biotechnology. The food industry recognized that potential benefits could be achieved with the help of modern biotechnology by upgrading raw materials, processes and end-products. With these goals in mind, a common objective was agreed on: to reach a consensus on responsible applications and "establish the conditions under which these applications could be brought to the market".

A major positive outcome from this dialogue in the Netherlands has been that the country now has in place novel food legislation that is supported by industry, consumers' groups and environmental activists.

One area of controversy that has been only partly resolved, however, is that of labelling. On the industry side, some companies are still reluctant to go beyond basic labelling requirements and identify biotech-based foods due to worry that such products will be singled out for criticism.

At the EU level, labelling of genetically-engineered foods remains a crucial outstanding question. Dr. Robert Hankin, of the foodstuffs section of the directorate-general for industrial affairs (DG III), highlights three aspects of existing European Commission proposals:

Scope. All new foods and food ingredients, including those produced using recombinant DNA technology, will be

covered by the proposed legislation, but it will not apply to foods that are "substantially equivalent" to existing foods.

Procedure. Simple cases that do not raise public health concerns will be identified through initial screening of applications by the food assessment body of one of the member States. "However, if any member State or the Commission considers it necessary, a full-scale safety evaluation will apply", Dr. Hankin said.

Labelling. The current Commission proposals envisage that labelling would be needed if there are significant differences between the novel food and the conventionally produced form. "Such differences might relate to the composition of the food its nutritional value or its method of preparation and also take account of cultural, ethical or public health factors".

For the future, the food industry aims to promote discussion and provide information on all aspects of food, including modern biotechnology, through a new, more formal industry group, the European Food Information Council (EUFIC). Companies involved include Cadbury, Coca Cola, Kraft Jacobs Suchard, Mars, Monsanto Europe, Nestlé and Unilever.

One of the objectives of the group is to foster a climate of opinion that does not discriminate against food products simply because they may have been using modern biotechnology. Task forces have been set up in France, the United Kingdom, the Netherlands, Spain, Switzerland and Germany.

Several vital concepts regarding risk assessment should be communicated to the public, according to Professor Jozef Schell of the Max Planck Institute (Cologne, Germany). He pointed out that today's agricultural practices are "one of the biggest sources of environmental pollution". If allowed to continue, there will be rapid and possibly irreversible deterioration of the environment, putting the sustainability of agriculture into question.

He also emphasized that plant breeding is one of the most effective methods of "improving agricultur l productivity without simultaneously destroying the environment". This applies to industrialized and developing countries and to intensive and extensive agriculture. If it is to be commercially viable and environmentally acceptable, agriculture must be productive, he added. To "diminisn the negative impact of agriculture on the environment, one should optimize productivity to obtain the maximum quality and yield for a given input".

"For plant breeding to contribute to the 'enormous problems of the future, the best techniques must be used, including genetic engineering", emphasized Professor Schell. "The resulting plants must then be compared to already available crops for their effects on health and on the environment". (Source: *Genetic Engineering News*, 1 January 1995)

Industrial microbiology

Enzyme process with environmental advantages

Under the title *Biotech Swears White is Green*, the Perth-based company, Biotech International Limited, announced an enzyme process with environmental advantages to process and leach paper and is set to take the next major step in the development of an environmentally-friendly biological paper pulp and bleaching process.

Following the successful isolation and laboratory testing of three micro-organisms from the thousands screened, Biotech International Limited is approaching the stage for the large-scale production of the enzymes and full mill trials in the next 12 months. The trio of micro-organisms were selected after a two-year search, starting in the forests of Western Australia, for fungi and bacteria which break down eucalyptus wood.

In April 1994, Biotech applied for international patents on the micro-organisms and their enzymes for application in pulping, pulp bleaching and water clarification. Patent coverage was sought for Australia, North America, Europe, Japan and China. If successful, the market potential is enormous both in Australia and overseas where each year some 1,400 mills produce more than 160 million tons of pulp and 230 million tons of paper valued at around $130 billion. Around 140 mills utilize eucalyptus which is grown in Australia, China, Chile, Spain and Brazil.

Traditionally, mills use a chlorine-based process in their operations, a process which has brought them under the environmental spotlight. Biotech's managing director, Saliba Sassine, said Biotech's enzymatic process in the pulp and bleaching stage of production is aimed at reducing chlorine use while at the same time lowering costs of production. Dr. Sassine says about a litre of enzyme would be needed to process each ton of pulp and market research shows operators would pay between $7 to $10 for enzyme product to treat each ton.

Further information: Biotech International, 2 Brodie Hall Drive, Bentley, WA. Tel.: (09) 470 4322; Fax: (09) 470 4283. (Source: *Australasian Biotechnology*, Vol. 4, No. 5, October 1994)

Re-use of spent enzymes

Professor N. Ogata and his research team of the Faculty of Science and Engineering of Sophia University and the Tokyo Women's Medical University have jointly developed a technique for easily recovering and re-using spent enzymes after use for reactions.

Enzymes were experimentally modified using a copolymer (IDc) of thermally responsive N-isopropylacrylamide (N-IPAAm) possessing reactive and groups at its chain terminals, and the characteristics accompanying temperature changes in the enzyme complex were studied. This IDc enzyme complex was confirmed to be separable, recoverable, and reusable from the reacted solution when made insoluble by changing the temperature, and retained its activity without changing the advanced structure.

The research team perceived that if polymers with aqueous solubility varying with temperature are bonded with enzymes, the aqueous solubility of the enzyme may be changed by the temperature. The polymer from N-isopropylacrylamide is dissolved in water at temperatures below 32° C and becomes hydrophobic as the temperature is raised, and was used to modify the enzyme lipase.

Carboxylic acid was bonded to the chain terminals of the polymer from N-isopropylacrylamide, and bonded with the amino groups in the lipase molecules. When olive oil was decomposed with modified lipase obtained in this manner, the lipase reacts in much the same way as ordinary lipase at below the critical temperature, but that when the temperature is raised, the reaction is terminated and the modified lipase precipitated.

The precipitated lipase can be recovered with ease from the reacted solution with a centrifugal separator, and when the temperature is lowered, it dissolves in water and returns to the reactive state. It was fully confirmed that the lipase is usable repeatedly for five times. This new technique is applicable to enzymes other than lipase, and by adding molecules such as dimethylacrylamide to polymer chains, it will become possible to adjust the critical temperature, in which case the enzyme aqueous solubility is changed within the range of 32–45° C.

Up till now, no technique had been available for recovering spent enzymes effectively, so industrial enzymes employed in the process of bioreactor manufacture were utilized in the form of "immobilized enzyme" by inclusion in polymer gel and exposure to the reaction solution. However, immobilized enzyme has a low reactivity compared with natural enzyme, so the new technology will allow improved reactivities of recovered enzymes. Further details available from Sophia University, Faculty of Science and Technology, 7-1, Kioicho, Chiyoda-ku, Tokyo 102. Tel.: +81-3-3238-3447; Fax: +81-3-3264-0867. (Source: *JETRO*, October 1994)

Process development

Intelligent software tools are becoming increasingly important to bioprocess design. Use of programs that simulate various operations carrying different loads can save both time and money, as the process can be modelled and results predicted in the virtual plant, before the first disc-stack centrifuge is ordered.

BioPro Designer® from Intelligen, Inc. (Scotch Plains, NJ), simulates several dozen unit operations, does equipment sizing and costing, offers batch and semi-continuous scheduling and creates economic reports. BioPro is offered for Windows as well as Mac platforms.

Since it can take a decade and $250 million to develop and market a therapeutic product, the firm advises that using a process simulator can speed up development, encourage accurate communication between departments and internal groups, reduce costs by optimizing the process and examine the environmental impact of various process alternatives.

The program offers interactive creation of a flowsheet, prompting the operator through development, allowing various modifications and limits to be inserted and offering unit operations from fluidized bed reactors to diafilters to flash evaporators. Finally, the reports that BioPro Designer can create include detailed cost analysis on areas from raw materials to waste treatment. (Source: *Genetic Engineering News*, 15 October 1994)

Mass production of chymosin with koji fungi

Dr. K. Kitamoto and his research team of Japan's National Research Institute of Brewing has applied gene recombination technology to establish technology using koji fungi for the mass production of the enzyme chymosin that is indispensable for manufacturing cheese.

Simply introducing chymosin genes into fungi could not improve the productivity of enzymes due to the action of the quality control function of fungi and the action of protease (protein degradation enzyme), but the productivity was improved by linking the gene of the enzyme possessed by fungi together with the gene of chymosin to create a fused protein. By applying the solid culture method using wheat bran, the productivity was increased about 500 times.

The mass production technology was established successfully in 1993 by recombining *Aspergillus oryzae*, a typical koji fungus, with the chymosin gene. However, in the initial stage, the productivity was as low as 0.1 mg of chymosin per litre of culturing liquid. The chymosin gene was linked to the koji fungus glucoamylase gene in the form of fused protein, by which the productivity was improved about five times. When solid culture was performed using wheat bran in a low pH environment, the mass production of 150 mg of chymosin per kg of culture bed became possible.

