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GENETIC ENGINEERING AND BIOTECHNOLOGY

1997/4

CONTENTS

SPECIAL ARTICLE:

Progressing Public-Private Sector Partnerships in International Agricultural Research and Development
by Clive James, Chair, ISAAA Board of Directors

NEWS AND EVENTS

COUNTRY NEWS

RESEARCH

APPLICATIONS

PATENTS AND INTELLECTUAL PROPERTY RIGHTS

BOOKS, JOURNALS, REVIEWS AND BIOINFORMATICS

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

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TO OUR READERS

Under the leadership of the new Director-General of UNIDO, who took office on 8 December 1997, a new programmatic approach for the Organization was developed, with services designed to help recipient countries solve their industrial development problems in the changing global economic environment. Ten packages of services that encompass the following areas of activities will constitute the core of future UNIDO services: Industrial Governance; Industrial Export Capacity-Building; Industrial Information Networking; International Industrial Partnerships; Quality and Certification for Industrial Competitiveness; Cleaner Production and Environment; Efficient Energy Development; Agro-related Industries Development; Local Industrial Development; and Women Entrepreneurship Development. These integrated packages of services are designed for both the public and private sectors.

Africa is the developing region where the transformed UNIDO and its new services will be first put to test. The services are designed to meet most demands of developing countries in rapidly changing global economic conditions. Once they are adapted and customized to attend to the specific needs of an individual country, these services will eventually promote the three E's of the UNIDO Business Plan: Economy, Environment and Employment by promoting a competitive economy; creating employment; and protecting the environment.

In this spirit, UNIDO has recently signed an agreement with the United Nations Conference on Trade and Development (UNCTAD), in which the complementary roles of the two organizations in investment and technology promotion and the related area of small and medium enterprise development are spelled out. Thus, UNIDO and UNCTAD have forged a new strategic alliance to boost investment in developing countries. The alliance harnesses the two organizations' comparative advantages to maximize delivery of services and avoid duplication, as part of the United Nations' efforts to pool the resources of its agencies.

While UNIDO will focus on advice and assistance on industrial sector issues and investment and technology promotion support, UNCTAD will concentrate on policy issues affecting investment promotion, including the regulatory and institutional framework for investment. These arrangements will also include the formation of new partnerships between the two organizations and the private sector of industry. Joint activities will take place at the country and global levels.

To attract investment and technology transfer to Africa, UNIDO offers a number of services to individual states. These include Build-Operate-Transfer (BOT) strategies, review and advice on legal framework, strengthening investment and technology related institutions; advice on organization, procedures, networking and operation set-up of national investment promotion agencies, preparation of promotional material, organizing promotional events such as Investment Promotion Fora and Techmarts, networking and subcontrating; and finally, on-the-job training for investment promotion personnel in UNIDO's Investment Promotion Offices in developed countries. Investment promotion events play a major role in laying the groundwork for new projects, not only for individual states, but also for regions.

Readers will be pleased to hear that the New Delhi component of the International Centre for Genetic Engineering and Biotechnology (ICGEB), now has a new Director, malaria researcher Virander Singh Chauhan, who hopes to spur modernization of the Centre under his leadership.

In the previous issue of *Genetic Engineering and Biotechnology,* on page 21 we should have given the following information on Brazil's biotechnology organization: Brazilian entrepreneurial biotechnology is represented by ABRABI, the Brazilian Association of Biotechnology Enterprises, which collects companies, incubators and research centres. Among these is Biominas Foundation (mentioned in our published text), which is one of the foremost members of ABRABI. The Biominas President, Guilherme Emrich, is a close associate and Vice-President of ABRABI. The President of ABRABI itself is Antonio Paes de Carvalho. We sincerely apologize for any inconvenience caused by this incomplete information. The address of ABRABI is as follows:

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CONTENTS

Page

A. SPECIAL ARTICLE 1

PROGRESSING PUBLIC-PRIVATE SECTOR PARTNERSHIPS IN INTERNATIONAL AGRICULTURAL RESEARCH AND DEVELOPMENT 1

B. NEWS AND EVENTS 37

UN and other organizations' news 37
Biodiversity indicators and implementation targets: Global Diversity Forum prepares for United Nations General Assembly review .. 37
Boosting seed supply 37
Cassava bacterial blight: a major threat to production 38
Regulatory issues 38
USDA amends regulations for GMOs 38
Blunt pharming talk 38
Microbial biotech regulations set 38
New US regulatory framework emerges for genetics 39
Task force finalizes genetic testing recommendations 39
EC food regulations published 39
Ethical issues 39
Europe/Japan face up to legal hurdles to cloning 39
US bioethicists say continue human cloning moratorium 39
Ethics of AZT studies in poorer countries attacked 39
AIDS trials ethics questioned 40
India fears patent and ethics abuses 40
Bioethical aspects of biotechnology in the agro-food sector—developing countries 40
EuropaBio ethical code put up for consultation 41
Bioethics convention 41
General 41
Moral lesson for policy makers 41
Genetically modified food 41
The Biotechnology Industry Organization (BIO) and SciQuest(sm) to form Internet Partnership 42
WTO overrides EU ban on BST-beef imports .. 42
Human cloning ban urged by Germany and France 42
ABIC '98 conference focuses on business of agriculture 42
Engineered maize condemned 42
Novartis' agribusiness 42
Bioprospecting deal 43
Sharp reaction to cloning 43
Europe's biotech sector to treble 43
New rules for GMOs 43
Amersham merges with P&U unit 44
Roche-Mannheim proposed merger 44
MRA agreement signals start of global harmonization 44
Public voice concerns 44

Page

Europe and the biotechnology gap 45
World environment 45
Biopharmaceuticals set for change 46

C. COUNTRY NEWS 47

Austria 47
EC urges Austria to end modified maize ban .. 47
Brazil 47
BIOLATINA 98 47
Canada 47
Canadian biotech regulations 47
Biotechnology boom 47
Help for Cuban Biopharmaceuticals 47
China 48
US China pact yields new cancer vaccines 48
Biotech key to self-sufficiency in China 48
Costa Rica 48
Indena, INBio enter collaboration 48
European Union 48
EU enforces biotech rules 48
EU to insist on product labelling 48
Public voice concerns 49
European patent directive 49
Germany 49
Biotech given a helping hand 49
Germany's herbal medicine industry 49
Hong Kong 50
Biotech in Hong Kong 50
India 51
India bans shrimp farming 51
Transgenics tops research agenda 51
Ireland 51
Biotech in Ireland 51
Irish biotechnology company update 52
BioResearch Ireland announces its first spin-off company 52
Italy 52
Gene Therapy Centre in JV with Boehringer Mannheim 52
Japan 52
Biotic pesticide to be developed to prevent anthracnose 52
Eight crops OK'd by Health Ministry 53
MITI to support tissue, organ research 53
Korea, Republic of 53
Government to develop biotechnology industry 53
Philippines 53
First-to-file system adopted 53
Russia 53
ABS in Moscow alliance 53
Russia steps into AIDS research arena 53
Switzerland 54
Import of genetically altered soya beans 54
Taiwan 54
Biotech panel set up 54
United Kingdom 54
Spearheads strategy to maintain bioscience industry in pole position 54

CONTENTS *(cont'd)*

Page

The IBIS project 54
Health and safety environment professionals .. 54
Biotech in Scotland 54
USA 55
EPA issues new requirements for biotech products 55
Phytoremediation activities 55
Amended biotech rules 55
NIH steps up malaria research 56

D. RESEARCH 57

Research on human genes 57
Key protein found for brain's dopamine-producing neurons 57
Human artificial chromosomes 57
Small molecule regenerates nerve tissue 57
Human haemoglobin from transgenic plants .. 57
Chimeric protein cytotoxic against KS tumours 58
Double first 58
Gene linked to autism 58
New yeast discovery hints at improved cancer treatment 58
First lymphatic growth factor identified 58
Stress proteins and human ageing 59
Map marks the X chromosome 59
Tumour suppressor gene 59
A cholera toxin effective in drug delivery 59
Engineered superantigen for efficient tumour killing 60
Sonodynamic therapy for selective destruction of tumour tissues 60
Common asthma gene isolated, cloned by Sequana in two years 60
Structure of mutant leptin resolved 60
Mechanism of IFN-resistant hepatitis elucidated 61
Endocrine cancer 61
Mouse multiple sclerosis model attenuated by IL-4 61
New type of DNA-free inheritance in yeast is spread by a BSE mechanism 61
Research on animal genes 62
Electroporation for creating transgenic fish 62
Transgenic cows produce human protein 62
Mouse gene of nerve cell apoptosis inducer enzyme CPP32 62
Mouse withdrawal genes 62
Circadian clock gene identified and cloned in mammals 63
Dolly—the science behind the sensation 63
DNA vaccine protects chimps against HIV ... 63
Research on plant genes 63
Expansins ripe for research 63
Thermoplastic polymer from cotton fibres 63
Effectiveness of gene isolation confirmed 64
Large DNA molecules transferred to plants ... 64
All's fair in larvae war 64
Transgenic potatoes 64
Researchers find pathways for nitrogen fixation 64

Page

Plastic from poplars 65
Engineering maize into chemicals 65
Tobacco gene encoding wound-induced protein kinase 65
Research on viral genes 65
Kaposi's sarcoma—associated herpes virus ... 65
Modified cold viruses 66
AIDS research 66
Research on bacterial genes 66
Salmonella bacteria used to hunt and attack cancer cells 66
Bacteria help to build honeycombs 66
Biological source of solar energy studied 67
Recombinant E.coli absorbs phosphate 67
Food biotechnology 67
Research instrumentation 67
Multiphoton imaging 67
Critters enjoy a glowing success 68
Infra-red spectroscopy basis of cervical cancer test, biotech firm 68
Lasers to screen cells 68
Biolog identifies over a thousand organisms ... 68
Carbon monoxide and the heme oxygenases ... 69
New sensations in biosensor design 69
Device to detect airborne biological warfare agents 69
Building the virtual laboratory 70
General 71
Scientists study bioluminescence 71
Genome study on diabetes in Africa 71
Drug delivery 71
TIGR releases EST data publicly 71
Telomerase seen as universal sign of cell's malignant transformation 72
Sequenced human genome 72
IBM Deep Blue to drug development 73
Protein yields catalytic key to telomerase 73
Parasite's food route under attack 73
Non-parenteral vaccines 73

E. APPLICATIONS 75

Pharmaceutical and medical applications 75
Study finds three-drug AIDS cocktail better than two 75
Fungus strain gives new drugs 75
Thalidomide prompts tumour responses 75
Complex vaccine may overcome quick change talents of HIV 75
Vaccine effective in laboratory against airborne black death 76
Cancer therapy 76
Demeter compounds found active against resistant bacteria 76
A cheaper, quicker way to monitor glucose ... 77
Vaccines 77
Promising results for HIV vaccine tests 77
Gene vaccine safe for humans 77
Risk from metals at work 78

CONTENTS *(cont'd)*

Page

Livestock applications 78
Conference reports on giant clam farming 78
Australians mass produce embryo clones 78
Plant-grown vaccines protect animals 78
Natural gum 79
Newcastle disease 79
Monoclonal antibodies produced in transgenic goat's milk 79
Agricultural applications 79
Antifreeze gene from white pine may help shield crops from frost 79
Sweet potato with edible leafstalk 79
Mildew resistance in wheat 80
Brazilian predator mite controls African cassava pest 80
Crops fight off aluminium 80
Genetically modified sugar beet for field trials 80
ICRISAT's ecofriendly gift to check chickpea pod borer 80
Food production and processing 81
Bittersweet biotech 81
Extraction industry applications 81
Plutonium eater eyed for nuke fuel 81
Industrial microbiology 81
Corn plastic 81
Enzymes have softer touch 81
Energy and environmental applications 81
Collaboration on bioreactor 81
Wastewater purification system 81
Bacterial strain could help pollution fight 82

F. PATENTS AND INTELLECTUAL PROPERTY RIGHTS 83

Europe to update bio-patent laws 83
MEPs agree protection for biotech inventions .. 83
Haemophiliacs win court case over blood products 83
Gene chip patent 83
Bill mandates patent extension if PTO dallies .. 83
Official fees in the European Patent Office reduced 84
One stop shopping for intellectual property ... 84

Page

G. BOOKS, JOURNALS, REVIEWS AND BIOINFORMATICS 85

Books, journals and reviews 85
Information systems for biotechnology 85
Crop protection compendium 85
Microbial pathogens handbook 85
Biodiversity, Science and Development: Towards a new partnership 85
Community Management and Common Property of Coastal Fisheries in Asia and the Pacific: Concepts, Methods and Experiences 85
Biosafety: Scientific Findings and Elements of a Protocol 85
Researchable Constraints in the Seed Sector in Developing Countries 85
Biopolitics: A Feminist and Ecological Reader on Biotechnology 86
Dynamic diversity 86
Especies útiles de un bosque tropical húmedo . 86
Bioprospecting in South Africa, Towards the Development of Equitable Partnerships 86
Seed Supply Systems in Developing Countries 86
Seed production and marketing in Asia and the Pacific 87
Biotechnology textbook 87
Book on biodiversity 87
Public controversy in biotech 87
Lost Crops of Africa Vol. I: Grains 87
Social change and conservation 87
Biotechnology 88
Gene technology 88
Bioinformatics 88
DNA vaccines 88
Online agriculture atlas 88
IDRC Website 88
BIOSAFE 88
Plant breeding news 89
Plant genome data and information center 89
IMGT database 89
Genes on the Internet 89
A Call to Action (CD-ROM) 90

A. SPECIAL ARTICLE

Progressing Public-Private Sector Partnerships in International Agricultural Research and Development

Clive James
Chair, ISAAA Board of Directors

No. 4-1997

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Executive Summary

The world's population is currently 5.8 billion and is expected to almost double by the year 2050 when approximately 90 percent of the global population will reside in the countries of the South. Compounding this situation, the additional food will have to be produced on the existing area, or less, of agricultural land without degrading the fragile natural resource base. Thus, one of the major challenges facing the world in the 21st century will be to achieve food security without degrading the natural resource base. Agricultural research and technological improvements will continue to be pre-requisites for increasing crop productivity. Industrial countries have benefited from agricultural research and development (R&D) investments by both public and private sectors, whereas developing countries, by and large, have relied on less than adequate funding, principally from the public sector. In the future it is imperative that developing countries invest significantly more public sector funding in agricultural R&D and also encourage more private sector investments.