Inside the cells of microbes are organs comparable to the quality control systems of industrial product production lines, and defective proteins are degraded by protease. When a koji fungus is incorporated with calf genes ordinarily not present, there is a high probability of the protein quality being checked by the microbe, but this check can be passed safely through fusion. In addition, the provision of a culturing environment enabling manifestation of the capabilities possessed by the koji fungus led to a considerable improvement in productivity.

In Western countries, chymosin is produced using *E. coli* or yeast to supplement chymosin deficiency. Compared with these microbes, the safety of koji fungus has been fully confirmed through the historical brewing of sake and shoyu, and the koji fungus intrinsically features a high enzyme productivity. There is also the advantage that it can be applied intact to enzyme manufacturing processes using other types of enzymes.

Further details from National Research Institute of Brewing, 2-6-30, Takinogawa, Kita-ku, Tokyo 114. Tel.: +81-3-3910-6235; Fax: +81-3-3910-6239. (Source: *JETRO*, October 1994)

Novel microbial redox enzymes for the enzymatic production of chiral synthons

Essential for the bioprocessing and chemical technology industries are new ways to overcome difficult or expensive processes. For example, although oligoreductase enzymes are of importance in these industries, two thirds of all known oligoreductases are NADP-dependent. As a result, they can only be used in preparative organic synthesis if the regeneration of the pyridine (P) nucleotides can be done at reasonable cost. These P nucleotides are the co-factors which provide the energy to catalyze the enzymatic reaction.

Suitable reductive regeneration methods do exist, but a European Commission-backed project has been working to develop alternative oxidative regeneration processes. Two technologies are now on offer by the CEC-VALUE Programme.

VAPOR Enzymes: Many micro-organisms possess enzymes which can reversibly transfer electrons between artificial 1-electron mediators and pyridine nucleotides. The term VAPOR was coined for these enzymes, as they are viologen accepting pyridine nucleotide oxido reductases. These VAPOR enzymes have been studied because they are catalysts for pyridine nucleotide regeneration and because they have interesting mechanisms of action between their 1-electron and 2-electron transfer steps. This work has led to the preparation of chiral compounds and three (as yet not commercially available) viologens have been synthesized.

New Electrochemical Cell: A new approach has been developed for an alternative electrochemical cell. Glucose

oxidase is able to communicate directly with an electrode via a conducting polymer. The enzyme is adsorbed to electrodes consisting of a platinum-coated membrane on which the conducting layer is applied. Thus the enzyme is in direct communication with the electrode via the conducting polymer. An advantage of this system is that there is no need for a mediator in the reaction medium.

Details from Phil O'Leary, BioResearch Ireland, Forbairt, Glasnevin, Dublin 9, Ireland. Tel.: 353-1-8370177; Fax: 353-1-837016. (Source: *Biotechnology Bulletin*, October 1994)

Energy and environmental applications

Photosynthesis secret unlocked

A recent discovery by a group of microbiologists at the University of Glasgow may light the way to a whole new generation of solar cells. After 12 years of work the team has uncovered the final part of the mystery of photosynthesis, the process by which plants convert light into energy. (Source: *Electronics Weekly*, 19 April 1995)

Freshwater pollution

As environmental U-turns go, the comment "if you want to do a bit for the environment, it's better to use phosphate-based detergents" is hardly less startling than a ringing endorsement for CFCs. The conclusion of an industry-sponsored study of how detergents affect algal blooms in surface waters claims that the critical factor in eutrophication is a lack of zooplankton—tiny organisms, such as water fleas—which normally eat algae; fertilization is only part of the problem.

Eutrophication is the progressive over-fertilization of water which the public sees as festering masses of algal blooms choking rivers and lakes, says Eric Johnston, an industrial consultant for the Scientific Committee on Phosphates in Europe (SCOPE), the phosphate industry-sponsored group which partially funded the research.

The major source of phosphates is agricultural fertilizers, but laundry detergents, which contain sodium tripolyphosphate (STPP) as a water softener, are "an attractive target for some legislators", Johnston adds.

However, according to a group of researchers based at the Netherlands Organization for Applied Scientific Research (TNO) in Den Helder, the University of Savoie and the University of Alicante, lakes and rivers are extremely complex ecosystems. Nutrients are taken up by both algae and rooted weeds. The latter act as shelter for fish larvae and zooplankton, both of which eat the algae and are, in turn, eaten by larger fish. The teams found that unpolluted lakes can absorb surprisingly large amounts of phosphates with no problems. Add a fertilizer, and more algae will grow but so will the populations of hungry zooplankton and fish. The ecosystem is balanced so there is no net increase in algae.

Problems only arise when the lake is already polluted, explains Martin Scholten, a TNO ecotoxicologist. Zooplankton are very sensitive to their environment, and many substances are toxic to them, he says. If any of these substances are present, the zooplankton population cannot increase.

Adding phosphates to this polluted system will cause unchecked algal growth. The floating slimy masses cut off the light supply, so the weeds die and decompose, using up dissolved oxygen, and causing sulphurous smells and midge plagues. Deprived of both shelter and food, the fish larvae starve. The lake is well on the way to catastrophe.

The SCOPE teams studied the behaviour of three types of enclosed microcosm of various sizes, containing water with different levels of pollutants and various species of algae, weeds, zooplankton and other freshwater life.

The teams added "artificial household waste water"—an unsavoury combination of fresh water and sewage—to these microcosms to simulate the stresses that various substances would exert. The waste water contained a detergent solution to mimic laundry water: either 3 g litre of phosphate-containing detergent or 5.2 g litre of a phosphate-free version. (Phosphate-free detergents use zeolites as water-softeners, which are less efficient so each wash needs more detergent.) Each type of microcosm was tested with control samples and both types of detergent.

Surprisingly, the teams found the highest algal densities and lowest numbers of zooplankton in the systems with the phosphate-free systems. Replacing the phosphate-free detergent with an identical amount of a phosphate-containing version also gave large algal densities and low zooplankton counts.

The key seems to be the amount of detergent rather than its components. Surfactants are known to pose environmental problems at higher concentrations, and little is known about the environmental impact of zeolites except that, as they are insoluble, they increase the volume of sewage sludge.

Meanwhile, another industry organization, the Centre Européen d'Etudes des Polyphosphates (CEEP), has helped fund a life-cycle analysis of laundry detergents, carried out by John Lester and Gary Morse of Imperial College, London. Lester and Morse concluded that switching from phosphate to phosphate-free detergents would have only a minor effect on the environment. The best way to help the environment is to minimize the use of all detergent constituents, and remove as many potentially harmful compounds as possible from waste water, they say. (Source, *Chemistry & Industry*, 16 January 1995)

Highly absorbent hydrogel

T. Kunioka and his research team of the Polymer Reaction Laboratory of the Polymer Chemical Department, National Institute of Materials and Chemical Research of the Agency of Industrial Science and Technology have succeeded in producing a new type of hydrogel featuring excellent water absorbance by using a biopolymer generated by microbes. It is capable of absorbing water to a maximum of about 3,500 times its own weight.

The water absorbance of hydrogel produced by biopolymers had previously been at best about several hundred times its own weight, so this is the first hydrogel with such a tremendous absorbance. Since hydrogel is biodegradable, it is gentle to the environment and disintegrates when scattered. The institute plans to advance research to apply the biogel to the manufacture of paper diapers and to the greening of deserts.

The biopolymer is poly(γ-glutamic acid) (PGA), a type of poly(amino acid), synthesized by a species of *Bacillus subtilis*, and is better known as the sticky threads of fermented soybean (natto). The research team has already established a technique for producing PGA at a high efficiency, and has also confirmed that when water containing PGA is irradiated with gamma radiation, a PGA

bridging reaction occurs and a swelled, transparent hydrogel containing water is generated.

When an aqueous solution containing PGA at 5 per cent was irradiated with a gamma beam of 19 kGy, a hydrogel was produced that absorbs water by about 3,500 times its own weight but which was rather fragile. Increasing the gamma ray irradiation and PGA density decreases the water absorbency, but the strength is increased. Also, when the hydrogel was dried after swelling, it swelled again when immersed in water and is repeatedly usable.

Chemically synthesized water absorbent polymers capable of absorbing water by 10,000 times their own weight are available, but are not degraded in the soil and have the effect of deteriorating the environment. The new hydrogel is biodegradable and exerts no adverse influence to the environment. However, when using water containing salt, the water absorbency is lowered to the level of synthetic counterparts, so research is to be advanced to make improvements in this area. Further details from National Institute of Materials and Chemical Research of the Agency of Industrial Science and Technology, Polymer Reaction Laboratory of the Polymer Chemical Department, 1-1, Higashi, Tsukuba City, Ibaraki, Pref. 305. Tel.: +81-298-54-6344; Fax: +81-298-54-6327. (Source: *JETRO*, November 1994)

Waste water treatment system using Kuragel

Kuraray Co. Ltd. of Japan has acquired a bright outlook to commercialize a waste water treatment system using "Kuragel", a gelled polyvinyl alcohol (PVA) produced by a unique forming technology, and which captures and immobilizes microbes by a special insolubility treatment.

Pilot plants are already in operation at several places, and the waste water treatment system's commercialization is in progress with the cooperation of waste water treatment system manufacturers. The gel consists of spheres of 3-5 mm, its specific gravity is 1.03 or close to that of water, and displays the effect of increasing fluidity and promoting agitation. Inside, it is porous with numerous holes of 1-10 micrometers, the water content inside the gel being as high as 95 per cent with its oxygen transmittivity (DK value) as high as 70 per cent, i.e. it features an environment ideal for microbe proliferation.

The method of using microbes for waste water treatment is in widespread use, but maintaining an environment ideal for microbe subsistence is difficult, and improving the treatment efficiency by raising the microbe density has the disadvantage of increasing the viscosity and making handling difficult.

In these respects, because "Kuragel" has numerous holes which retain microbes with stability, roughly 20,000 mg of microbes can subsist in a litre of treatment water. This is a microbe density that is 3-6 times that of conventional microbe treatment systems, and the treatment capacity is increased proportionally. As a result, with an existing facility, its size can be halved with the same treatment capacity.

Already, a sewage treatment pilot plant has been constructed in a residential complex jointly with the Okayama Prefectural Environmental Health Center for sewage treatment using Kuragel, and highly satisfactory results have been confirmed. The original water's total nitrogen content (TN value) is being reduced from 25-44 to 9-18, and the biological oxygen demand (BOD) reduced to less than 20.

To prevent water quality degradation of rivers and lakes, new nitrogen and phosphorus discharge standards are being prescribed legally and waste water treatment controls are being intensified, which is certain to raise a demand for small-scale waste water treatment systems. Against this backdrop, the company is presently striving to commercialize Kuragel with the cooperation of waste water treatment system manufacturers as a waste water treatment system for use by small- and medium-scale enterprises and residential combinates. Further details from Kuraray Co. Ltd, Public Relations & General Affairs Dept., 3-8-2, Nihonbashi, Chuo-ku, Tokyo 103,. Tel.: +81-3-3277-3305; Fax: +81-3-3277-3295. (Source: *JETRO*, November 1994)

Plants to test for toxins

Scientists at the Saskatchewan Research Council in Canada will be testing the toxicity of base metals on four aquatic plants and minute phytoplankton to determine their role in developing faster, more efficient and less costly tests to screen toxicity in mining and pulp mill effluents.

Numerous tests in the USA have used plant bioassays to measure toxicity, but most have focused on measuring responses of a single organism. SRC hopes to improve these protocols by using Canadian species, a broader spectrum of organisms, and methods to determine whether mixtures of chemicals in effluents have the potential to be toxic. (Source: *The Agbiotech Bulletin*, Vol. 3, No. 2, February 1995)

New biological wastewater process

Biological treatment of wastewater can have a number of advantages over physico-chemical processes, particularly flexibility and cost. Unfortunately, such advantages can be outweighed by the problems associated with the attendant sludge disposal problems. These problems will worsen with the banning of disposal-at-sea changes in legislation relating to land-spreading and landfilling of sludge and the high capital and operating costs of incineration plants. Sludge disposal is often more of a problem for industrial wastewater treatment since the sludge may contain heavy metals or other toxins.

The Bio-Logic Process is a suspended growth, biological treatment process, created and maintained by a novel high rate oxygenation and mixing system. It achieves the primary objective, that of giving a good final effluent quality, and produces minimal or, in some cases, zero sludge for disposal. Extended trials have been carried out in sewage and animal waste treatment applications and are now under way in industrial wastewater treatment. EA Technology has laboratory scale bioreactors for experimental trials to test the technical feasibility of a given application. Pilot scale trials are carried out with a trailer-mounted transportable bioreactor. Details from Business Development Environmental & Process Technologies Division, EA Technology Ltd., Capenhurst, Chester CH1 6ES, UK, or on 051 347 2522. Fax: 051 347 2138. (Source: *Biotechnology Bulletin*, January 1995)

Culturing of algae storing liquid fuel using sewage treatment water as nutrient

Japan's National Institute for Resources and Environment of the Agency of Industrial Science and

Technology has succeeded in culturing an algae storing liquid fuel using sewage treatment water as the nutrient, and has developed technology for recovering the liquid fuel under much less severe conditions than in the past.

Sewage treatment water ordinarily drained away is used as the culture liquid, so the manufacturing cost is reduced considerably. Algae proliferate using the nitrogen and phosphorus in the sewage treatment water as nutrients, so the process can also suppress lake and river eutrophication. The stored liquid fuel is anticipated to serve as an alternative fuel in place of fossil fuel. The algae is still at the research stage, but may allow cost reduction of liquid fuels.

The algae used is *Botryococcus braunii* that belongs to the green algae family and stores a liquid hydrocarbon known as botryocouene up to about one half its own dry weight, synthesized from carbon dioxide (CO_2) gas. As long as there is sunlight and a nutrition source, this algae proliferates while fixing CO_2 and storing liquified fuel, so is expected to enable the production of an environmentally friendly type of energy.

In experiments, about 1,200 mg of the algae was placed in a 2-l culturing tank made of glass, then cultured for one month under CO_2 and light. When the algae was cultured while supplying sewage treatment water continuously, about 200 mg of algae can be extracted continuously per litre of culturing liquid each week. Algae produced in a culture bed contains 50-58 per cent of liquid fuel, but that produced with sewage treatment liquid contains about 50 per cent of liquid fuel. The sewage treatment water after aerobic biological treatment primarily contains nitric acid ions as the nutrient since *B. braunii* is highly compatible with nitric acid ions as the nitrogen source.

Meanwhile, recovery experiments were conducted under the conditions of 200° C and pressure of 40-50 Pa to cause thermochemical liquefaction. The product from the reaction container is cooled and depressurized, and is an oil resembling heavy oil, which mixes with water and contains gaseous carbon dioxide and a semi-solid substance called char. The oil is recovered by static separation, the char combusted together with oil, and the hydrophilic components undergo repeated sewage water treatment. Ultimately, only ash remains when the gas and char components are combusted.

The Institute earlier confirmed that the liquid fuel contained in the algae can be recovered efficiently by using a catalyst at 300° C and a pressure of 100 Pa, but this time established technology for extracting the liquid fuel under less severe conditions without using catalyst. Further details from National Institute for Resources and Environment, AIST, 16-3, Onogawa, Tsukiba City, Ibaraki Pref. 305. Tel.: +81-298-58-8111; Fax: +81-298-58-8118. (Source: *JETRO*, October 1994)

Cleaning system reduces feed waste

A newly developed cleaning system for fish farms is currently being tested at Ytteroy Sjoprodukter in Norway. The system will mean lowered emissions of "leftovers" and faeces. It will also monitor the feeding habits of the fish, which may reduce feeding costs.

Scientists at SINTEF NHL (Norway R&D agency) are behind the cleaning system which was installed at Ytteroy Sjoprodukter, and is in the process of building up a commercial halibut farm.

The cleaning system, which goes under the name of "Particle Trap", was developed for use in closed aquaculture systems. The trap has two functions: it gathers food remains and faeces from the waste water so that these do not return untreated to the sea, and it also continuously records the amount of feed present in the water so that the quantity and timing of meals can be regulated.

The Particle Trap has already shown that for a while, the fish were being given too much food. Subsequently the amount of food had to be increased because virtually none of it was going to waste. Feed is a major cost element and if this system enables one to accurately adjust the quantity given to the fish it will cut costs.

The fish farm has a total of 8,500 halibut, and the Particle Trap is being tried out in three tanks that hold a total of about 2,000 fish. Two tanks have built-in shelves on which the halibut can lie, another development which is due to the NHL researchers. The idea was to increase the effective area of the tank by allowing the fish to lie on both the bottom and the shelves. Halibut are bottom-living fish that prefer to lie on the floor of the tank. But it soon gets crowded down there. That is why the shelves were put in which the fish seem to like The Particle Trap also functions well in that tank. Water in the tanks is changed continuously. So far, the waste is not recycled, but work is under way to develop disinfection processes that would allow it to be used as fertilizer, for example.

How it works

The principle of the Particle Trap is that the water outlet in the middle of the tank is divided into two. The main pipe goes vertically up in the tank with a strainer at the top, so that most of the water is discharged without carrying food remains or faeces with it. The other pipe lies right at the bottom of the tank and collects the particles.

"We remove so much water here that the bottom sludge is taken by a pipe to a collector where it is separated, so that the particles fall to the bottom and can be collected, while the water is released", says Arve Berg, a SINTEF NHL scientist.

Two types of particle trap have been developed. One of them requires a swirl or current eddy in the centre of the tank, and is intended for salmon, which prefer to swim in rapidly flowing water. This version has been patented by SINTEF, and has been industrialized by Rupro Plast of Lokken.