To meet the challenge of future global food security requires new partnerships between the public and private sectors in agricultural R&D and agribusiness; these partnerships will serve to optimize and integrate the respective comparative advantages of the partners in their quest to achieve mutual objectives. During the 1990s there has been a growing awareness in both public and private sectors of the significant benefits that can be derived from such public-private sector collaboration. This publication aims to present information that supports the need for public-private sector partnerships by reviewing public and private investments in agricultural R&D during the last decade, when there has been a decline in official development assistance to countries of the South. Three examples of public-private sector partnerships are presented to illustrate that there are opportunities for collaboration which result in win-win situations and contribute to global food security.

Recent estimates suggest that in the decade 1987 to 1997, official development assistance (ODA) to agriculture has declined by 50 percent. Furthermore during the same period, national governments have provided less support to agriculture in developing countries. This does not bode well for the future, which highlights the importance of developing new partnerships between the public and private sectors. It is noteworthy that public sector ODA funding for all sectors is $60 billion annually, whereas private sector investment from the North in the South is $170 billion per year, and growing, equivalent to almost three times that of the public sector ODA. In 1990 global investments in agricultural R&D by the public sector were estimated at $17.3 billion, with $8.8 billion invested by developing countries, and $8.5 billion by industrial countries. Industrial countries typically invest 2 percent of agricultural GDP in public R&D whereas the corresponding figure for developing countries is 0.5 percent, a quarter of the industrial country investment. In the 1960s in the United States, private sector R&D investments were 5 percent less than corresponding investments by the public sector; however, by 1995 private sector R&D investment was 27 percent more than that of the public sector. Whereas private sector investment in developing countries is lower than public sector R&D, the same trend is observed in countries such as Colombia where private sector R&D investment, expressed as a percentage of the national R&D investments, increased from 22 percent in 1970 to 37 percent in 1991.

Corporations involved internationally in agriculture are involved in a broad range of activities that include fertilizer, crop protection, seed industry, animal health and biotechnology. The scale of operations in each of these market areas is reviewed, and the major corporations characterized in terms of global revenues, R&D, and the structure of the global markets by region and product, using recent data for 1996. Industry considers 5 to 7 percent of revenue as the minimum investment necessary to ensure an acceptable level of competitiveness in the marketplace, and the average R&D investment for 15 crop protection and seed companies in 1996 was 10.6 percent. Whereas direct comparisons with the public sector are not possible, private sector R&D investments are judged to be considerably higher than those of the public sector.

The global fertilizer market in 1995/1996 was $50 billion, with the private sector responsible for at least half of the market. On a global basis 60 percent of fertilizer is consumed in developing countries, and more specifically 63, 61 and 48 percent of nitrogen, phosphate, and potash respectively, are used by developing countries. The crop protection global market was valued at $31.25 billion in 1996, with herbicides, insecticides, fungicides, and transgenic crops representing 48, 28, 19, and 1 percent respectively of the world market; it is noteworthy that the global market for transgenic seed increased from $75 million in 1995 to $235 million in 1996, an increase of 213

percent. Seventy-two percent of the world crop protection market is in industrial countries and 28 percent in developing countries. The major countries for crop protection products are the United States (28 percent), Japan (12 percent), and the major crops on which crop protection products are used are cereals (19 percent), followed by maize (12 percent), rice (11 percent), soybean (9 percent) and cotton (8 percent). The global area of commercial transgenic crops, where the dominant traits are herbicide tolerance, and insect or virus resistance, increased by a factor of 4.5 from 7.0 million acres (2.8 million ha.) in 1996 to 31.5 million acres (12.8 million ha.) in 1997.

The value of the seed industry is estimated at $45 billion per year, equally divided into three segments: commercial seed, farmer-saved seed, and seed supplied by Governments, a prevalent practice in developing countries and centrally planned economies. Consumption of agricultural seed, which includes farm-saved seed is 120 million tons per year. Asia and the Commonwealth of Independent States (CIS) are the largest consumers of seed. In recent years the global seed market has been relatively stagnant, except in Asia where consumption has increased by 18 percent, with rice representing one-third of the total seed used. Cereals dominate the global seed market, accounting for two-thirds of the 120 million tons, wheat (35 million tons) being the dominant crop. The top 25 seed corporations had a total revenue of $8 billion in 1996. The world market for animal health products in 1995/ 1996 was $14.4 billion, with pharmaceuticals representing just under half. Cattle account for 32 percent of the global animal health supplies, followed by pigs (23 percent), poultry (18 percent), and sheep (6 percent). Approximately 66 percent of the animal health market is in industrial countries with 34 percent in developing countries.

Many of the transnational corporations have parallel involvement in many of the sub-sectors; hence one corporation may have interests in areas that include fertilizer, crop protection, seed and animal health, and with biotechnology being a common denominator of increasing importance in R&D. The need to create the minimum critical mass in R&D and marketing has led to many mergers and alliances in the private sector; biotechnology has been the major factor that has triggered consolidation in the industry in recent years and this trend is likely to continue. Investments in biotechnology have been significant with an estimated $10 billion invested by the United States alone in biotechnology R&D in 1995, of which $2 billion was in agricultural biotechnology. The market for biotechnology products in the United States was estimated at $304 million in 1996, and the global market for transgenic crops is projected to reach $2 to $3 billion in the year 2000, $6 billion in 2005, and $20 billion in 2010.

There is no greater incentive for collaboration between the public and private sectors in agricultural research than the enormous challenge posed by global food security, which will require that limited resources be used in the most effective way to develop sustainable agricultural systems that also conserve natural resources. The significant investment of the private sector in biotechnology, perhaps more than any other single factor, has clearly demonstrated the need for, and significant advantages associated with collaboration between the public and the private sectors in agriculture. Global private sector investments in agricultural and food R&D are conservatively estimated at $11 billion in industrial countries, and $2 billion in developing countries, compared with $8.5 billion and $8.8 billion by the public and private sectors respectively, for a public/private global total of $30 billion.

It is evident that $30 billion in global investment for agricultural R&D is inadequate to meet future needs and it is, therefore, vital that the two major players, the public and private sectors, involved in agricultural R&D on the global scene collaborate to address the important and impending challenge of global food security. Governments of developing countries, the donor community, and the private sector must take the necessary and urgent steps to stimulate the building of partnerships. It is encouraging to note that there are several successful initiatives already underway to build new partnerships between the public and private sectors. Three of these public-private initiatives are the founding of the International Service for the Acquisition of Agri-Biotech Applications (ISAAA) in 1991, the establishment of the Private Sector Committee of the CGIAR in 1995, and the formation of a Public-Private Sector Consortium by CAB International in 1995 to support the development of a Global Electronic Compendium for Crop Protection. These three initiatives, which are quite different in character, are described in more detail in the text, and can serve as models for emulation and improvement in future public-private sector partnerships.

Introduction

The world's population is currently 5.8 billion and is expected to almost double by the year 2050. Ninety-seven percent of this population increase will occur in developing countries in Africa, Asia and Latin America (Swaminathan 1995). Even with today's 5.8 billion population, 800 million people are deprived of adequate food supplies and 1.3 billion people, equivalent to 30 percent of the population of the developing world, live in abject poverty, and barely survive on one dollar per day or less, for food, shelter, and other essential needs. A high proportion of the poor people live in rural areas where the natural resource base is fragile and deteriorating. The challenge for the future is global food security, which will require at least a doubling or preferably tripling, of food production by the year 2050 to meet the needs of the rapidly growing population of up to 11 billion people, ninety percent of whom will reside in the developing countries of the South. Compounding the situation, this additional food will have to be produced on the existing area, or less, of agricultural land. The enormity of the challenge of food security is best illustrated by the fact that in the next fifty years the global population will consume twice as much food as has ever been consumed since agriculture began 10,000 years ago.

Agricultural research and technological improvements are, and will continue to be prerequisites for increasing agricultural productivity and generating income for farmers and the rural work force. This in turn will help to alleviate poverty, which is primarily a rural phenomenon, but also afflicts the urban poor; 75 percent of the poor in Africa and Asia live in rural areas. Given that economic growth is the best antidote to poverty, and that few countries have achieved economic growth without agricultural growth, it follows that agriculture, a principal sector in most developing countries, can contribute significantly to growth and development and should be accorded a high priority. During the last decade, however, investments in agriculture, at both the national and international levels, have declined. There is an urgent need to reverse this trend, which, if left unchecked, can threaten global food security.

Industrial countries have benefited from agricultural research and development (R&D) investments in both the public and private sectors, but developing countries have by and large relied on public sector support from national programs and from international organizations such as the international centers of the Consultative Group on International Agricultural Research (CGIAR). In the future it is imperative that developing countries invest significantly more public sector funding in agricultural R&D and also encourage the indigenous and international private sectors to participate in activities where they have comparative advantages. To meet the challenge of global food security requires new partnerships in agricultural R&D between the public and private sectors that optimize the comparative advantages of each in pursuit of mutual objectives. Forging these new public-private sector partnerships would promote the most effective use of limited global resources for the development of sustainable agricultural systems. In the last decade governments in industrial countries have encouraged increased participation by the private sector in agricultural R&D, a trend that is being mirrored in many developing countries. During the 1990s there has been a growing awareness, in both the public and private sectors, of the significant benefits that can be derived from such collaboration.

This publication is not an exhaustive analysis of public and private sector investments in agricultural R&D; rather, it presents general information that demonstrates the need for public-private sector partnerships, with particular emphasis on developing countries. In order to provide a global contextual framework in which to view the activities of the public and private sectors, the declining official development assistance to agriculture as well as public and private sector investments in agricultural R&D are briefly reviewed; for the latter, selected activities of the private sector active in international agricultural R&D are characterized. The need for collaboration between the private and public sector is discussed and three different initiatives are described that involve collaboration between the public and the private sectors, aimed at building new partnerships for the future.

Declining Support for Developing Country Agriculture

A recent International Food Policy Research Institute (IFPRI) study (Brown and Haddad 1994) reported that the proportion of official development assistance (ODA) devoted to agriculture decreased from 20 per cent in 1980 to 14 per cent in 1990. The study also showed that real external assistance to agriculture for developing countries declined from $12 billion[1] in 1980 to $10 billion in 1990. More recent estimates (World Bank 1997) suggest that in the decade 1987 to 1997 official development assistance for agriculture has declined by 50 percent. Although there are many reasons for this decline, the following are believed to be the major factors. First, there are those within the development assistance community who (i) reject the view that investment in agriculture is a prerequisite for economic growth in developing countries, and (ii) contest the reported high private and social rates of return of 20 percent or more attributed to agricultural research projects. Second, during the 1980s and 1990s, bilateral and multilateral agencies that provided development assistance, assigned a higher priority to environmental protection, which reduced the amount of funds available for support to agriculture. This change in priority occurred at the same time donor agencies were being forced to deal with their own domestic economic constraints. Consequently, donors were unable to satisfy all of the new and competing demands, such as significant financial aid to Eastern Europe and the countries of the former Soviet Union.

In the past, ODA and official investment assistance have been important for obtaining additional financial support from national programs for agricultural research. There is now evidence that this external support is declining at the same time developing countries are providing less support to agricultural R&D. External assistance to national agricultural research systems (NARS) is estimated to be 35 percent for Sub-Saharan Africa, 26 percent for Asia and the Pacific, and 7 percent for Latin America and the Caribbean. The breadth of support for agriculture from the donor community tends to be narrow and, therefore, is vulnerable. For example, the World Bank provides 25 percent of the total agricultural R&D support to developing countries, and two thirds of the World Bank's $817 million to developing countries during the period 1981 to 1987 was limited to six projects (Anderson *et al.* 1994). One positive development is the World Bank's revitalized Rural Development Program which increased lending to $3.9 billion for 56 projects in 1997, after several years of decline. Similarly the International Finance Corporation's financing of food and agri-business continued to grow in 1997 to $814 million for 27 projects (World Bank 1997).

In summary, declining support of public sector funds from ODA to aid agricultural research in developing countries does not bode well for the future, which highlights the importance of increased participation by the private sector in partnership with the public sector. It is noteworthy that public sector ODA funding for all sectors is currently estimated at approximately $60 billion annually, whereas private sector investments from the North for all sectors in the developing countries of the South are estimated at more than $170 billion per year (Serageldin and Sfeir-Younis 1996), equivalent to almost three times that of public sector ODA.