The other principle is based on gravity, in that the particles fall to the bottom of a sludge pot before they are sucked out into the collector. This is most suitable for flatfish such as halibut, which prefer water with a low current velocity.

"The Particle Trap is a tool that monitors the appetite of the fish in real time, offering a basis for controlling the amount and timing of meals. It is neither economic nor environmentally friendly to feed fish when they are not hungry, so that food is wasted", says Arve Berg. "We can say the same of giving fish too little food, because this means that they have to be kept for longer before they can be harvested". (Source: *Gemini*, November 1994)

Breakthrough for bioreactor

Studies carried out by SINTEF Oslo have demonstrated that oily waste can be cleaned by using biological methods.

When oil tanks are cleaned out, the oil companies are left with oil-sludge that is difficult to get rid of. Esso

Norge A S has carried out successful tests in which oily sludge has been composted. SINTEF has monitored the tests and determined that most environmentally harmful compounds in the oil are degraded. "We cannot obtain total cleaning, but this type of treatment is better than just dumping the sludge, says Ove Bergersen, a microbiologist.

Composting is currently being tried out as a means of dealing with many different types of waste, and the technique is on the verge of a breakthrough. It started with the treatment of sewage sludge from purification plants in a bioreactor. SINTEF Oslo has helped to further develop the technique, and two bioreactors with capacities of 25 and 40 cubic metres respectively are in operation. Several local authorities have shown interest in starting similar facilities.

The principle is simple: sludge and bark are filled into a rotating tank. By controlling the temperature, ventilation and humidity, the mass is converted in the course of 14 days to a steaming heap of compost with a temperature of 60-70° C. After stowing for a month, the sewage sludge has turned into an attractive, odourless soil improvement agent.

Ove Bergersen sees a great deal of potential for this technology in the future. For example, the bioreactor can be used to deal with waste from the fishing, meat-packing and food industries, as well as manure and sorted domestic waste. Local trials of composting domestic waste have already started in many parts of Norway. (Source: *Gemini*, November 1994)

Bacteria in jelly purifies water

By adding bacteria embedded in jelly to waste water from Norwegian dairies, researchers at SINTEF have managed both to purify the water and to precipitate out proteins that can serve as animal feed.

An average sized dairy generates up to 240 cubic metres of waste water per day, or about 200 litres per minute. This waste water, mainly originating from the cleaning processes, contains fat, proteins and lactose as the dominant contaminants. If discharged to the public sewage system, the lactose in the waste water will lead to a rapid depletion of oxygen in the water, leaving no or little oxygen for the microbial degradation of other compounds.

"When our selected bacteria, embedded in a jelly, are added, they will convert the lactose into organic acids, and the waste water becomes acidic. The process does not consume oxygen, and in the acidic water the proteins precipitate out as small lumps. By adding small amounts of gas to the water, bubbles are formed around the lumps, and the cheese-like material floats to the surface where it is easily collected. In this way, we combine biological and chemical purification processes to set up a beneficial circle: waste milk is returned to the farm as feed", says Nils Dyrset, project manager at SINTEF Applied Chemistry.

A similar process has already been tested by some dairies, but in this process commercial inorganic acids are added to make the waste water acidic. Disadvantages of this process are the cost of the added acid, and that the lactose leaves the purification plant untreated.

"The financial benefits to the dairies are small", Dyrset points out. "The primary incentive for the project is the environmental aspect". (Source: *Gemini*, November 1994)

F. PATENTS AND INTELLECTUAL PROPERTY RIGHTS

EPO rules against patentability of plants

The European Patent Office has come out against the patentability of plant species *per se*. In what is seen as a precedential ruling, the EPO restricted the scope of a patent previously granted jointly to the Belgian seeds company Plant Genetic Systems (PGS) and Biogen of the United States. While Greenpeace has hailed the decision "as a decisive move to defend nature", PGS is playing down any implications.

The patent in question relates to the tolerance of plants to glutamine synthetase inhibitors, such as the Hoechst herbicide *Basta*. The original 1991 patent included a claim to all plant cells and plants which contain the specific gene. (Extracted from *European Chemical News*, 27 February - 5 March 1995)

Drug makers expect benefits from US-China patent accord

The patent and copyright enforcement agreement reached by the United States and China will result in stepped-up enforcement of intellectual property protection for pharmaceutical patents and trademarks, says a spokesman for United States name-brand drug manufacturers.

The new agreement, announced in Beijing on 26 February, provides for the establishment of government task forces in China to oversee the implementation of intellectual property in that nation and more effective means for companies to enforce their rights in China.

The trade pact also provides for the establishment of a process for frequent bilateral consultations between United States and Chinese officials on enforcement of intellectual property rights, and greater transparency in the grant and enforcement of intellectual property rights.

The drug makers have urged the Clinton Administration to designate five nations—Brazil, Argentina, India, Singapore and Turkey—as "priority foreign countries" under the special 301 trade law. This Federal statute identifies the most serious offenders of world-wide intellectual property rights. (Source: *Chemical Marketing Reporter*, 13 March 1995)

Recent legislation

Biodiversity Treaty

During the June 1992 Earth Summit, formally known as the United Nations Conference on Environment and Development, the United States refused to sign the biodiversity accord developed during the conference. The accord was designed to curb the destruction of species, habitats and ecosystems. Then-President George Bush said the pact did not sufficiently protect the intellectual property rights of United States companies and put too many restraints on biotechnology. The United States position changed under the Clinton Administration, which has indicated a willingness to sign the treaty.

The change in the United States position is based upon the Clinton Administration's belief that an interpretive agreement on the intellectual property rights section of the Biodiversity Accord will protect the rights of United States companies. The Administration has already circulated drafts of such an interpretive agreement and feels that its interpretation will be widely accepted.

The biotechnology industry, once a fierce foe of the treaty, has been mollified by Clinton's efforts to address three major concerns. The first is the protection of intellectual property rights, which would be addressed by the interpretive agreement. The second is technology transfer to developing countries and the third is the handling of genetically modified organisms. With respect to the last issue, the industry believes that the biodiversity treaty should not be interpreted to presume that a protocol, in addition to the treaty, is necessary for these organisms.

The impact of the United States agreement to the Biodiversity Treaty, with the interpretive agreement discussed above, must be analysed in conjunction with the provisions of the GATT. Other countries seem to realize that access to United States technology will be limited unless United States companies have some assurance that their rights will be respected and protected abroad.

GATT

On 15 April 1994, the United States, as well as 109 other countries and the European Union, signed the Final Act, embodying the results of the Uruguay Round of negotiations on the General Agreement on Tariffs and Trade (GATT). This Act was the culmination of a contentious multilateral set of negotiations on the basic structure of international trade and touches upon virtually every international transaction. In addition, the Act established a World Trade Organization (WTO), which will be the body charged with the responsibility for enforcing the provisions of the Act.

In general, the Act served to lower barriers to trade and to standardize the requirements for imports among its signatory countries (Members). Of primary importance to the biotechnology industry are the Act's provisions addressing the trade-related aspects of intellectual property rights.

Under the Act, each Member must provide no less favourable treatment to other Members than it would to its own citizens with respect to its protection of intellectual property rights. Furthermore, any protection afforded to one Member must be afforded to all Members, under the Most Favoured Nation clause. Thus United States companies can expect to see a higher level of protection of their intellectual property rights than has existed in the past.

Patent Act Modifications

The principal modifications to the United States Patent, Trademark and Copyright Act involve the legislation implementing the intellectual property provisions of the GATT. The issue of primary concern to the biotechnological industry is the 20-year limit imposed by the GATT on the life of patents.

Under current US law, a patent has a life of 17 years from the date of issuance and is issued to the first person to invent a product. This differs from the patent law of most industrialized nations, who grant 20 years from the date of filing and issue patents to the first person to file an application on a particular product. The Clinton Administration has proposed adopting the same patent term but

appears to have ignored circumstances that arise in the United States patent system that delay the issuance of a patent.

These delays are caused by, among other things, the time needed to resolve "interference" proceedings, where the Patent and Trademark Office (PTO) or the federal courts determine the identity of the first person to invent the product; and the PTO's requirement for clinical data to support inventions claiming a therapeutic effect. The effect of these, and any other, delays is to decrease the effective life of a patent, if the term is measured from date of filing.

To combat this, the biotechnology industry has lobbied hard on Capitol Hill for legislation that would ensure that the patent term would be no less than 20 years from the date of filing. The most recent proposal is to restore up to 5 years of patent life lost due to appeals to the PTO. Unfortunately, this legislation has proven so controversial that, as of the date of publication, no vote on it has occurred. It is difficult to predict, therefore, exactly what US patent law will be once Congress has passed the legislation implementing the provisions of the GATT.