Public Sector Investments in Agricultural R&D

In the 1960s industrial countries accounted for approximately two-thirds of the total public sector investments in global agricultural research. It was not until 1990 that developing countries invested marginally more than industrial countries in agricultural R&D. In 1990 global investments in agricultural R&D by the public sector were estimated at $17.3 billion, with $8.8 billion invested by developing countries and $8.5 billion by industrial countries (Alston and Pardey 1996).

One of the most useful and meaningful methods for comparing national agricultural research expenditures is to express them as a percentage of the corresponding national agricultural gross domestic product (GDP); Anderson *et al.* (1994) reported these as "agricultural research intensity ratios". Data for the period 1961 to 1993 is shown in Table 1.

1) All data in this publication are given in US dollars ($).

Table 1: Investments in Agricultural R&D
(expressed as percentage of national agricultural GDP)

Region or Country	Number of Countries	1961-65	1971-75	1981-85	Most Recent Year
Developing Regions					
Sub-Saharan Africa, (excluding South Africa)	17	0.42	0.67	0.76	0.58[a]
South Africa	1	1.39	1.53	2.02	2.59[a]
Asia and the Pacific (excluding China)	15	0.14	0.22	0.32	-
China	1	0.57	0.44	0.42	0.42[b]
Latin America and the Caribbean	26	0.30	0.46	0.58	-
West Asia and North Africa	13	0.28	0.50	0.52	-
Developed Countries	18	0.96	1.41	2.03	-
United States	1	1.32	1.36	1.93	2.22[c]
Australia	1	1.54	3.56	4.52	4.42[d]

[a]1991 estimate, [b]1993 [c]1992 [d]1988.
Source: Pardey and Alston, (1995).

The data in Table 1 indicate that industrial country investments show continued growth, with at least 2 per cent of agricultural GDP invested in R&D by the early 1980s; the average investment by eighteen industrial countries in the early 1980s was 2.03 percent, with the United States reporting 2.22 percent in 1992 and Australia 4.42 percent in 1988. Corresponding developing country expenditures averaged approximately 0.5 percent in the early 1980s, equivalent to one-fourth of the amount invested by industrial countries. Whereas public sector investments in agricultural R&D in developing countries doubled on average between the 1960s and the early 1980s, the initial rapid growth during the early 1960s slowed during the 1970s, and by the 1980s investments had either leveled off (China at 0.42 percent) or declined, with seventeen Sub-Saharan Africa countries showing a significant decrease, from 0.76 percent in 1981 to 1985, to 0.58 percent in 1991. It is noteworthy that the Republic of South Africa's investment in agricultural research continued to increase, from 1.39 percent in the 1960s to 2.02 percent in the early 1980s, to 2.59 percent in 1991, and compared favorably with investment in industrial countries such as the United States, which reported 2.22 percent for 1992.

In summary, recent global investments in public agricultural research show that developing countries invest approximately 0.5 percent of agricultural GDP in agricultural R&D, one-fourth of the amount invested by industrial countries, which average 2 percent. The significant growth in public spending on agricultural research in the 1960s in developing countries has leveled off or declined in some countries, and there is growing concern that current investments will not be adequate for delivering the technology contribution necessary to increase food productivity sufficiently to ensure food security in the future. Given that global resources devoted to agricultural R&D are inadequate, one of the options that must be explored is better use of current allocated global resources, including the integration of public and private sector research resources, so that limited global resources can be used to achieve mutual objectives more effectively and efficiently at the national and international levels.

Private Sector Investments in Agricultural R&D and Estimates of Global Markets for Selected Products

There are no comprehensive and uniformly generated global estimates of private sector investments in agricultural R&D for industrial and developing countries. However, some data from selected industrial countries, where most of the private sector investments are made, provide an indication of the scale and scope of investment *vis-a-vis* the public sector. In the early 1960s private sector agricultural R&D expenditures in the United States were about $250 million annually, approximately 5 percent less than corresponding public sector expenditures. Recent estimates (United States Department of Agriculture 1995) for the United States indicate that in-house private sector agricultural research expenditures for 1992 were $3.3 billion, 27 percent more than the corresponding amount spent by the U.S. public sector. The data in Table 2 show the trends in private sector spending for various activities during the period 1960 to 1992. It is noteworthy that private sector agricultural R&D spending in the United States increased almost twenty-fold during this period, with real expenditures (expressed in 1980 dollars) increasing by a factor of three, from $511 million in 1960 to $1,648 million in 1992 (Alston and Pardey 1996). During the 1960s and 1970s, spending on agricultural research by the private sector showed real growth rates of more than 4.5 percent per year and exceeded corresponding public sector spending. Despite the fact that U.S. private expenditures in agricultural R&D grew at lower real growth rates in the 1980s, compared with the 1960s and 1970s, the total investment by the U.S. private sector in 1992 was $700 million greater than the public sector. The highest rate of growth in the 1970s was in chemicals, which was also the only activity to decline in the 1980s, when postharvest and food processing investments increased rapidly from $456 million in 1982 to $1,088 million in 1992.

Although available data do not allow precise comparisons and breakdown of public and private sector spending in agricultural R&D, the trend in the United States - higher spending in the 1970s and 1980s by the private sector compared with that of the public sector - is probably representative of the spending in most other industrial countries. Comparable data for agricultural and food R&D in the United States, United Kingdom, and France for the mid-1980s indicate that annual private sector expenditures were $2,400 million, $530 million and $270 million, respectively, equivalent to 49, 47, and 39 percent of total spending by both the public and private sectors (Anderson 1996), and these percentages are likely to have increased significantly in the interim period.

Expenditures on agricultural R&D by the indigenous and international private sectors in developing countries are much lower than in industrial countries and are concentrated in a few of the larger and more advanced developing countries, such as Argentina, Brazil, India, and

Table 2: Trends in Private Sector Spending on Agricultural R&D: Input-Oriented, Postharvest and Food Processing, 1960 to 1992
(millions of current dollars)

Year	Input-Oriented				Postharvest & Food Processing	Total	
	Chemicals	Agricultural machinery	Veterinary/ Pharma-ceuticals	Plant breeding		Current	Real
1960	9.7	75.9	6.0	5.6	80.0	177.2	511.9
1970	126.0	89.1	45.0	26.3	206.1	492.5	839.0
1980	1,390.0	287.0	111.0	96.7	456.1	1,340.8	1,340.8
1992	1,123.0	394.0	306.0	399.7	1,088.0	3,310.7	1,648.0

Source: Adapted from United States Department of Agriculture (1995).

Mexico (Pray and Echeverria 1991). More recent data (Falconi 1992, 1993) show that in the 1970s and 1980s private sector investments in agricultural R&D in some developing countries increased faster than public sector investments, similar to the trend in the United States. For example, private sector investments (expressed as a percent of total R&D expenditures) in Colombia, increased from 22 percent in 1970 to 37 percent in 1991, and in Ecuador from 19 percent in 1986 to 27 percent in 1991. This trend is not surprising because it occurred at a time when many developing countries introduced policies to encourage increased participation by the private sector in agricultural R&D.

Given the nature of the market place and the competition among private sector corporations, comprehensive data on agricultural R&D is not readily available in the public domain. However, much can be gleaned about the scale and scope of private sector activities in an international context. In this paper, 1996 data from industry sources has been used to characterize the international markets for selected products, and to estimate R&D expenditures, expressed as a percentage of revenues. These activities are discussed in the following section.

Activities of the Private Sector in International Agricultural R&D

Corporations active in international agricultural research include a large number of companies from the North and fewer, but an increasing number of, indigenous companies from the South. The companies from the North range in size from small corporations, often with specialized applications and operations in one or few industrial countries, to large transnationals with global operations in many industrial and developing countries. Companies from the South are generally smaller and focus on their home country or region. Recent acquisitions - the successive acquisitions by Seminis of the Empresa La Moderna-ELM (Pulsar) Group from Mexico of Asgrow Seed, Peto Seed, Royal Sluis, and DNAP - however, indicate that some of the larger companies from the South are expanding their base of activities and becoming transnational.

The private sector has broad-ranging activities in agricultural research focused on the development, production, and distribution of products and services that lend themselves to commercialization. The private sector's major activities are in the industrial countries where currently there are more opportunities for commercialization than in developing countries, but this is changing. Most private sector activities in the developing world take place in the most advanced developing countries and favor working with large and wealthy commercial farmers and plantations rather than with small, subsistence, and resource-poor farmers. The corporations from the North and South that are active in agricultural R&D and are potential partners for public sector institutes are engaged in very diverse activities, some of which are listed below:

- acquisition, exchange, distribution and improvement of genetic stocks of crops, forest species, livestock and fish, using conventional and biotechnology applications;
- production and distribution of improved seed and livestock to meet international needs;
- production of fertilizers and development of management practices to optimize crop production;
- development of diagnostics to detect diseases in crops, animals, and fish;
- production of pesticides and pesticide application within the context of chemical control or integrated pest management;
- development of strategies to ensure responsible deployment of resistance genes in crops that will optimize durability of the genes;
- development and production of vaccines and other disease control agents for animal diseases;
- processing, storage, and use of food and feed products, including control of post-harvest losses;
- global strategic planning and policy analysis aimed at developing commercial agriculture-based products to meet global needs;

Private sector activities in agricultural research, such as those listed above, are conducted by industry groups that can be conveniently classified according to the following product types:

- fertilizers;
- seeds;
- crop protection;
- crop and microbial biotechnology products;
- animal genetic stocks, including biotechnology-based technologies;
- animal health products;
- food and food processing;
- forestry;
- fisheries;
- machinery and equipment.

The above classification, based on product groups, can be used to match and compare the activities of the private sector with those of the public sector. To provide an indication of the scale of the private sector's international activities, recent data on global markets for selected major industry groups have been collated, with major compa-

nies identified and listed according to their estimated global markets or their estimated R&D expenditures. Data have been collated for fertilizers, seeds, crop protection, animal health, and biotechnology. Many of the large transnational companies are listed in several of the groups, indicating that they are involved in several areas; for example, some companies have operations in seeds, agricultural chemicals (pesticides), as well as in crop and animal biotechnology.

Estimates of R&D Expenditures for Selected Corporations

The data in Table 3 list 1996 annual revenues and R&D expenditures for selected agricultural companies in crop protection and in seeds; the intent is to provide a better understanding of the scale and scope of current R&D expenditures by the private sector. R&D expenditures range from 14.8 percent of total revenue, to 5.9 percent, with an average of 10.6 percent. In general, industry considers 5 to 7 percent of revenue as the minimum investment necessary to ensure an acceptable level of competitiveness in the market place. Estimates of R&D expenditures by indigenous companies in developing countries suggest that on average R&D expenditures as a percentage of revenue are significantly lower, ranging from 1 to 5 percent, as compared with 5 to 10 percent or more in industrial countries. Whereas the percent R&D expenditure data in Table 3 cannot be compared directly with corresponding spending by the public sector on R&D, it is judged that percent R&D expenditures in the private sector are considerably higher than in the public sector.

Table 3: Annual Revenue and R&D Expenditures in 1996 for Selected Crop Protection and Seed Corporations
(US$ millions)

Company	Annual Revenue	R&D Expenditure	Expressed as Percent of Revenue
Crop Protection Corporations			
Novartis	4,175	373	8.9
Monsanto	2,872	170	5.9
Zeneca	2,849	260	9.1
DuPont	2,515	258	10.3
AgrEvo	2,451	283	11.6
Bayer	2,305	305	13.2
Rhone-Poulenc	2,174	174	8.0
DowElanco	2,005	210	10.5
Cyanamid	1,989	165	8.3
BASF	1,506	184	12.2
Seed Corporations			
Pioneer	1,600	133	8.3
Novartis	970	122	12.6
Limagrain	660	60	9.1
Advanta	470	53	11.3
DeKalb	387	41	10.6
Seminis	380	47	12.4
KWS	350	47	13.4
Cargill	250	37	14.8

Source: For Crop Protection Corporations: Wood Mackenzie 1997. For Seed Corporations: compiled by Clive James 1997.

Fertilizer Industry

The annual global fertilizer market was estimated at $50 billion in 1995/96, as shown in Table 4, with nitrogen at $35 million representing the major component in terms of value and tonnage, followed by phosphate at $11.2 million, and potash at $4.0 million. Data in Table 5 show that developing countries use 63 percent of the nitrogen consumed on a global basis, 61 percent of phosphate, but only 48 percent of the potash. On average about 60 percent of global fertilizer is consumed in developing countries, and the private sector is responsible for at least half of the total global production. Due to significantly higher prices in 1995/1996, the global fertilizer market was estimated at approximately $50 billion. The major fertilizer producers active in the international market are listed in Table A-1 of the Appendix.

Doubling food production will require significantly more use of fertilizers despite the significant effort underway to develop crop varieties that are more responsive to fertilizers. Such increased use of fertilizer will exacerbate a situation that is already of environmental concern; that is, even with the current usage rate of fertilizer, intensified agriculture is resulting in nitrate levels in groundwater well above accepted tolerance levels. Various technologies are being investigated to determine the potential for increasing the efficiency of nitrogen utilization and for using nitrogen-fixing organisms to develop cereals that can fix some of their own nitrogen supply, thereby decreasing dependence on inorganic nitrogen. Use of mycorhiza is also being explored as a means to increase the extraction efficiency of phosphate and other elements that are not available in sufficient quantities for crops growing in marginal areas, such as acid soils.

Crop Protection Industry

Global food, feed and fiber losses due to the combined effect of weeds, insect pests, and pathogens, are estimated to reduce yield by approximately 35 percent. The annual value of the global crop protection market in 1996 was $31.25 billion (Wood Mackenzie 1997). Herbicides represent 48 percent of the world crop protection market, insecticides 28 percent, fungicides 19 percent, growth regulators 4 percent, and transgenic seed less than 1 percent as shown in Table 6. The major difference between the global market in 1995 and 1996, and previous years, is the first commercialization of products derived from crop biotechnology, principally in North America; it is noteworthy that the global market for transgenic seed increased from $75 million in 1995 to $235 million in 1996 - an increase of 213 percent. Whereas herbicides are far more important than insecticides and fungicides in North America, Europe, and other industrial countries, with the exception of Latin America, insecticides predominate in developing countries. Approximately 72 percent ($22.6 billion) of the annual $31.3 billion global crop protection market is in

Table 4: The Global Fertilizer Market (1995/1996)

Type of Nutrient	Millions of Tons	Annual Value* ($ Billions)
Nitrogen (N)	78.7	35.0
Phosphate (P_2O_5)	31.0	11.2
Potash (K_2O)	21.1	4.0
Total	**130.8**	**50.2**

* Global value.

Source: International Fertilizer Development Center (IFDC) 1997

Table 5: Estimated Fertilizer Consumption in Industrial and Developing Countries 1995/1996 (million nutrient tons)

Nutrient	Industrial Countries	Developing Countries	Worldwide
Nitrogen (N)	28.8	49.9	78.7
Phosphate (P_2O_5)	12.0	19.0	31.0
Potash (K_2O)	12.1	9.0	21.1
Total	**52.9**	**77.9**	**130.8**

Source: International Fertilizer Development Center (IFDC) 1997

industrial countries of the North; 28 percent ($8.6 billion) is in developing countries of the South; note that this is a small change from 1994 when 25 percent of pesticides were used in developing countries. Nine countries consume 82 percent of pesticides, and the two major markets in the industrial North are the United States (28 percent) and Japan (12 percent), followed by several European Union countries and Canada, which consume 2 to 9 percent. Brazil and Argentina, at 6 and 3 percent respectively, are the only significant pesticide consumers from the South.

In terms of crops, horticultural crops (fruit and vegetables) are by far the most important, consuming just over 25 percent of pesticides, as shown in Table 7. The other major crops, which consume from 16 to 2 percent of the global supply are, in descending order of priority, cereals (small grains), maize, rice, soybean, cotton, sugar beet, and oil seed rape (canola). The segmented market for different pesticide products indicates that more insecticide (35 percent) is used on fruit and vegetables than any other crop category, followed in order of importance by cotton (19 percent), rice (13 percent) and maize (8 percent). The major use of herbicides is for cereals (19 percent), maize (18 percent), soybean (17 percent), fruit and vegetables (13 percent) and rice (9 percent). For fungicides, the major consuming crops are fruit and vegetables (46 percent), cereals (25 percent) and rice (15 percent).

Table 6: Global Crop Protection Market in 1996, by Group, by Principal Country and by Region

The Key Crop Protection Groups: 1995/1996

	Estimated Sales $ Millions		
Group	**1995**	**1996**	**% Change**
Herbicides	14,280	15,050	+5.4
Insecticides	8,750	8,745	-0.1
Fungicides	5,855	5,895	+0.7
Plant growth Regulators & Others	1,380	1,325	-4.0
Biotechnology Products	75	235	+213.3
Total	**30,265**	**31,250**	**+3.3**

Principal Countries' Percent Shares of the 1996 Global Crop Protection Market

USA	27.8
Japan	12.4
France	8.7
Brazil	6.2
Germany	4.0
Italy	3.3
Canada	2.8
United Kingdom	2.8
Argentina	2.8
Others	17.8
Total	**100.0**

Crop Protection Revenues 1996, by Region ($ millions)

	Herbicides	**Insecticides**	**Fungicides**	**Others**	**Biotech**	**Total**
North America	6,275	2,040	680	340	235	9,570
West Europe	3,605	1,420	2,510	600	0	8,135
East Europe	510	368	180	22	0	1,080
Japan	1,270	1,310	1,220	80	0	3,880
Industrial Countries	**11,660**	**5,138**	**4,590**	**1,042**	**235**	**22,665**
Latin America	2,035	1,005	520	140	0	3,700
Rest of East Asia	970	1,455	630	100	0	3,155
Rest of World	385	1,147	155	43	0	1,730
Developing Countries	**3,390**	**3,607**	**1,305**	**283**	**0**	**8,585**
Total	**15,050**	**8,745**	**5,895**	**1,325**	**235**	**31,250**

Source: Wood Mackenzie (1997)

Table 7: Global Crop Protection Market in 1996, by Crop, and by Crop Protection Product/Crop

Total Crop Protection Market by Crop	$ Million
Fruit and Vegetables	8,185
Cereals	4,955
Maize	3,655
Rice	3,380
Soybean	2,800
Cotton	2,639
Sugar Beet	827
Oilseed Rape/Canola	546
Others	4,263
TOTAL	**31,250**

Herbicide Market by Principal Crop	$ Million
Cereals	2,850
Maize	2,735
Soybean	2,590
Fruit and Vegetables	2,020
Rice	1,280
Sugar Beet	640
Cotton	600
Oilseed Rape/Canola	425
Others	1,910
TOTAL	**15,050**

Fungicide Market by Principal Crop	$ Million
Fruit and Vegetables	2,715
Cereals	1,490
Rice	870
Others	820
TOTAL	**5,895**

Insecticide Market by Principal Crop	$ Million
Fruit and Vegetables	3,070
Cotton	1,620
Rice	1,140
Maize	720
Others	2,195
TOTAL	**8,745**

Source: Wood Mackenzie (1997).

With the advent of biotechnology, some conventional insecticides are being substituted by novel genes - for example, *Bacillus thuringiensis (Bt)* - that confer resistance to insects through development of transgenic crops in which the active gene has been incorporated. In 1997, on a global basis, 9.9 million acres (4.0 million hectares) of transgenic crops resistant to insects were grown commercially. Similarly, 17 million acres (6.9 million ha.) of herbicide tolerant transgenic crops were grown in 1997 (James 1997). Currently, industrial countries consume considerably more herbicides than developing countries, but this is likely to change. Labor shortages and higher labor prices will lead to reduced use of hand-weeding for crops such as rice, and more herbicides will be applied, perhaps in conjunction with use of herbicide-tolerant varieties. Use of herbicides on rice in developing countries is likely to increase as the present trend to favor direct seeding in irrigated areas over traditional transplanting becomes more pronounced, and if more attention is focused on rainfed rice, where weeds are more of a problem. Water constraints associated with irrigated rice production will lead to less optimal control of weeds, which, in conjunction with the other factors noted above, could lead to significant increases in herbicide use on rice, more than 90 percent of which is grown and consumed in Asia.

Concern for the environment, large-scale commercialization of transgenic crops with resistance to insects, herbicides and plant pathogens, and widespread implementation of integrated pest management (IPM) are all factors that will likely have a significant effect on the structure of the crop protection market in the future. The private sector, however, will continue to dominate the crop protection market and will probably become more dominant as technologies become more sophisticated and

as penetration of markets in the developing countries of Asia and Latin America, and to a lesser extent Africa, advances.

The principal companies involved in the international crop protection industry are transnationals with headquarters based in Europe (7), the United States (7), and Japan (9). Companies involved in crop protection are by and large also those involved in the chemical, pharmaceutical, seed and agribiotechnology industries. The principal companies involved and their respective share of the global market are listed in Table A-2 of the Appendix. The turnover of the companies ranges from $0.26 billion to $4.2 billion per year, and the leading ten companies account for approximately 80 percent of the $31.25 billion global market.

The crop protection industry has gone through a consolidation phase that featured mergers and takeovers, the most recent of which occurred in March 1996 with the merger of Ciba and Sandoz to form Novartis. Novartis, which will benefit from the combined pesticide markets of both Ciba and Sandoz, is now the largest crop protection company in the world, with sales of $4.175 billion in 1996 (see Table A-2). In 1995, Hoechst and Scherring merged to form AgrEvo, which is now ranked the fifth largest corporation involved in crop protection, with 1996 revenues of $2.5 billion. Whereas the incentive for the merger between Ciba and Sandoz was driven mainly by the needs of the pharmaceutical industry, it nevertheless has important implications for the crop protection industry, which is anticipating more mergers in the coming decade.

A survey of pesticide usage in the United States (Anonymous 1995) for the period 1991 to 1993 showed that use, as measured by volume of active ingredients, continued in 1993 a ten-year pattern of nearly flat growth, which was due to lower application rates of more potent compounds and more efficient use of pesticides. Twenty new active ingredients were registered in the United States in 1993, the highest number since 1975, with regulation costs estimated at $303 million or 3.6 percent of pesticide revenues.

Seed Industry

The value of the global seed trade is estimated at $45 billion annually, equally divided among the three different segments (Rabobank 1994): commercial seed, which is dominated by the private sector; farm-saved seed; and seed from government institutions. The latter is particularly prevalent in developing countries and in centrally planned economies. For example, in Africa, governments completely control the seed industry in 60 percent of the countries, and both the government and private sectors are active in 28 percent of the countries. Consumption of agricultural seed, which includes farm-saved seed, is approximately 120 million tons per year, and global consumption has been stable since about 1980. Asia and the Commonwealth of Independent States are the largest consumers of seeds, approximately 38.4 and 37.3 million tons respectively, in 1990, and together represent approximately two-thirds of the world market, as shown in Table 8. Consumption has been stagnant during the last decade, except in Asia, where consumption has increased by 18 percent since 1980; one-third of the seed used in Asia is rice.

Cereals dominate the world seed market, accounting for approximately two-thirds of the 120 million ton market, as shown in Table 9. Wheat is the major cereal crop for the seed market (35 million tons) followed by rice (13 million tons), barley (11.1 million tons), and maize (6.8 million tons); root and tuber crops are deceptively high, at 33.3 million tons, because of the high water content of "seed tubers". Of the $15 billion annual market in commercial seed, horticultural seed accounts for only $1.75 billion, and this includes both vegetable and flower seed. In 1990 approximately $13 billion of the $15 billion commercial seed market was in the OECD countries. The European Union ($5.8 billion), the United States ($4.5 billion), and Japan ($2.7 billion) were the largest markets; Turkey, Argentina, and Brazil were also important.

The private sector dominates the $15 billion annual global commercial seed market. There are approximately 1,500 seed companies worldwide, of which 600 are based in the United States and 400 in Europe. The twenty principal seed companies that are active internationally have a total market of $7.8 billion (Cailliez 1997) and are listed in Table A-3 and, with the exception of Empresas La Moderna, S.A.-ELM (Pulsar), which is based in Mexico, are transnationals based in the United States (5), Europe (12), and Japan (2). The annual turnover of the companies ranges from approximately $0.12 billion to $1.6 billion per year. Their combined turnover of $7.8 billion, is about half of the global commercial seed market. The market shares of these companies are expected to increase in the future. Of these 20 seed companies, approximately 75 percent are specialized seed companies, and the other 25 percent are owned by larger corporations with diversified interests.

Until the 1960s the seed industry comprised traditional seed companies that specialized in the improvement, pro-

Table 8: Total World Consumption of Agricultural Seed, by Continent
(millions of tons, incl. farm-saved seed)

Region	1980	1985	1990
Commonwealth of Independent States (CIS)	41.7	37.7	37.3
South America	4.3	4.4	4.2
Europe	23.2	23.6	21.3
North & Central America	10.9	10.4	11.0
Asia	32.6	35.0	38.4
Africa	3.9	4.3	4.6
Oceania	1.2	1.4	1.1
Total (World)	**118.8**	**117.7**	**118.7**

Source: FAO (Rabobank, 1994)

Table 9: Total World Consumption of Agricultural Seed, by Crop (millions of tons)

Crop	1980	1985	1990
Wheat	34.0	33.2	35.0
Barley	11.8	11.6	11.1
Rice	11.5	12.2	13.0
Maize	6.4	6.5	6.8
Other grains	9.5	9.3	8.9
Root/tuber crops	36.8	35.4	33.3
Pulses	3.4	3.9	4.0
Oilseeds	5.4	5.6	6.6
Total	**118.8**	**117.7**	**118.7**

Source: FAO (Rabobank, 1994)

duction and distribution of seed. During the late 1960s several transnational corporations with activities in farm chemicals and pharmaceuticals acquired seed companies to capture the range of products and services for the agricultural industry within one corporate structure, thus providing them with the necessary R&D critical mass and benefiting from economies of scale. After a decade or so, however, some of the transnationals sold their acquired seed operations, for several reasons: incompatibility with an evolving business strategy, lower margins than expected in seed operations where they lacked business linkages and experience, and a realization that the opportunities for using the seed industry to capture and market proprietary transgenic crops was a longer-term venture than they had anticipated. In the 1980s and 1990s acquisitions and mergers have resulted in fewer but larger seed companies, a trend that is expected to continue into the next decade, ultimately resulting in a few very large companies dominating the international market. This trend is fueled by the long-term investments in research that are necessary to ensure competitiveness and an international marketing structure to effectively compete in the global market.