European Union

In order to guarantee free movement of goods throughout various countries in Europe, the European Union (EU), formerly the European Economic Community, or EEC, has adopted various Directives. These have the force of European law. Among the areas addressed by the Directives are the requirements for approval to market a medical device, standards for protocols for clinical trials of medicinal products and harmonization of standards for good laboratory practices.

Medicinal products include drugs, biologics and biotechnological products. Under the Mutual Recognition and Centralized Procedure, effective 1 January 1995, manufacturers may apply for approval to market throughout the EU with a single application. This new procedure standardizes the various regulatory requirements of the European Countries for medicinal products.

Medical devices are regulated separately and, under a Directive which also took effect 1 January 1995, a standard approval process will be implemented over the next three years. By June 1998, all medical devices marketed anywhere within the EU must have received approval. In order to receive approval, a medical device manufacturer must demonstrate the safety and efficacy of the device and must pass an audit of its Quality Assurance system. This makes the new EU system analogous to FDA's PMA requirements. The major difference lies in the amount of clinical data required by the EU, which varies depending upon the device's intended use and risk posed to the patent. (Extracted from *Genetic Engineering News*, January 1995)

US Patent Office reverses decision on species-wide patent

The United States Patent and Trademark Office (PTO) has reversed its controversial decision to grant a species-wide patent on genetically-engineered cotton to Agracetus, Inc., a subsidiary of the giant chemical company W. R. Grace. The patent gives Agracetus exclusive rights over all genetically-engineered cotton, regardless of the gene transfer method employed or trait modified.

The PTO's original decision to grant a patent covering an entire species drew criticism from the United States Department of Agriculture (USDA), commercial competitors, and public-interest organizations. All were concerned about the implications of giving one company too much control over the implementation of a new technology.

The new PTO ruling came in response to a challenge from both USDA and an unidentified competitor. The reversal decision must withstand several appeals before it is final. The patent remains in force while the appeals are pending.

The notion of a patent covering an entire species is especially troubling to developing countries that harbour diverse species of potentially important plants. Such a country, for example, may find that a multinational company has obtained a broad patent covering an important indigenous plant, and for 20 years has the right to restrict all genetic engineering with regard to that plant. Patents give the holders the right to control the use of inventions in research and development as well as to prohibit sale.

Farm advocacy groups like the Rural Advancement Foundation International (RAFI) have led the international opposition to the broad species patents. RAFI has recently challenged another species patent issued by the European Patent Office on the soybean. RAFI charged that the patent, also held by Agracetus, was a threat to world food security. According to RAFI, soybeans are one of the world's most important crops, valued at $27 billion annually.

Sources: Associated Press, "Plant Gene", 19 December 1994; Rural Advancement Foundation International, "NGO's Challenge W. R. Grace's Species Patent on Soybeans from the European Patent Office", Press Release, 1 December 1994. (Source: *The Gene Exchange*, December 1994)

Genencor obtains European patent for enzyme technology

Genencor International has received a European patent for recombinant enzyme technology, despite opposition from the company's competitors.

Genencor originally received the patent in 1991 for its work on recombinant subtilisin enzymes. The patent covers specific changes at a number of amino acid positions in subtilisin, including methionine. Three of Genencor's competitors filed oppositions to the patent at the time.

The technology allows for the development of enzymes with superior properties, such as oxidative stability, which is important in detergent formulations containing bleaching agents, Genencor says.

The subtilisin molecule is among the largest commercial biotechnology products world-wide, and used primarily in detergent and other cleaning products. It also has application in starch processing, silver recovery and food processing.

On a different note, Genencor has obtained a United States patent covering a fungal expression system which is used in the production of commercial and development stage polypeptides. The company obtained the patent after a 10-year review. The patent describes a production process developed by Genencor for a range of proteins. The claims cover DNA sequences, modified *Aspergillus* host cells and procedures for fermenting the cells. Genencor says the technology allows it to express and secrete proteins at high yields and with exceptional quality. The patent forms the basis for manufacturing the chymosin enzyme, which is required in curdling milk during cheese making. (Source: *Chemical Marketing Reporter*, 6 February 1995)

New US patent review guidelines established

The United States Patent and Trademark Office (PTO) has issued new patent review guidelines that should help biotech companies establish a proprietary position in the market-place sooner. The PTO's action, announced at a press conference, also will make it easier for them to raise money.

To lure a wealthy partner to develop a new medicine, a biotech company needs a patent to assure the prospective partner of a proprietary position in the market prior to sinking money into clinical trials. But the PTO has required clinical trials as proof of utility, a fundamental prerequisite to patentability. *In vitro* and animal studies now will suffice to prove usefulness.

In October 1994, at an extraordinary hearing at the United States Patent and Trademark Office in San Diego, about 60 biotech company representatives, venture capitalists, patent attorneys and other interested parties described the problems patent examiners were creating for the industry.

"What this means is that the milestone of achieving an issued patent will come earlier, and so it will reduce an awful lot of the uncertainty that has existed in planning R&D", says William H. Rastetter, president and CEO of IDEC Pharmaceuticals Corp. (San Diego, California). Under the new guidelines, explains Rastetter, a typical patent might issue in four years instead of eight. Those years, he says, are the time when the bulk of the $120 million it takes to bring a typical biotech product to market are spent. The new guidelines can now offer that investment patent protection.

The biggest benefits will come as biotech companies developing products search for corporate partners that can supply capital.

However, the impact on start-ups would be modest, since capital remains scarce. Final guidelines will issue in March 1995.

The change in the guidelines comes just in time to mitigate some damage that the General Agreement on Trade and Tariffs (GATT) legislation may do. The patent term has been changed from 17 years from grant to 20 years from original filing. Since even under the new guidelines most biotech patents will take more than three years to issue, this amounts to shortening the effective patent term.

Moreover, GATT legislation also changed the law so that interferences by foreign applicants have become much easier.

The oldest case has dragged on for seven years on an 11-year-old patent application. The new patent term creates an incentive for the party with the weaker case to avoid settling, in order to shorten the effective life of the patent.

On the positive side, the administration has now agreed not to oppose an amendment to the GATT legislation which would restore the 17-year-from-grant patent term option. (Extracted from *Genetic Engineering News*, January 1995)

European biotechnology patent laws

The European Union is embroiled in a row over a new directive on the legal protection of biotechnology inventions. The draft directive has made slow progress as the current disagreement between the Council of Ministers, the European Commission and the European Parliament remains unresolved. The three have until the end of January 1995 to hammer out an agreement.

The Commission first put forward a draft directive on patenting biotechnology inventions in 1988. Its purpose was to ensure that patent law developed uniformly across the EU. It also set out "to try to establish a clear frontier between what is patentable and what is excluded", according to the Commission.

The Council revised the Commission's offering but this version was not well accepted by the European Parliament. Briefly, the argument is over the extent to which it will be possible to patent "life", particularly human life.

The parties began talks in a last ditch attempt to reach agreement, but was postponed because the Commission tabled an amended directive, agreed with the Council of Ministers, just two days before the planned meeting, giving MEPs too little time to consider the proposals. The new wording includes the clause: "industrially applicable patents obtained by technical means from the human body should not be unpatentable because of their human origin".

While industry could live with the proposed changes, it is not going to complain too loudly if the directive does fail. The European patent system has changed over the past five years. There is no longer the pressing need to change the European patent legislation that there seemed to be when the Commission first started to consider the subject. Since then the European Patent Office in Munich has come to terms with patent applications for living organisms.

If the Council, the Commission and Parliament fail to agree, MEPs could vote to reject the draft directive, although that appears unlikely. So it looks like the saga of a biotechnology patent directive may continue for many months yet. (Source: *Chemistry & Industry*, 16 January 1995)

Intellectual property and biotechnology

Protection for intellectual properties takes a variety of forms. Trade secrets are protected by common law if they are kept confidential, even though they cannot be registered. Patents, on the other hand, secure a limited monopoly on a technique or product in exchange for a complete disclosure of an invention.

Only products considered new and useful, which are not obvious and which involve patentable subject matter are eligible for patent protection. In other words, the patented technology must be original and have predictably useful functions, it cannot be obvious to anyone with expertise, and it must be something that national laws allow an inventor to hold a patent on—medical treatments, for example, are not patentable subject matter in Canada. With a patent, an inventor can prevent others from practising the invention without permission; however, patents do not grant any positive rights, that is, they are not equivalent to regulatory approval.

Plant Breeders' Rights (PBR) protect only the reproductive material from new varieties; for example, if rights are granted on a new variety of apple, only the seeds and trees are protected, not the apples themselves, and only if the new variety is considered to be distinct, uniform and stable.

Other forms of proprietary rights include copyrights and trade marks.

Copyright covers the form in which ideas are expressed, such as a paper or floppy disk containing a

description of a new product. Trade marks cover distinguishing words or designs.

Intellectual property protection has advantages and disadvantages. Property protection secures investments by granting a monopoly which can prevent competition and result in licensing revenues. Disadvantages include the risks involved in disclosing the invention to competitors and the relatively high legal costs.