Mergers and acquisitions are not the only way critical mass for R&D is being created in the industry. Collaborative arrangements, which range from cooperative R&D agreements to cross-licensing, are becoming prevalent, with Pioneer Hi-Bred International recently reporting that it has 800 agreements with various private and public organizations. In 1995, ELM (Pulsar) of Mexico acquired Asgrow Seed owned by Upjohn, added Peto Seed and Royal Sluis to its portfolio later in the year, and in early 1996 acquired DNAP, a small agricultural biotechnology company. In February 1996 there was a merger between the seed operations of Zeneca (formerly ICI, United Kingdom) and Suiker Unie, which owns the Vander Have Group from the Netherlands. The two corporations view the merger as an opportunity to mobilize the necessary critical mass for research, to benefit from the complementarity in their respective operations, and to increase the probability that the newly formed company will be one of a few large companies to dominate the market in the coming decades.

In March 1996, Sandoz and Ciba merged to form Novartis, which now is the second largest seed company in the world, with a turnover of $907 million in 1994. The former operations of Sandoz were estimated at $727 million and included four companies, Hilleshog NK (France), Northrup King (United States), S&G Seeds (the Netherlands), and Rogers (United States), with subsidiaries in twenty-five countries, and those of Ciba were in ten or more countries, with operations estimated at $180 million. Seed industry representatives expect such mergers to continue as companies attempt to build the minimum critical mass necessary for efficient R&D operations to be implemented and for products to be more competitive in the international marketplace.

In August 1997 DuPont announced a $1.7 billion investment in Pioneer Hi-Bred International. The alliance between the two companies represents a joint venture called "Optima Quality Products" which allows Pioneer to enhance the value of its germplasm, mainly maize, and provides DuPont with an effective delivery vehicle for marketing its broad range of output traits that confer enhanced nutritional value to food and feed products. In developing countries, where it is estimated that 80 percent of seed is currently supplied by government organizations or by farmer-saved seed, private sector activity in the seed industry is expected to become increasingly strong. Private sector growth is likely to be particularly important in Asia,(where most of the industrial country-based seed transnationals are active along with the Thailand-based CP Seed Company), as well as in Latin America and selected countries in Africa. As the former centrally planned economies of Eastern Europe and the Commonwealth of Independent States become politically and economically stable, these regions should also experience significant growth of the private sector seed industry.

Animal Health

The world market for animal health products was estimated to be $14.4 billion in 1995 (Wood Mackenzie 1997), as shown in Table 10. Animal health products are divided into four categories: nutritional feed additives; medicinal feed additives; biologicals; and pharmaceuticals. [These categories are defined in detail in the footnote of Table 10.] Pharmaceuticals represent just under half of the global market of animal health products, and nutritional feed additives approximately one-third. More than half of the total global pharmaceutical market of $6.4 billion is in the OECD countries, with sales of $2.1 billion in Europe, $1.9 billion in North America, $1.1 billion in East Asia, and $850 million in Latin America.

The data in Table 11 indicate that cattle account for 32 percent of the global market supply of animal health products (of which approximately half is pharmaceuticals) followed by pigs (23 percent), poultry (18 percent), and sheep (6 percent). In developed countries, care of domestic pets is a significant and growing market, making up approximately 20 percent of the global market in animal health products.

The animal health industry has many similarities to the crop protection industry in that the principal companies active internationally are either part of, or have association with, large transnationals that have operations in chemicals, pharmaceuticals, and biotechnology. Global sales of animal health products are dominated by the private sector. The top ten companies [see Table A-4], accounted for 60 percent of the world market of $14.4 billion in 1995. With the exception of the Tortuga Corporation (Brazil), all the principal companies are transnationals based in the United States (9), Europe (13), or

Table 10: Global Animal Health Sales in 1995, by Product Group and Region ($ millions)

Regions:	Nutritional Feed Additives	Medicinal Feed Additives	Biologicals	Pharmaceuticals	Total
North America	1,042	675	530	1,858	4,105
Western Europe	1,092	492	645	2,066	4,295
East Asia (China, Southeast Asia, Australia)	757	445	377	1,121	2,700
Eastern Europe	435	185	140	280	1,040
Latin America	294	198	358	850	1,700
Rest of World (Africa, Middle East, India)	170	95	90	175	530
World Total	**3,790**	**2,090**	**2,140**	**6,350**	**14,370**

Note. Product categories included the following: nutritional feed additives include vitamins, minerals, amino acids, non-protein nitrogen and other nutritionals; medicinal feed additives include antibiotics, antibacterials, anticoccidials, growth promotants, and other medicinals; biologicals include livestock biologicals, poultry biologicals, and companion animals; pharmaceuticals include antimicrobials, parasiticides, and performance enhancers.

Source: Wood Mackenzie (1997)

Table 11: Global Animal Health Sales by Product Group & Animal Species, 1995 ($ millions)

Animal Species	Nutritional Feed Additives	Medicinal Feed Additives	Biologicals	Pharma ceuticals	Total
Cattle	1,025	440	610	2,475	4,550
Pigs	1,100	730	285	1,120	3,235
Sheep	130	95	145	485	855
Poultry	1,065	765	500	240	2,570
Pets/Other	470	60	600	2,030	3,160
Total	**3,790**	**2,090**	**2,140**	**6,350**	**14,370**

Source: Wood Mackenzie (1997).

Japan (2), but they have significant and growing business in the developing countries estimated to be approximately 35 percent of the global market of $14.4 billion in 1995.

Biotechnology

Private sector investments in biotechnology are multidisciplinary in the sectors of medicine, pharmaceuticals, agriculture, and industrial applications such as fermentation. Because most private sector R&D investments are subject to a degree of confidentiality and many of the companies investing in biotechnology have multi-sector investments in biotechnology research, it is difficult to dis-aggregate the proportion of R&D investments devoted to agriculture. Thus, because there are no precise data available on biotechnology R&D expenditures, and because estimates are not always comparable due to lack of uniform methodology for consolidating and comparing data, the intent here is to describe the scope and scale of the investments and highlight order-of-magnitude differences.

Global R&D investments in 1990 by both public and private sectors in biotechnology for all sectors were estimated to be $11 billion, of which $6 billion was in the United States, $3 billion in Europe, and $2 billion in Japan; the private sector in Japan invested $1.4 billion (70 percent) of the total $2 billion (Persley 1990). Estimates of the relative contributions of the public and private sectors in the different biotechnology markets in 1985 (Persley 1990) are detailed in Tables 12, 13, and 14; they indicate that 50 percent of total global investments were in the USA, 25 percent in Europe, 15 percent in Japan and the balance of 10 percent in other countries. The estimates also show that global R&D expenditure in biotechnology by the private sector was $2.7 billion, slightly more than twice the $1.3 billion by the public sector. Corresponding comparisons for agricultural biotechnology indicate that slightly more than 60 percent of the investments were by the private sector and the balance by the public sector. Of the total $900 million spent in 1985 in agricultural biotechnology R&D by the public and private sectors, $550 million, equivalent to almost two-thirds of total expenditures, was spent by the private sector. Of the $900 million invested by both the public and private sector on agricultural biotechnology, two-thirds was spent on seed, and the balance on microbiology applications.

More recent data for 1995 on investments, revenues, and R&D expenditures show that there has been a dramatic increase in the decade 1985 to 1995. In the United States alone total sales of new biotechnology-based products in all sectors were almost $9.3 billion in 1995. It is estimated that sales will grow at 12 percent per year to reach $34 billion by the year 2006 (Ernst & Young 1995). More specifically, Table 15 shows that in 1995 sales of agricultural biotechnology products in the United States were approximately $100 million with an R&D expenditure of $2 billion; the corresponding sales for pharmaceutical products in 1995 were $7 billion sales and $8 billion in R&D. In 1996 the U.S. sales of agribiotech products increased to $304 million and this figure is expected to increase by 20 percent per year (Ernst & Young 1996). It is estimated that of the $10.8 billion total sales of biotechnology products in the United States in 1996, human therapeutics represented 75 percent of total sales, human diagnostics 17 percent, agriculture 3 percent, specialties 3 percent, and non-medical diagnostics 2 percent (Ernst & Young 1996, Persley 1997).

Table 12: 1985 Global Estimates of R&D Expenditures on Biotechnology, by Country or Region ($ millions)

Country or Region	Private sector	Public sector	Total
United States	1,500	600	2,100
European Union	700	300	1,000
Japan	400	200	600
Others	100	200	300
Total	**2,700**	**1,300**	**4,000**

Source: Persley, 1990.

Table 13: 1985 Global Estimates of R&D Expenditures on Biotechnology, Private and Public Sectors ($ millions)

Sector	Agricultural biotechnology	Other	Total
Private	550	2,150	2,700
Public	350	950	1,300
Total	**900**	**3,300**	**4,000**

Source: Persley, 1990.

Table 14: 1985 R&D Global Expenditures on Agricultural Biotechnology, by Application ($ millions)

Application	Private sector	Public sector	Total
Seeds	350	250	600
Microbiology	200	100	300
Total	**550**	**350**	**900**

Source: Persley, 1990.

Table 15: Sales and R&D Expenditures for Biotechnology Products in the United States, 1995 and 1996 ($ millions)

	1995	1996
Pharmaceutical Sales	7,000	8,600
Pharmaceutical R&D	8,000	N/A
Agricultural Sales	100	304
Agricultural R&D	2,000	N/A
Other Sales	2,200	1,896
Total Sales	**9,300**	**10,800**

Source: Compiled by Clive James and derived from Ernst & Young (1995), Ernst & Young (1996), & Wood Mackenzie (1997).

Whereas a high proportion of the R&D investments in agri-biotechnology are undertaken by the private sector, various public institutions and organizations that serve domestic and international interests are assigning higher priority to biotechnology. The World Bank has lent $100 million in support of biotechnology, whilst the Rockefeller Foundation and bilateral agencies, including those in the United States, U.K. and the Netherlands, have invested $200 million during the last decade (Brenner 1996). National research agencies such as USDA, BBSRC in the United Kingdom, and CSIRO in Australia, have also made significant investments in biotechnology. The CGIAR international agricultural research centers estimate that biotechnology expenditures are currently $22.4 million per year, of which $10 million is spent on animal biotechnology and the balance of approximately $12 billion on crop biotechnology by a total of eight centers (CGIAR 1996).

In terms of sales of agri-biotech products, it is estimated that transgenic seed comprise two-thirds to three-fourths of total sales of agri-biotech products. The People's Republic of China was the first country to commercialize transgenics in the early 1990s with the introduction of virus resistant tobacco, which was later followed by a virus resistant tomato. In 1994, Calgene obtained the first approval in the United States to commercialize a genetically modified food product, when the company marketed its Flavr Savr™ delayed ripening tomato. By 1996 approximately 7 million acres (2.8 million ha.) of seven principal transgenic crops (tobacco, cotton, soybean, corn, canola, tomato, and potato) were grown commercially on a significant area in the following six countries, listed in descending order of acreage: United States, China, Canada, Argentina, Australia, and Mexico. By trait, virus resistance accounted for 40 percent of the transgenic acreage in 1996, followed by insect resistance (37 percent), herbicide tolerance (23 percent), with quality traits accounting for less than 1 percent (James & Krattiger 1996). In 1997 the global area of transgenics increased significantly to 31.5 million acres (12.8 million ha.), with seven crops grown in six countries, as in 1996, with at least forty transgenic crops approved in at least one country (James 1997). Thus, the 1997 acreage of 31.5 million acres (8.1 million ha.) increased by a factor of 4.5 from the 7.0 million acres (2.8 million ha.) in 1996. The United States continued to be the principal grower of transgenic crops in 1997 and its share of global acreage increased from 51 percent in 1996 to 64 percent in 1997, equivalent to 20.1 million acres or 8.1 million hectares. The relative areas occupied by the four transgenic traits were also significantly different in 1996 and 1997. Herbicide tolerance, the third ranking trait in 1996, occupying 23 percent of the area, moved to the top ranking position in 1997 with 54 percent of the global area. Insect resistance was fairly stable with 37 percent in 1996 and 31 percent in 1997, with virus resistance decreasing sharply from 40 percent in 1996 to 14 percent in 1997; quality traits occupied less than 1 percent of total area in both 1996 and 1997. More comprehensive information on the benefits associated with new transgenic crops will be available following analysis of 1997 data, when the first substantial acreage of transgenics was planted globally, however initial results indicate that the benefits are significant (James 1997). Transgenic crops have been well received in North America, with a very high percentage of farmers planting transgenic crops in 1996, electing to plant again in 1997; many transgenic products were unavailable to potential growers in North America in 1997 because of shortage of transgenic seed supplies, and therefore reported acreages of transgenic crops are lower than the acreages planned by farmers.

There are numerous potential opportunities for applying biotechnology in developing countries, but for commercial reasons many of these will not be pursued by the private sector. These opportunities often exist for what are termed *orphan commodities* (Persley 1989; James and Persley 1991); for example, low-value, vegetatively propagated crops such as cassava and sweet potatoes, which are important primarily as staples for poor people in the developing world. Similarly, crops grown over a relatively small area would not be attractive to the private sector, even though these crops may make a vital contribution to the diet of poor people in a specific country or region. Given that basic biotechnology knowledge is broadly applicable to diverse problems, industry often has a comparative advantage in developing the most cost-effective solutions to many problems in the developing world. This situation represents a challenge to both developing countries and to international development agencies (James and Persley 1990), to develop effective biotechnology transfer programs to benefit subsistence farmers and orphan crops in developing countries.

Assuming equal research competence in the private and public sectors in the industrial countries, and acknowledging that industry's principal objective is product delivery, it is reasonable to suggest that the private sector will continue to be the principal, although not the only, generator of biotechnology products for agriculture. The comparative advantage of industry lies in several areas:

- Large R&D resources for funding long-term and sometimes high return, but speculative, agricultural projects.

- Diversity, from small, dedicated biotechnology companies to large transnational corporations that have extensive and increasingly collaborative research links with the public sector, particularly universities.
- Critical mass of scientific research resources, which is of paramount importance in biotechnology. These resources often are consolidated within a core research group in the private sector (e.g. in a life sciences department), which is a cost-effective way to provide common research support for two significant product development markets - medicine and agriculture.
- Knowledge of and expertise in marketing and distribution systems.
- Access to global markets and the associated advantages of economies of scale, which allow development costs to be amortized over long periods in large markets.

The advent of biotechnology has resulted in a significant change in the relative investments of the public and private sectors in agriculture, with the private sector now investing significantly more than the public sector in biotechnology R&D. As the adoption of biotechnology-based products in agriculture becomes more widespread, this gap between public and private sector investments is expected to be maintained or increase. This trend will be accentuated by current government policies, in both industrial and developing countries, that encourage participation by the private sector in areas where it has comparative advantages over the public sector. Estimates of future markets for agricultural biotechnology products vary; industry sources suggest that a realistic estimate is $3 billion to $5 billion for total sales at the farm level by the year 2000. Of this, seeds are predicted to comprise approximately $2 billion to $3 billion, with the balance in veterinary products and microbiology-based products. The increased market for agricultural biotechnology products is expected to be at the expense of existing markets, with some restructuring of those markets, rather than by major expansion of current markets (Persley, 1990). The global market for transgenic crops is projected to increase from $0.5 billion in 1996, to $2 to $3 billion in the year 2000, to $6 billion in 2005, and to $20 billion in 2010.

Summary of Private Sector Activities in Agricultural R & D

In summary, the private sector plays a major global role in agricultural R&D. The importance of its role is evident from the data presented in this section and in the appendix, even though these data do not include all the activities of the private sector; for example, the subsectors of post harvest/food processing and agricultural machinery, which are not featured, represent significant investments that are dominated by the private sector. In the future, private sector investments in agriculture and food are expected to increase faster than investments by the public sector, in both industrial and developing countries. Anderson *et al.* (1994) noted that, as farmers use more purchased inputs and as the value-added in agriculture increasingly moves off the farm to the marketing and processing subsectors, it is likely that the incentives for private sector investments in agricultural research will grow. With current private sector global revenues in fertilizers, seeds, pesticides and animal health alone estimated conservatively at approximately $80 billion per year, the private sector is an essential partner for the global public sector engaged in agricultural research.

The Need for Collaboration between the Public and Private Sectors

There is no greater incentive for collaboration between the public and private sectors in agricultural research than the enormous challenge posed by global food security, which will require that limited global resources be used in the most effective way to develop sustainable systems that also conserve natural resources. The urgency of this challenge cannot be overstated. Knowledgeable observers judge that the current joint investments of the public and private sectors in agricultural research are inadequate, to double (or preferably triple) agricultural production in the next fifty years. Furthermore, this is occurring at the same time external aid to agricultural research, which is viewed by many to be the catalyst that will stimulate economic growth in developing countries, and as the best antidote for poverty, is declining.

There is, and will continue to be, a critical and essential role for governments in developing countries to address policy issues in agriculture and to implement technical programs that optimize social welfare for the public good. Governments should not view for-profit private sector activities as detrimental to the public good because these private sector activities often are the most effective way – for example, in seed production and distribution - to

achieve national goals set by governments. The collective goal must be to build partnerships that optimize the comparative advantages of the public and private sectors to achieve mutual goals. Governments have access to many policy instruments to encourage and stimulate private sector investments in joint venture programs, and donors can facilitate implementation of such collaborative programs (Anderson et al. 1994).

It is noteworthy that in the last decade there has been a strong trend for governments of donor countries to encourage, and in some cases require, increased participation by the private sector in agricultural research. Many of the more advanced developing countries have emulated this trend and established policies that encourage increased participation by the private sector in areas where it has comparative advantage. Whereas in the past policymakers in developing countries did not always recognize the private sector as an important resource for national programs, there has been a marked and progressive change in which the private sector is now generally acknowledged to be a key player in research and development. This view is endorsed by the international development and finance community, which recognizes the private sector in the North and the South as an increasingly important national and international resource (James and Persley 1990).

The significant investment of the private sector in biotechnology, perhaps more than any other single factor, has clearly demonstrated the need for and significant advantages associated with collaboration between the public and private sectors in agricultural research and development. Indeed the requirement for a minimum critical mass in R&D, particularly in biotechnology, has been the major stimulus for most of the mergers and acquisitions within the private sector. The development of biotechnology applications is capital intensive, requiring substantial long-term investments, which often can be mobilized only by the private sector. Thus, most investments in biotechnology are made by the private sector. A major challenge for both the private sector and the public sector is to find ways to collaborate in sharing and transferring appropriate new and superior technologies, which often are proprietary, from the private sector in the industrial countries to the public sector in the developing countries.

Collaboration between the public and private sectors is essential in planning future research strategies that are global in coverage, and requires cooperation by all the major entities in agricultural research in industrial and developing countries. This cooperation should ensure that limited global resources in agricultural research are used in the most effective way to strategically address the issue of food security in the developing world by optimizing the comparative advantages of the public and private sectors. Assuming that data from selected industrial and developing countries are representative, current private sector investments in agriculture and food R&D are conservatively estimated to be about $11 billion in the industrial countries and $2 billion in the developing countries; this compares with $8.5 and $8.8 billion, respectively, by the public sector. The issue here is not the precision of the estimates; rather, it is that both the public and private sectors are spending, independently, a total of approximately $30 billion on agricultural R&D. This $30 billion investment is inadequate to meet current global agricultural R&D needs. In addition, it does not benefit from the considerable efficiencies that could accrue if the same $30 billion were invested in a more coordinated manner by the public and private sectors. It is, therefore, vital that the two major players, the public and private sectors, involved in agricultural R&D on the global scene collaborate to address the important and impending challenge of global food security. Governments of developing countries, the donor community, and the private sector must take the necessary and urgent steps to initiate the building of partnerships. It is encouraging to note that there is cause for cautious optimism because several initiatives are already underway to build new partnerships between the public and private sectors. Three of these public-private initiatives are the founding of the International Service for the Acquisition of Biotech Applications (ISAAA) in 1991, the establishment of the Private Sector Committee of the CGIAR in 1995, and the formation of a Public-Private Sector Consortium by CAB International to support the development of a Global Electronic Crop Protection Compendium (CPC). These three initiatives, which are quite different in character, are described in the following pages.

Founding of The International Service for the Acquisition of Agri-biotech Applications (ISAAA)

The Mission

The mission of the International Service for the Acquisition of Agri-Biotech Applications is to help alleviate poverty by increasing crop productivity and income generation, particularly for resource-poor farmers, and to create a safer environment and promote a more sustainable agricultural development. ISAAA's objective is the transfer and delivery of appropriate biotechnology products, particularly proprietary technology from the private sector in the North, to developing countries in the South by building partnerships between institutions in the South and the private sector in the North.

The Need

In the past, developing countries, and the institutes which have assisted them with agricultural research, have had the privilege of freely accessing non-proprietary traditional technology from the public sector in the industrial countries. With the advent of new biotechnology applications, however, this situation is changing. The new applications are increasingly proprietary, and are owned primarily by private sector corporations in industrial countries, which account for the majority of the investment in biotechnology R&D on a global basis. The greatest need for agribiotechnology, however, is in the developing countries. The benefits of biotechnology generally are not accessible to developing countries due to institutional, political, and infrastructural constraints and to a lack of financial resources. The applications of agribiotechnology offer promising means to a more sustainable agriculture and a safer environment; for example, by providing alternatives to the use of toxic conventional pesticides. Conventional technology alone can no longer increase food, feed and fiber productivity at a growth rate fast enough to keep up with population growth and still respond to environmental and sustainability pressures. There is consensus in the scientific community that biotechnology is an essential element for increasing food, feed and fiber productivity in the future.

The Institutional Response

A new institutional mechanism, ISAAA, sponsored by public and private sector institutions, was created to transfer agri-biotech applications from industrial countries in the North, particularly proprietary technology from the private sector, to developing countries (James 1991, James and Krattiger 1993). ISAAA's role and comparative advantage as an honest broker is to bring together institutions from national programs in the South and from the private sector in the North, into partnerships to transfer biotechnology applications. Thus, ISAAA is not an executor but a facilitator. ISAAA's organizational structure permits both the public and private sectors to work together as true partners in an international biotechnology program for the benefit of the developing world. Acknowledging that technology adoption by resource poor farmers is, and probably always will be, challenging and difficult, emphasizes the importance of ISAAA's mission in its quest for equity in technology transfer. In the absence of organizations such as ISAAA, developing countries may be denied the opportunity to access the full potential that current and future superior biotechnology applications offer.

To assist developing countries in the acquisition and application of proprietary biotechnology applications, ISAAA was founded as a not-for-profit international organization. It is cosponsored by a troika of donor groups: philanthropic foundations, bilateral organizations and corporations from the private sector that provide financial support and share biotechnology applications. More than $13 million has been provided by a group of eighteen donors in support of ISAAA's program. ISAAA is a small, responsive, nonbureaucratic, international network. Two ISAAA Centers are already established in the North, the AmeriCenter at Cornell University in the United States and the *Euro*Center at the John Innes Centre, Norwich Research Park, United Kingdom. These two Northern Centers evaluate and monitor available technology applications and products for transfer to the South; links are maintained with Japan through a liaison group. The two Centers in the South are hosted by CGIAR centers which facilitates close cooperation with the international agricultural research centers (IARCs). The ISAAA *Afri*Center, established in 1994, is hosted by the International Potato Center on the ILRI campus in Nairobi, Kenya, and the ISAAA *SEAsia*Center is hosted by the International Rice Research Institute (IRRI) at its campus in Los Baños, the Philippines; plans to establish the *Lati*Center which will serve the needs of South America, are under consideration. Programmatic, organizational and policy guidance is provided by an International Board of Directors of prominent individuals representing developing and industrial countries, public and private sectors, and professional interest groups, including environmental protection.

ISAAA is funded by fixed-term commitments through a donor support group that includes a balanced representation of public and private sector institutions. No core funding is being mobilized, allowing full flexibility for changes in future directions without encumbering donors with long-term and less flexible core commitments. The fixed-term funding strategy exposes the program to regular peer review when accessing competitive international funding. Early tangible expressions of support from the public and private sectors were evident by the significant grants awarded to ISAAA by eighteen donors.

The Program

ISAAA has initiated a pilot program that uses a five step strategy to provide the following services:

- assist developing countries in identifying biotechnology needs and priorities and in assessing potential socioeconomic impacts, in a demand-driven program;
- monitor and evaluate the availability of appropriate biotechnology applications, particularly proprietary technologies from the private sector in industrialized countries;
- provide "honest broker" services, by matching needs with appropriate proprietary technologies;
- mobilize funding from donor agencies for client countries to implement projects;
- counsel developing countries on the safe and responsible testing of biotechnology products and provide targeted assistance for the implementation of biosafety and food safety regulatory procedures, socioeconomic analysis, the management of resistance genes, and intellectual property rights.

The Strategy

The strategy is to focus on the safe and effective introduction of near-term biotechnology applications that already have been tested in industrial countries, particularly to:

- emphasize applications to increase the productivity of food crops in the near-term, particularly *orphan commodities* grown by resource-poor farmers; contribute to sustainable agriculture and a safer environment through the development of alternative technologies to conventional toxic pesticides; and assign high priority to horticulture and forestry;
- concentrate on three classes of plant biotechnology applications: tissue culture, diagnostics, and transgenic crops; and
- assign priority to the assessment of benefits and constraints of biotechnology in developing countries, including biosafety and food safety considerations, and the responsible deployment of resistance genes to optimize durability.

ISAAA implements a demand-driven program that responds to the priority needs of twelve target national programs in Africa (Egypt, Kenya, and Zimbabwe), Asia (Indonesia, Malaysia, the Philippines, Thailand, and Vietnam) and Latin America (Argentina, Brazil, Costa Rica, and Mexico). These target countries were selected because they are developing nations that have some capability in agribiotechnology and the political will to play a leadership role in biotechnology transfer. Establishment of ISAAA centers in the South provides a physical location from where diffusion of technology to neighboring countries with similar needs can be achieved effectively at marginal cost.