It pays for inventors to know the rules involved in proprietary rights, the first being the requirement to maintain confidentiality until a patent is filed. Otherwise, a competitor can be "first to file" the patent, and possibly gain the monopoly. Inventors should also know the rules so that they can avoid the costs involved in unsuccessful applications resulting from a failure to meet required standards.

A significant degree of difference exists in the proprietary laws of different countries, and in the speed with which patents are considered, granted or rejected. This can mean that there are sometimes advantages to pursuing a patent in another country first. International trade agreements are leading to more uniform regulations world-wide. (Source: *The Agbiotech Bulletin*, Vol. 3, No. 3, March 1995)

G. BIO-INFORMATICS

Mine of information

MINE—the Microbial Information Network Europe—is a new database accessible through the Deutsches Institut für Medizinische Dokumentation und Information (DIMDI, Cologne, FRG). Launched and supported by the European Commission, it is an English language factual database containing information about strain cultures of bacteria, fungi, and yeasts from national culture collections of 12 European countries. A document contains:

- The taxonomy of the described micro-organism;
- Its origin;
- Culture conditions;
- Applications;
- Genetic information;
- Data on pathogenicity;
- Data on preservation, handling, etc.

Menus provide access to:

- Information about certain species and strains (when the species name or the strain number is known);
- Strains with special features (i.e., special origin, chemical and biological properties, culture conditions);
- Addresses of the MINE Member Collections;
- Recipes of the culture media on which the strains are growing.

The original data are supplied by national culture collections taking part in the MINE project (so-called Member Collections). Some of the data come from "Affiliated Collections", which cooperate with the MINE Member Collections. The integration of the data is performed by two Data Integrating Nodes, one of which works on bacteria (LMG, Ghent, Belgium), the other on fungi and yeasts (CBS, Baarn, the Netherlands). DIMDI receives the integrated and standardized data from the two institutes and operates as the so-called Central Database Node to make the database available on-line.

Altogether, 33 institutions are cooperating in the project, which is coordinated by the Royal Dutch Academy of Arts and Sciences. For more information, contact Mrs. Sylvia Herrmann, DIMDI, Weisshausstr. 27, D-50939 Köln, FRG. Tel.: +49 221 47241.

World Patents Index and Biotechnology Abstracts available on-line

Derwent Publications (London, UK) and the Scientific and Technical Information Network (STN International, Karlsruhe, FRG) have announced the release of the World Patents Index database and Biotechnology Abstracts on the STN service. The World Patents Index offers more than 6 million patent inventions from around the world.

STN International, which has recently celebrated its 10th anniversary, is jointly operated by Fachinformationszentrum (FIZ) Karlsruhe, Chemical Abstracts Service (CAS, Colombus, Ohio, USA), and the Japan Information Centre of Science and Technology (JICST, Tokyo, Japan). Derwent Publications has provided scientific and technical information to business, industry, government and research institutes throughout the world for more than 40 years.

For more information concerning the release of the Derwent databases on STN, contact Shirley Bailey-Wood, Marketing Department, Derwent Publications Ltd., Derwent House, 14 Great Queen Street, London WC2B 5DF, UK. Tel.: +44 71 344 2800; Fax: +44 71 344 2821. STN International can be contacted c o FIZ Karlsruhe, Postfach 2465, D-76012 Karlsruhe, FRG. Tel.: +49 7247 808 555; electronic mailbox STNmail (id:HLPDESKK).

Microbes in society

Power Unseen—How Microbes Rule the World by Dr. Bernard Dixon, the former editor of *New Scientist*, is a collection of stories about the many diverse and unexpected ways in which microbes affect the world. Each of the 75 vignettes centres on a different character, from "makers" to "destroyers", "deceivers" to "supporters", through to "artisans" predicted to shape our future.

The 256-page hardback book, which contains 16 black-and-white photographs, is priced at £16.99. For more information, contact W.H. Freeman/Spektrum, 20 Beaumont Street, Oxford OX1 2NQ. Tel.: +44 865 726 975; Fax: +44 865 790 391.

Genome research software helps scientists sort through DNA data

As the international effort to unravel the human genome accelerates, information management has become a formidable task. The DNA sequence data in the public electronic library known as GenBank already is doubling every 20 months, before concerted sequencing efforts hit their stride.

The National Center for Biotechnology Information, which manages GenBank, has answered many a molecular biologist's dream with a software system that combines current information about genes, where they are located, the products they make and any medical literature about them. When a scientist finds a new gene sequence or protein, the system makes it a 15-minute task to learn whether it also exists in other species and if so, how it works in that environment.

A new component of the integrated system, which is called Entrez, automatically searches for similarities between gene sequences and finds articles that are on related topics. The findings are then incorporated into the database.

The new service is available on CD-ROM or through the Internet, for reporters at the annual short course in mammalian genetics at the Jackson Laboratory in Bar Harbor, Maine

BioCatalysis database launched

Synopsys Scientific Chemical Systems Ltd. has developed a new chemical reaction database, *BioCatalysis*, designed to provide reliable, up-to-date information on the use of biomolecules as catalysts in organic synthesis.

Chemical companies and academic researchers are currently focusing a great deal of attention on the use of enzymes and micro-organisms in synthesis, both as catalysts for novel processes and as versatile alternatives to traditional methods. Advantages offered by biocatalysts include excellent chemo-, regio- and enantio-selectivity, coupled with important environmental benefits.

A thorough and systematic coverage of the literature on biocatalysis is assured by Professors Bryan Jones (University of Toronto) and Herbert Holland (Brock University), who are responsible for the selection of suitable material for the database.

The database offers easy access to the increasingly important subject of biomolecule-mediated organic synthesis and is supplied for use with popular reaction searching systems, including REACCS, ORAC and ISIS host. Details from: Dr. Julian Hayward, Synopsis Scientific Systems Ltd., 175 Woodhouse Lane, Leeds LS2 3AR or on 0113 245 3339; Fax: 0113 243 8733.

BioCommerce Abstracts available on CD-ROM

You can now search over 300,000 news items on the biotechnology industry, anything from patents to products, finance to fermentation and companies from Abbott to Zynaxis. The new CD-ROM version of *Abstracts in BioCommerce* combines simple, full colour, function key driven retrieval software with the largest database of business abstracts available on CD-ROM. Details from: BioCommerce Data Ltd., 95 High Street, Slough, Berkshire SL1 1DH or on 01753 511777; Fax: 01753 512239.

Engineering Processes for Bioseparations

A new book on downstream processing, edited by Lawrence R. Weatherley of the Department of Chemical Engineering, The Queen's University of Belfast, has two main objectives. First, it focuses on the application of existing separation techniques to the recovery and purification of biologically derived products. The complexities and breadth of problems associated with biological separations are discussed with reference to both high-value, low volume and bulk products. The specific engineering techniques presented include the main unit operations of extraction, solid-liquid operations, membrane separations, and the use of electrokinetic techniques.

Second, the book examines the state of knowledge of new techniques which are either of recent application to the area or which have potential in the future. These include aqueous two-phase processes, electrophoretic separations, near-critical fluid extraction and intensified processes. Details of the book, priced at £40.00, and other bio-titles from: Butterworth Heinemann, Linacre House, Jordan Hill, Oxford OX2 8DP, UK, or on 0865 310366; Fax: 0865 310898.

Explciting Biotechnology

by Vivian Moses and Sheila Moses

Exploiting Biotechnology provides a basic knowledge of biotechnology: how products are chosen, manufactured and marketed, as well as how new avenues for development are identified and managed. The authors discuss the most relevant aspects of biology and chemistry, and then go on to survey the most significant developments in biotechnology in recent years together with those likely to bear fruit in the future. Combined with technology, the chapters on management, manufacturing, patents, regulation and public policies, views and perceptions complete the picture. (1994), 280 pp., Cloth ISBN: 3-7186-5570-5. List price $64.00/£40.00. Paper ISBN: 3-7186-5571-3. List price: $28.00/£18.00.

Human genome research advice

A report on the priorities and opportunities in United Kingdom genome research highlights the ways in which genetics benefits the treatment of medical conditions, such as heart disease, cancer and diabetes. It emphasizes the importance of close cooperation between all parties involved – industry, the Government, research charities, and academia.

The report, *The Human Genome Mapping Project in the UK—Priorities and Opportunities in Genome Research*, was produced for the Advisory Committee on Human Genome Research by an independent group of leading geneticists chaired by Professor Kay Davies, and was commissioned by the United Kingdom Office of Science and Technology. The report's findings recognize the United Kingdom's strengths in human genetics research, and makes recommendations in genetic mapping, comparative mapping, DNA sequencing, genome informatics, commercial opportunities, and public education and training. Industry should become more involved with the Human Genome Mapping Project. More widespread use should be made of existing genetic resources in industry, in the charities, and in academia. Copies: from HMSO, price £9.95, ISBN 0-11-4300 99-2.