Program Achievements

Approximately twelve ISAAA projects have been developed, brokered, and implemented or are under development. The most advanced model project involves Monsanto's donation in 1991 of coat protein genes to Mexico for the control of potato viruses (PVX/PVY); the project is funded by the Rockefeller Foundation and features technology transfer and training of Mexican scientists. The transgenic potatoes, developed by Mexican scientists, are currently being field-tested in Mexico and results are promising. Monsanto has also agreed to a South-South transfer of the PVX/PVY technology that will allow Mexico to share this technology with Kenya. A companion project assisted Mexico in developing the infrastructure and regulatory biosafety and food safety procedures for testing and introducing recombinant products. Discussions between Mexico and Monsanto in 1996/1997 led to another donation of a gene that confers resistance to the economically important potato leaf virus (PLRV); this technology transfer is aimed specifically at varieties, such as Rosita, that are grown exclusively by resource-poor farmers.

Other ISAAA projects include:

- Diagnostic for black rot of crucifers, one of the most important diseases of cabbage in Asia (Washington State University/Asian Vegetable Research and Development Center -AVRDC).
- Development and transfer of several diagnostics for maize diseases in Brazil (Pioneer Hi-Bred International/EMBRAPA).
- Diagnostic for Tomato Spotted Wilt Virus (TSWV) in horticultural crops in Indonesia and other countries in S.E. Asia (Novartis Seeds/Indonesia).

- Insect-resistant cotton (Monsanto/Brazil/Argentina).
- Transfer of a selectable marker gene in cassava (Sandoz/CIAT).
- Tissue culture-based pilot production facility for more productive, virus-free banana seedlings (South Africa/Costa Rica/Kenya/Uganda).
- Improved and healthier fruit trees with the application of diagnostics (Germany/South Africa/Zimbabwe).
- Breeding for maize streak virus resistance in maize (John Innes Center, United Kingdom/Kenya/Pan Africa).
- Micropropagation and distribution of multipurpose trees (Mondi Corporation, South Africa/Kenya).

Projects under development include:

- Transgenic sweet potatoes resistant to Feathery Mottle Virus, one of the most devastating virus diseases of sweet potatoes in Africa (Monsanto/Kenya/Rwanda/Tanzania/Uganda).
- S.E. Asia Network for the development and testing of transgenic papaya that is resistant to papaya Ring Spot Virus, and with a delayed ripening gene that reduces postharvest losses (ISAAA's target countries in S.E. Asia)

Project Support Activities

ISAAA initiated a series of activities to support project implementation. These include an initiative on biosafety, socioeconomic analysis, management of proprietary science and technologies, intellectual property rights, issues related to biodiversity, and deployment and management of crops resistant to insects (*Bt*). A series of five biosafety workshops were conducted in Argentina, Costa Rica, and Indonesia, and two in Kenya. An initiative to staff a full time position to provide support in the important area of proprietary science will be implemented early in 1998.

Investment in Human Capital, ISAAA's Fellowship Program

Recognizing that human capital and training are the most important factors for sustainable and successful projects, ISAAA has a strong fellowship program. Training, an element in all ISAAA projects, is essential to build capacity and sustainability vis-a-vis biotechnology in national programs and to preclude dependency of developing countries on industrial countries for the new technologies. To date, ISAAA has arranged mid-career training for thirty-five scientists from eleven countries in tissue-culture, transformation, regeneration, diagnostics and molecular biology. Unlike traditional training programs, which usually have involved the public sector in the industrial countries, a noteworthy feature of the ISAAA Fellowship Program is that most of the project-specific, hands-on training, has been undertaken with the private sector corporations, rather than with the public sector.

Four regional biosafety workshops organized in Latin America (2), Asia and Africa have provided training for almost 300 regulatory officials and scientists from developing countries in the promulgation and implementation of biosafety guidelines. In the workshops, representatives from the industrial country public sector regulatory agencies and from private sector corporations (which are the major users of biosafety regulations) have shared their experience with colleagues from the developing countries. The thrust of the biosafety activities is to build capacity in regulatory oversight in national programs. For projects that involve genetically engineered plants, ISAAA ensures that products are tested and introduced in a safe and effective way, and preferably in harmony with existing biosafety regulations in various industrial countries. A similar series of training activities will be initiated in 1998 to address the complex issues related to the management of proprietary science and technologies. Socioeconomic activities and studies are incorporated in all projects including those dealing with recombinant technology.

Summary

In summary, the ISAAA experience has already demonstrated that partnerships can be built between the public and private sectors to their mutual advantage, and that a series of win-win options can be negotiated. These options include a partnership between the public sector in a developing country and a private sector corporation in an industrial country that involves outright donation of a biotechnology application by the private sector corporation; a joint venture that involves a contribution of technology from the two partners (for example, adapted germplasm from the developing country and a gene that confers added value from the private sector corporation) with an arrangement for development costs and return on investments to be shared by both parties; and a partnership between two private sector corporations, one from the North and one from the South, to commercialize a product by optimizing the comparative advantages of the partners.

Establishment of the Private Sector Committee of the CGIAR

Proposal to Establish the Committee

At the CGIAR Ministerial-Level Meeting in Lucerne, Switzerland, 9—10 February 1995, ministers, heads of organizations and delegates representing the membership of the Consultative Group on International Agricultural Research (CGIAR) recommended that the CGIAR broaden its partnership within the global agricultural research system. More specifically, as part of their Declaration and Action Program statement, the Ministerial-Level meeting encouraged the CGIAR to convene a committee of the private sector as a means of improving the dialogue among the CGIAR, the private sector, and members of the civil society interested in the same issues as the CGIAR. Interaction between the committee and the CGIAR was envisioned to be collaborative and of a consultative nature. The CGIAR was urged to work in closer partnership and collaboration with the private sector in the North and in the South to design and conduct joint research programs, and to ensure that the CGIAR's research agenda reflects the views and goals of global and regional partners in agricultural research. Under the leadership of the Chairman of the CGIAR, Mr Ismail Serageldin, a proposal was developed, discussed, and agreed to by the CGIAR, to establish the committee which first met in December 1995.

Terms of Reference of the Committee

The Committee interacts with the CGIAR to provide a private sector perspective on the current status of global agricultural research and future needs. It serves as a link between the CGIAR and the agricultural private sector organizations at large, in the North and the South, and facilitates the liaison between the agricultural private sector and the CGIAR. Through rotation of membership, over time the committee will incorporate representative views of a broad cross section of the private sector in relation to policies, strategies, research priorities, and program activities in agricultural research and development in the North and in the South.

The CGIAR initiative to form the committee aims at encouraging the private sector to foster and develop new programmatic partnerships that exploit fully the respective strengths, network of relationships, and comparative advantages of the CGIAR and the private sector.

The Committee brings to the CGIAR its perspectives on issues such as the following:

- current and future needs and priorities for agricultural research and development in the developing countries;
- current and future strategies of the private sector, especially in the South, to respond to those needs;
- private sector views on CGIAR policies, strategies and activities, including views on recent private sector research breakthroughs or cutting-edge technologies that the private sector would be willing to share with the CGIAR;
- identification of program thrusts that represent an opportunity for the private sector and the CGIAR to collaborate and to optimize the comparative advantage of the respective partners to achieve mutual goals and objectives; and
- evolution of a new partnership between the private sector and the CGIAR that will represent a holistic and all-encompassing global approach to food security.

The Committee expects to carry out its work by:

- meeting two times per year, for approximately two days at locations in the North and in the South (these meetings may or may not coincide with the Mid-Term-Meeting and International Centers Week of the CGIAR);
- interacting with the various elements of the CGIAR system and the clients that it serves in the developing countries;
- consulting with the CGIAR and its Chairman, as necessary;
- organizing meetings, workshops and consultations to broaden interactions between CGIAR and private sector institutions; and
- presenting to the CGIAR views and proposals emerging from the committee's deliberations.

The Committee is represented at CGIAR meetings through attendance by the Co-Chairs.

Composition and Membership of the Committee

The Committee has ten private sector members, including two Co-Chairs, one from the North and one from the South. Half of the members are from the private sector in the North, the other half from the private sector in the South. Members were selected from small, medium and large companies and represent the major activities of the private sectors in the North and South focusing on the

particular areas where the CGIAR is active, (for example, genetic improvement and management of crops, livestock, forest and fisheries; soil fertility; conservation and utilization of genetic resources; formulation of government food policies; and conservation and management of natural resources). The committee has reasonable geographic coverage and is a manageable size. Members are senior executives from the private sector who are leaders in their respective fields, have experience in strategic planning and policy decisions and have a broad range of professional backgrounds in the principal areas where the private sector and the CGIAR are active.

Initial Areas of Interest Identified by the Committee

The Committee has identified the following four topics for exploration and dialogue with the CGIAR:

- biotechnology—members are involved in the current Biotechnology Review in the CGIAR;
- intellectual property rights, genetic resources and biodiversity policy;
- mechanisms of interaction between the CGIAR, NARS and the private sector; and
- international centers and private sector practices in research and research management.

Summary

In summary, the establishment of the Private Sector Committee of the CGIAR represents an important development that should provide mutual benefits. The CGIAR, with a current annual budget of over $300 million (equivalent to 4 percent of public sector spending on agricultural research in the developing countries) is the single largest public sector investor in international agricultural R&D. The significant impact of the international centers of the CGIAR on productivity and production of staples, such as wheat and rice, is well documented and internationally recognized, evident by Dr. Norman Borlaug being awarded the Nobel Peace Prize in 1970 for his pioneering work on the semidwarf wheats. More recent objectives of the CGIAR focus on food self-reliance rather than food self-sufficiency, acknowledging that both agricultural and economic growth can alleviate poverty and the need for an eco-regional perspective to develop sustainable systems that conserve natural resources and protect the environment. The private sector faces the same challenges. These challenges demand more resources than the public and private sectors can marshal independently, and thus, it is both logical and desirable for the public and private sectors to collaborate in the pursuit of a goal that is vital for the future survival of the global community - food security.

Establishment by CAB International (CABI) of a Public-Private Sector Consortium to Support Development of the Global Electronic Compendium for Crop Protection (CPC)

It is estimated that crop pests (weeds, insects, diseases) reduce global crop production by up to 35 percent. Authoritative and current information on crop protection is a prerequisite for the development of knowledge-based pest management policies and strategies that optimize productivity and thus contribute to future world food security through the implementation of effective integrated pest management strategies. Workshops conducted by CABI in 1989 and 1992/1993 facilitated consultation with representative crop protection specialists from developing countries to determine the needs and priorities of national programs vis-a-vis crop protection. The lack of authoritative and current information, without which well-informed knowledge-based decisions are impossible, was determined to be an urgent priority need. Accordingly, workshop participants strongly endorsed the need for a Global Electronic Compendium for Crop Protection that would meet the needs of diverse users responsible for various aspects of crop protection globally.

In 1994 CABI conducted an extensive survey, focused on S.E. Asia, to determine the specific needs of different user groups in order to ensure that the Compendium would respond to needs and was demand-driven. The user survey determined strong demand for the Compendium from policy-makers responsible for crop protection in government and regional crop protection organizations, quarantine officers, researchers, extensionists, university teachers, agro-chemical industry personnel, and pest control managers implementing pest management schemes.

In early 1995 CABI made a decision to initiate the development of the Global Electronic Crop Protection Compendium in two modules (CABI 1996). Module 1 of the Global Compendium was developed during the first two years (1995 to 1997), starting with a focus on South East Asia and extended in the second two year period (1997 to 1999), with delivery of the Global Compendium scheduled for mid 1999. The development cost for the Compendium for the four year period 1995 to 1999 is $ 3

million, divided equally at $1.5 million for the first and second two year phases. Subject to successful resourcing of the development funds, CABI has made an up-front commitment to update the Compendium annually, using revenues from sales of the Compendium in industrial countries to update the product and offering preferential prices to developing countries to ensure affordability and equitable access to the product. CABI elected to form a public-private sector consortium to resource the compendium, thus facilitating broad participation by representatives of different user groups. Members derive significant benefits from the comparative advantages that CABI, as the developer of the compendium, offers the consortium. The following attributes characterize the compendium:

The Concept

The principal objective is to develop a knowledge-based multi-media electronic crop protection compendium that is global in scope; authoritative and current in content; capable of being operated in a user friendly mode, with a CD-ROM, or networked on a personal computer; and affordable to users in both the public and private sectors in developing and industrial countries. The Compendium provides a knowledge platform that allows users in developed and developing countries to easily access authoritative and current information on crop protection; the information can be readily applied to facilitate decisions in relation to all aspects of crop protection with a focus on integrated pest management. The Global Compendium will provide basic information on up to 20,000 pests/beneficial organisms, and detailed information on 2,000 insect pests, diseases, weeds and their natural enemies on 150 crops in 150 countries.

Content

The Compendium is a state-of-the-art information tool that will support knowledge-based decisions in crop protection and facilitate efficient international knowledge exchange in the following areas:

- ***integrated pest management,*** through comprehensive description of the full range of pest management practices in illustrated data sheets for the organisms of significance for crop protection, backed by a database of worldwide publications reflecting the experience of IPM in the field;
- ***crop protection and quarantine,*** through commodity-related lists of up to 20,000 pests, pathogens and weeds, plus electronically generated pest distribution maps which will optimize the cost effectiveness of pest risk analysis (PRA);
- ***biological control,*** through a facility to list and prioritize natural enemies for particular pests, their geographic distribution, and their use in IPM systems;
- ***pesticide usage data,*** classified by country, crop, and pest type for selected countries.