American type culture collection

Vector NT for Windows 3.1—Intelligent Software for Molecular Biology

Rockville, Maryland, USA, May 1994—American Type Culture Collection (ATCC), in partnership with InforMax Inc., announces an innovative, knowledge-based software product, Vector NT, designed to automate many cloning applications. Vector NT is capable of designing new genetic molecules automatically, utilizing user's specifications for the desired molecule. The software contains over 3,000 rules for genetic engineering designing.

Vector NT includes a database of 80 commonly used vectors, including vectors available from the ATCC, and permits transferring changes to molecules in child-parent trees. New molecules can be added to the database by importing files in GenBank, EMBL, or ASCII formats. All molecules can be analysed to identify sequences for PCR primers, restriction sites, open reading frames, and sequence motifs. The user has complete flexibility in adding new enzymes or motif descriptions.

For your free demonstration disk and tutorial documentation or to place an order, contact the ATCC by telephone (800-638-6597), Fax (301-816-4361), Internet email (request@atcc.org), or mail at ATCC/Marketing, 12301 Parklawn Dr., Rockville, MD, 20852, USA.

Green Alliance Briefing Document on deliberate release

The Green Alliance Briefing Document *Why are Environmental Groups concerned about Release of Genetically Modified Organisms into the Environment?* is well worth tracking down. Prepared with support from the Baring Foundation, The Network for Social Change and WWF, the document focuses on the following concerns:

1. Genes inserted into micro-organisms, plants and animals, that could not have got there by conventional breeding, will over time be spread to other organisms.
2. We do not know enough about ecological interactions to be able to accurately predict what the long-term consequences will be of the presence of these introduced genes in the environment.
3. Changes to the environment may not be noticed early.
4. The regulatory system controlling releases to the environment has not taken on board the concept of "genetic pollution" – in other words, the spread of genes in the environment, when they could not have got there by natural means, is not seen as environmental damage in itself.
5. Work with viruses poses particular risks.

6. Genetic modification may not further the development of "sustainable" agriculture.
7. The development of herbicide-resistant plants could cause changes in the patterns of herbicide use in agriculture in ways that will be more environmentally damaging than at present.
8. Efforts to engineer top predators such as fish could lead to ecological disruption.
9. Liability for damage caused by GMOs needs special provision.
10. The regulatory system does not give enough scope for consultation with the public.

The Green Alliance's work on biotechnology includes providing a critique of the development of the regulatory system, facilitating liaison between environmental groups and the regulatory authorities, and encouraging dialogue between industry and public interest groups. The organization has been monitoring biotechnology issues since 1987 and its Director, Julie Hill, has been a member of the United Kingdom Government's Advisory Committee on Release to the Environment (ACRE) since 1990. Details from: The Green Alliance, 49 Wellington Street, London WC2E 7BN or on 0171 836 0341. Fax: 0171 240 9205. E-mail: grailliance@gn.apc.org.

Biocommerce Data's UK Biotechnology Handbook

The *UK Biotechnology Handbook '94* provides detailed profiles of over 700 organizations involved in biotechnology, including over 200 new entries. This figure includes over 360 companies as well as more than 100 universities and research institutes, 30 venture capital providers, over 175 service providers and 30 government agencies.

Details of the publication, priced at £110.00 plus £4.00 p&p, from: BioCommerce Data Ltd., Prudential Buildings, 95 High Street, Slough SL1 1DH or on 0753 511 777. Fax: 0753 512 239.

Biological products

With its first issue planned for January 1995, *Biological Products* will be an international journal devoted to the safety, efficacy, quality control and production consistency of products made by or from biological entities. Annual subscription price: £140.00. Details from: Butterworth Heinemann, Linacre House, Jordan Hill, Oxford OX2 8DP, UK, or on 0865 310366. Fax: 0865 314519.

SCREEN Newsletter

The first issue of the SCREEN *Newsletter* was published in May. The SCREEN (Swift Community Risk Evaluation Effort Network) Project is funded by the EU-BIOTECH programme as a "horizontal activity", concerning the assessment of the ethical and socio-economic effects and technological risks associated with biotechnology. It is hoped that the collected data will help to keep the industry, legislators, regulators and researchers up to date with the latest releases of GMOs and research on and regulation of novel foods and property rights. The first issue covers events in Germany and the United Kingdom, while the second issue will turn to look at Belgium, Holland and Ireland. Additional information, not included in the newsletter, can be accessed via the SCREEN Bulletin Board.

Details from: Dr. Gert de Vries, ProBio Partners, Meerweg 6, 9625 PJ Overschild, the Netherlands. Tel.: +31 5966 321; Fax: +31 5966 508. In the United Kingdom, the contact is Jonathan F.A. Thomas, Rarfon Ltd., Elm Tree House, Southover High Street, Lewes BN7 1JB. Tel.: +44 (0) 273 474 744; Fax: +44 (0) 273 474 828.

Irish Biotechnology Sourcebook 1994

What is billed as the first comprehensive guide to Irish biotechnology has just been published by BioResearch Ireland. The *Irish Biotechnology Sourcebook 1994* contains information on over 160 biotechnology-based companies, or companies involved in relevant R&D or distribution activities. A number of other sections are devoted to research projects under way in universities and research institutes, cell and tissue culture collections and support and regulatory organizations. Details from: Desiree Breslin, BioResearch Ireland, Forbairt, Glasnevin, Dublin 9, Ireland or on +353 1 837 0177. Fax: +353 1 837 0176.

GenEthics News

David King, previously of the Genetics Forum, has launched a newsletter on genetic engineering issues. Given its provenance, biotechnologists will not be surprised to find the first issue of GenEthics News brimming over with critical articles on such issues as BST, the release of genetically-engineered plants, patents on life and the labelling of genetically-engineered foods. But such ethical and environmental issues can only become more important—and the bi-monthly newsletter is something of a snip. The first year's subscription rate is £14.95. Subscription inquiries to GenEthics News, FREEPOST (LON 6013), P.O. Box 6313, London N16 0BR or from David King direct on 071-249 0175.

People, Plants, and Patents

The impact of intellectual property on biodiversity, conservation, trade, and rural society

by The Crucible Group

Decisions about intellectual property, particularly for plant life, have major implications for food security, agriculture, rural development, and the environment for every country in the world. For the developing world, in particular, the impact of intellectual property on farmers, rural societies, and biological diversity will be profoundly important.

People, Plants, and Patents examines intellectual property and the patenting of life forms as bluntly and as fairly as possible. *People, Plants, and Patents* identifies the major issues and the range of policy alternatives in this extraordinarily important, fast-changing, and politicized field. The book is also available in French and Spanish. IDRC 1994, 100 pp. ISBN 0-88936-725-6, CA $12.95. The book may be ordered from CODE International, 323 Chapel, Ottawa, Canada K1N 7Z2.

Plant Genome Database

The USDA Plant Genome Database (PGD) is available over Internet from the National Agricultural Library at Beltsville, Maryland. PGD contains data for maize, soybean, small grains, rice and tomato, as well as data on *Arabidopsis*, a plant model for genetic research. Information centres on genetic maps and loci; there is also data on probes, clones, references, researchers and germplasm. PGD researchers will add data on other crops as it becomes available.

Contact: Doug Bigwood at (301) 504-6613 or Fax: (301) 504-7098; Internet: pgenome *a* nalusda.gov.

Ag Biotech Economic Prospects

Agricultural Biotechnology: An Economic Prospect describes the economic, scientific and social factors that will influence the future of biotechnology in agriculture. Ultimately, the use of biotechnology in the agrifood sector will depend on consumer demand for biotechnology-derived products, state authors M. Caswell, K. Fuglie and C. Klotz. Demand for biotech by farmers and food processors is derived from expected profitability, while supply of biotech products will be affected by public policies, producer expectations and consumer demand.

The book is published by the Resources and Technology Division, Economic Research Service, USDA. It is listed as Agricultural Economic Report No. 687.

Bibliography on Biotech and Sustainable Agriculture

This new bibliography contains citations and key words to 127 books, reports and magazine and journal articles regarding the compatibility of bioengineered crops and agricultural products with sustainable cultural practices. Although the bibliography is not exhaustive, it provides a foundation for understanding the debate on this issue. The scope of literature covered is broad, including the impact of biotechnology on technical deployment of alternative control methods, such as integrated pest management, as well as cultural, social, and international issues.

Contact: To obtain a copy of *Biotechnology and Sustainable Agriculture: A Bibliography*, send a self-addressed label to the Biotechnology Information Centre, National Agricultural Library, 4th Floor, 10301 Baltimore Blvd., Beltsville, MD USA 20705-2351. The bibliography is also available at the NAL gopher at: gopher.nalusda.gov; or via WWW at http: www.inform.umd.edu EdRes Topic AgrEnv Biotech. Look under Information Centres Biotech Info Centre Bibliographies.

World Technology Policies—The Longman Guide to World Science and Technology

Paul Cunningham and Brendan Barker

This book has been compiled in order to update the series of Longman guides which have for the past 10 years been following the technological progress of a wide variety of countries. In uncomplicated language the guide seeks to produce a comprehensive reference book covering the mechanisms through which Governments and the wider community encourage technological advancement in both developed and developing countries. The guide begins with overviews of four sectors which have experienced major changes in policy in recent years (defence, information technology, environment and new materials). It then examines the policies and organizations involved in technology on every continent.

If a business was considering buying this book, it would probably be doing so as part of its research into countries with which it might form new links or strengthen existing ones. The information the business would require would therefore need to be reliably up to date. As the guides' introduction accepts, however, this type of reference book feeds on and at the same time is plagued by the organic growth of both science and governments' policies. This growth quickly ages sections of the text.

The second factor which a company would require is evidence of the politics which invariably motivate the spending of government money and changes in the emphasis and direction of policies. In order to provide an impartial guide the editors have, however, included little reference to politics. This factual reporting also results in little analysis of whether current systems of policies are likely to produce different results from their predecessors.

As a thorough introduction to the subject the guide is a useful tool. Researchers whether acting for a Government, a business or in academia will find it an invaluable starting point.

Longman, Harlow, Essex, 1992, £145.00, ISBN 0-582-05730-2.

Seeds of Change: The Living Treasure

by Kenny Ausubel

Harper San Francisco, 1994, 232 pp. $18.00.

Seeds of Change, Kenny Ausubel's slick, glossy account of the heirloom seeds movement and the seed company he founded is comprehensive and beautifully designed. Ausubel's strengths—a breezy, accessible style and a genius for public relations—have already brought the issues of plant genetic resources to a broader audience than ever before. His weaknesses—a penchant for superficial explanations and a tendency to adopt uncritically the ideology of activists he admires—will make many in the genetic resource professions wince with discomfort.

Seeds of Change, Inc., is a private company based in Santa Fe, New Mexico, that sells certified organic, open-pollinated, and heirloom varieties of vegetables, herbs, and flowers. The company sells 530 varieties of 132 types of crops, including 61 different tomato varieties (12 of them heirlooms), six varieties of quinoa, and several tobaccos. Founded in 1989 by Ausubel and master gardener Gabriel Howearth, Seeds of Change sells seeds wholesale to health food and garden stores and retail to backyard gardeners by mail order and through seed racks in hundreds of locations, including the gift shops of the Smithsonian museums in Washington, D.C.

Ausubel's book tells the fascinating story of the company and the movement to enlist backyard gardeners in protecting biodiversity.

The book simultaneously explores the issues of plant genetic diversity, variety protection and plant patenting, the merits of open-pollinated versus hybrid varieties, etc.

The book, like the company's lovely seed catalogue, is enlivened by stunning images of landscapes and botanical details. Many readers will enjoy a short collection of recipes celebrating plant diversity contributed by master chefs, and a short resource list at the end will lead the inquisitive to other groups involved with seed saving, organic gardening, and the politics of genetic and cultural diversity.

Irish genetic conservation

An Irish Genetic Resources Conservation Trust (IGRCT) has been established to support practical projects on animal and plant genetic resources conservation in Ireland. Current projects include: conservation strategy for Galway sheep, a native breed which has recently been endangered; a register of rare breeds of domesticated animals in Ireland; conservation of ecotypes of native flora of agricultural and economic importance already listed as endangered; and support for a heritage apple collection project by the Irish Seed Savers Association. The IGRCT intends to create a mutually beneficial forum between community, university, NGO and governmental Irish groups involved in genetic resources conservation. The IGRCT welcomes contact and communications from other groups in Europe involved in similar activities, to share ideas and information.

For further information contact: Charli. Spillane, IGRCT, 52 Cramton Sq:. Temple Bar, Dublin 2, Ireland. Tel.: (353-1) 677 40 52; Email:cspillne *a* mail.tcd.ie

Canadian biotechnology law text released

A new text offers a comprehensive analysis of the state of Canadian law as it relates to biotechnology. *Biotechnology and the Law in Canada* covers in detail the major legal issues that concern the biotechnology industry, including proprietary rights, marketing options, and domestic and international licensing. There is a particular emphasis on legal issues pertaining to the pharmaceutical industry. However, the book also contains sections on plant breeders' rights, the legal use of animals in research and testing, and biotechnology regulatory law. Fully updated in 1994, the book explores the implications of NAFTA, the new Quebec Civil Code, amendments to the Canadian Patent Act and recommendations concerning property rights of human tissue.

Biotechnology and the Law in Canada is written by Randall W. Marusyk and Margaret S. Swain and is published by Les Éditions Yvon Blais Inc., Box 180, Cowansville, Quebec, J2K 3H6. Tel.: (514) 263-1086; Fax: 263-9256.

Biosafety for Sustainable Agriculture: Sharing Biotechnology Regulatory Experience of the Western Hemisphere

by Anatole F. Krattiger and Arno Rosemarin (editors)

The editors state that "the ultimate objective" of their book is "to outline how to build upon existing experience in order to assist the countries of Africa, Asia, the Americas and Eastern Europe to further develop biosafety regulatory mechanisms appropriate for their own needs, circumstances, objectives and priorities in agriculture, biotechnology and the environment".

Published by the International Service for the Acquisition of Agri-biotech Applications (ISAAA) and the Stockholm Environment Institute (SEI); 278 pp. 1994

Genetically Modified Organisms: A Guide to Biosafety

by George T. Tzotzos (editor)

This book was commissioned by the Informal Working Group on Biosafety of UNIDO UNEP WHO FAO and was prepared by the UNIDO Secretariat in cooperation with ICGEB. The book is intended to help scientists and regulators to conceptualize the major issues underlying biotechnology safety as well as to understand how these affect policies to regulate biotechnology. It reviews a large array of biotech applications and focuses on risk assessment procedures. In this context, it analyses potential adverse impacts on health and the environment and pays due attention to mitigation procedures.

A Primer on Biotechnology

An easy-access book is now available for those baffled by terms like PCR, antisense, DNA libraries, artificial chromosomes or genetic engineering in general.

Genes at Work uses analogies and diagrams to illustrate many of the concepts and explains how biotechnology is being used, associated techniques and where the technology is heading. The book explores many of the possibilities biotechnology has to offer, as well as the technical hurdles that have yet to be overcome. Written by experts in the field, the book is nevertheless geared for the high school or undergraduate student, or the informed lay person.

Contact: *Genes at Work* is available for $32.95 (US), including postage and handling. Make orders payable to CSIRO Information Services, Box 89 (314 Albert Street), East Melbourne, Victoria, Australia 3002. Tel.: Int+(613) 418-7217; Fax: Int+(613) 419-0459.

Biotechnology Report 1994-95

An overview of the state of the global biotech industry over the last year is provided in *The Biotechnology Report 1994-95*.

The book covers a wide range of topics, from financing trends to regulatory issues, commercial strategies and regional development. A substantial part of the book is given over to pharmaceuticals, including diagnostics, therapeutics and drug delivery. However, agbiotech, advances in enabling technologies and contract research opportunities are also covered to a lesser extent.

According to the publisher, the work is a "yearbook of events and analysis", intended as a representative "snapshot" of the diverse elements of the biotech industry. It provides this through selected information on the capabilities and knowledge of small research-intensive firms as well as the larger players, as well as underlying issues, such as financing, marketing and public acceptance.

A list of further references is also supplied, as well as a directory of selected firms and contacts for various biotech associations around the world.

Contact: Copies of *The Biotechnology Report 1994-95* cost $155 per copy. Make payment to Campden Publishing Ltd., Tech West Centre, 4 Warple Way, London W3 0UE, UK. Tel.: Int+(44 81) 749-6655; Fax: Int+(44 81) 749-1718.

UK biotechnology sector shows strong growth

Recent predictions of fast growth in the UK biotechnology industry are supported by the latest edition of the UK Biotechnology Handbook, produced by the BioIndustry Association (BIA) and BioCommerce Data which has over 200 new entries this year. A number of companies have now completed public offerings and several US biotechnology companies have established British subsidiaries.

The UK Biotechnology Handbook '94 provides detailed profiles of over 700 organizations involved in biotechnology including over 360 companies, as well as more than 100 universities and research institutes, 30 venture capital providers, over 175 service providers and 30 government agencies. The fifth edition of this key reference book also includes nine in-depth review articles by expert authors dealing with such topics as valuation and financing, intellectual property protection, the growth potential of the United Kingdom bioscience sector, European legislation, standards, government grants and the new Biotechnology and Biological Sciences Research Council (BBSRC). The articles are topical and informative and provide information complementary to the directory listings.

BioCommerce Data Ltd. specializes in business related biotechnology information and publishes bulletins and databases dealing with the commercial aspects of biotechnology and information resources for this sector as well as providing mailing list and consultancy services on a worldwide basis.

For further details contact: BioCommerce Data Ltd., Prudential Buildings, 95 High Street, Slough SL1 1DH, UK. Tel.: +44 (0) 753 511 777; Fax: +44 (0) 753 512 239