Module 1 of the Compendium, available as of mid 1997, has global relevance while focusing on the major pests of South-East Asia and the Pacific; it includes the following novel combination of features, on CD-ROM, updated annually, and can be migrated to the World Wide Web:

- ***pest data sheets:*** detailed data sheets for about 1,000 pests (including insects, diseases and weeds) and their natural enemies, written by 500 specialists. Focus on: identity, geographic distribution, biology, economic impact, control, with special attention paid to integrated pest management (IPM). Editing facilities to cut, paste, export, import and customize.
- ***crops and countries:*** data sheets on about 150 crops and 150 countries.
- ***basic data:*** names, distribution and host range for 12,000 pests and natural enemies.
- ***pictures:*** data sheets are linked to thousands of pictures of pests, natural enemies, crops or crop damage, usually in colour.
- ***maps:*** geographic data are automatically projected as distribution maps, global and regional, which can be overlaid with the distribution of a crop or natural enemy.
- ***relational database:*** factual data are stored in a multi-dimensional database, allowing retrieval of, for example, all fungi causing necrosis on the leaves of rice in China.
- ***hyperlinks:*** "soft" linking allows any word in any text to be used to seek related information, e.g. a country, a pest, a crop, a glossary definition, a reference.
- ***user notes:*** every data sheet has its own personal notepad, allowing in-context local storage of the user's personal experience of that item. Every data sheet has an optional second notepad, designed for corporate networking of shared information.
- ***diagnostic keys:*** a series of illustrated diagnostic keys to major groups of insects, and to nematode and weed species. Some are dichotomous; some (CABIKEYs) give multi-entry access, allowing the user to choose an approach to identification.
- ***taxonomic framework:*** every organism is placed in a taxonomic framework, which can be displayed and used for navigation.
- ***bibliographic references:*** 60,000 references, most with abstracts, either cited in the data sheets or important to IPM, including inaccessible "grey" literature

from several Asian countries. Powerful retrieval tool, offering natural-language searching.

- ***glossary***: hyperlinked glossary of pest management terms; includes data on pesticide uses and environmental impact from the *Pesticide Manual*.
- ***production statistics***: global crop production data, by country, including land use and pesticide trade statistics from FAO, with automatic charting facility.
- ***pesticide usage data***: data for selected Asian countries from the *Landell Mills Database*.
- ***open architecture***: modular structure allows links to be made to external information resources, such as additional bibliographic databases, and the World Wide Web.
- ***World Wide Web links***: automatic launch of Web browser, with selected links from a Crop Protection Compendium Home Page (http://pest.cabweb.org/cpc/cpchp.htm).

Geographical Scope:
The scope is global coverage. Module 1 of the Global Compendium focuses on South East Asia, chosen because the crop protection problems of the region encompass those of other tropical and subtropical regions. The Global Compendium to be completed in mid 1999 will extend coverage to include up to 20,000 pests and natural enemies on 150 crops in 150 countries.

User groups:
A survey of user needs identified strong demand for the Compendium from extensionists, the agrochemical industry, quarantine officers, research scientists, university teachers, policy makers in government departments, and Regional Plant Protection Organizations.

Training:
The Electronic Compendium has a powerful and very important role to play in educational training at universities and other learning institutions. It also has an important role as a professional training tool for updating staff on new developments in crop protection in diverse organizations ranging from quarantine agencies, public sector institutions and private sector corporations, to organizations with responsibilities in crop protection.

Technological Considerations:
The Compendium uses original applications of the latest information technology (IT) to allow users friendly access to the most current and comprehensive data information and knowledge-base that will facilitate the development of solutions to practical problems in crop protection and pest management; thus the Compendium establishes a leadership role in the use of information technology for the benefit of all members of the global crop protection community.

Sustainability:
Subject to availability of funding from the Consortium for the development of the Global Compendium, CABI is committed to annual updating of the Compendium, revenue from sales in developed countries being used to offset annual updating costs.

CABI's Comparative Advantage:
As an international institution, CABI is dedicated to providing information that will contribute to more well informed, knowledge-based decisions; CABI can also greatly facilitate the effective exchange of information in the global crop protection community which will benefit both the consortium members and all the users of the Compendium. CABI's comparative advantage as the developer of the Compendium is related to many factors, including the following:

- its long experience in compiling and disseminating authoritative information in support of agriculture and forestry; it is the repository of the largest, most comprehensive, and extensive historical data base on agriculture in the world;
- its widely respected bibliographic database, CAB ABSTRACTS (comprising more than 3.5 million abstracts, of which more than 0.5 million relate to crop protection), specially enhanced through additional national contributions on IPM;
- its unique biosystematic expertise linked to practical application of biological control and IPM programs;
- its independent, inter-governmental status;
- construction of the Compendium is the responsibility of CABI which compiles information at regional and international levels, through coordinated input from the world's best-informed specialists who provide data of the quality required to be widely accepted as a reliable authority.

Affordability of the Compendium:
The purchase price of the Compendium is set so that it is affordable to the different user groups; there are differential prices for developed and developing countries, with reductions for bulk purchases and sponsorship.

The Compendium Consortium
The project to develop the *Crop Protection Compendium* is an initiative under the aegis of an International Devel-

opment Consortium, organized by CABI, and currently comprises 22 members; 12 are from the public sector and 10 are from the private sector. As of October 1997, 22 members had already committed more than two-thirds of the total funding of $3 million required to complete the project; negotiations are currently underway with several potential new members to resource the balance of funding required. The 22 members of the Consortium are listed below in alphabetical order:

- Asian Development Bank (ADB)
- AgrEvo, Germany
- Australian Centre for International Agricultural Research (ACIAR), Australia
- CAB International, UK
- Canadian International Development Agency (CIDA)
- Cyanamid, USA
- Danish Government Institute of Seed Pathology / Danish International Development Agency (DGISP/DANIDA), Denmark
- DowElanco, USA
- DuPont, USA
- Gesellschaft für Technische Zusammenarbeit (GTZ), Germany
- International Development Research Center (IDRC), Canada
- International Rice Research Institute (IRRI), Philippines
- Monsanto, USA
- Novartis Crop Protection, Switzerland
- Overseas Development Administration (ODA; now DFID), UK
- Pioneer Hi-Bred International, USA
- Rohm & Haas, USA
- Sumitomo Chemical Company Limited, Japan
- Swiss Development Cooperation (SDC), Switzerland
- United Nations Development Program (UNDP)
- United States Department of Agriculture - Animal and Plant Health Inspection Service (USDA-APHIS)
- Zeneca Agrochemicals, UK

Consortium members can contribute to single or multiple units of membership and are offered privileges in recognition of their grant support, essential for the development of the Compendium. These include: membership in the Consortium which directs the future development of the Compendium; a complimentary copy of the Compendium, that can be networked and updated at no charge until the year 2002; and an option to purchase a specified number of copies at significant discounts to the published price in industrial countries.

Summary

In conclusion, in the context of this publication, it is appropriate to assess the benefits of the consortium approach, which represents a partnership facilitated by CABI, between public sector institutions and private sector corporations. The major benefit is that the Consortium approach allows a unique and state-of-the-art product to be developed to meet the common needs of different users in the most cost-effective way, using pooled resources from Consortium members. Whereas the monetary benefits are substantial, they are judged to be insignificant compared with the less tangible benefits that result from partnerships and cooperation *per se*. Simply stated, the Consortium members, collectively, have benefited from an authoritative product, funded through affordable contributions, that no single member of the Consortium could possibly have developed on their own. As a consequence of cooperation during the development of the Compendium, Consortium members can also greatly facilitate the adoption of the CPC as an internationally recognized knowledge-base, to facilitate improved and well informed decisions vis-a-vis crop protection. For example, different views on quarantine issues often arise because agencies have access to inadequate or incomplete information. The advent of a knowledge-base that has benefited from the inputs and experience of diverse organizations involved in all the different aspects of crop protection, and where data is validated and updated annually, is judged to be an important development; this is particularly important when globalization of agricultural trade is underway and where constraints associated with non-tariff trade barriers are becoming increasingly important. Finally, the concept that the Compendium is "owned" by Consortium members provides the incentive and motivation for active participation and the full exploitation of the comparative advantages of respective members for their collective and mutual benefit. In this context, the Electronic Note Pad, featured in the Compendium, provides an opportunity for all Compendium users (not only Consortium members) to share information on any aspect of crop protection with CABI, which in turn can utilize it to update the Compendium. Thus, participation in the future development of the Compendium can be broadened, through the use of the Electronic Note Pad, to include all users in a global network that can effectively exchange information and better serve the needs of the global crop protection community. The Compendium has the potential to allow crop protection specialists in developing countries to benefit from

novel, state-of-the-art IT technology that will enable them to be equitable participants in a global network, and share information that in the past resided in gray literature, or was never documented; for example, information on crop protection practices in subsistence farming in developing countries. Similarly, the Compendium provides an excellent vehicle for the countries of the South to exchange information and harmonize understanding with the North, and likewise between the public and the private sector. In the 21st century, one of the challenges will be to forge new partnerships so that use of limited resources can be optimized. Experience with the development of the Crop Protection Compendium indicates that opportunities to further explore are the establishment of consortia, where common needs can be met with the collective action of members whose respective comparative advantages and diverse viewpoints can be mobilized cost-effectively to meet mutual goals and objectives.

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Appendix

Table A-1: **Principal Fertilizer Companies** *
(Listed alphabetically for Nitrogen, Phosphate & Potash producers)

Company	Country
Nitrogen/Ammonia (N)	
Arcadian	USA
CF Industries	USA
DSM Agro BV	Netherlands
Farmland Industries Inc.	USA
ICI Fertilizer	UK
Kemira Oy	Finland
National Fertilizer Ltd.	India
Norak Hydro As.	Norway
Pemex	Mexico
Pupuk Kaltim	Indonesia
Rashtriya Chemicals & Fertilizers Ltd.	India
Phosphate (P_2O_5)	
CF Industries	USA
Freeport McMoran Resource Partners	USA
ICW/SIAPE/SAEPA	Tunisia
IMC Fertilizer Group Inc.	USA
Occidental Chemical Corp. Ag.Products	USA
OCP	Morocco
Texas Gulf Inc.	USA
Potash (K_2O)	
Arab Potash Company	Jordan
Entreprise Miniére et Chimique	France
Dead Sea Works	Israel
IMC Fertilizer Group Inc.	USA
Kali and Salz	Germany
Kallum Chemicals	Canada
Potash Corporation of Saskatchewan	Canada

* List excludes producers in China, Former Soviet Union, and Central Europe
Source: Communication from International Fertilizer Industry Association (IFIA), Paris, France.

Table A-2: **Major Plant Protection Companies** (Based On Estimated 1996 Global Sales of Crop Protection Products)

Rank	Name	Country	Approx. Sales (US$ Million)
1	Novartis	Switzerland	4,175
2	Monsanto	USA	2,872
3	Zeneca	UK	2,849
4	DuPont	USA	2,515
5	AgrEvo	Germany	2,451
6	Bayer	Germany	2,305
7	Rhône-Poulenc	France	2,174
8	DowElanco	USA	2,005
9	Cyanamid	USA	1,989
10	BASF	Germany	1,506
11	Sumitomo	Japan	648
12	FMC	USA	595
13	Rohm & Haas	USA	514
14	Ishihara	Japan	495
15	Makhetshim-Agan	Israel	472
16	Kumiai	Japan	464
17	Nihon Nohyaku	Japan	376
18	Sankyo	Japan	371
19	Uniroyal	USA	353
20	Hokko	Japan	330
21	Takeda	Japan	321
22	Nissan	Japan	320
23	Nufarm (Fernz)	New Zealand	317
24	Atochem	France	265
25	Nippon Soda	Japan	264
Total (US$ Million)			**30,946**

Source: Wood Mackenzie (1997).

Table A-3: **Major International Seed Companies** (Ranked by Worldwide Sales 1996)

Rank	Name	Country	Approx. Sales (Million US $)	Crops								Marketing Regions				
				Cereals	Maize	Oilseed	Forage	Sugar-beet	Protein Crops	Flower & Vegs.	Cotton /Rice	North America	Europe	South America	Asia	Africa
1	Pioneer	USA	1,600	X	X	X	X					X	X	X	X	X
2	Novartis	Switzerland	970		X	X	X	X	X	X		X	X	X	X	X
3	Limagrain	France	660	X	X	X	X	X	X	X		X	X	X	X	X
4	Monsanto	USA	600	X	X	X			X		X	X	X	X	X	
5	Advanta	Netherlands /U.K.	470	X	X	X	X	X	X	X		X	X	X	X	X
6	Takii	Japan	450				X			X		X	X		X	
7	Dekalb Plant Genetics	USA	387		X	X	X					X	X	X	X	X
8	Seminis	Mexico	380		X	X	X		X	X		X	X	X		X
9	Sakata	Japan	360							X					X	
10	KWS	Germany	350	X	X	X	X	X	X	X		X	X	X	X	
11	Cargill	USA	250	X	X	X				X	X	X	X	X	X	
12	Cebeco	Netherlands	170	X	X	X	X		X	X		X	X			
13	Pau Euralis	France	162	X	X	X						X	X			
14	Svalof Welbull	Sweden	160	X	X	X	X		X	X		X	X	X		
15	RAGT	France	150	X	X	X	X						X			
16	Mycogen (Dow Elanco)	USA	147	X	X	X	X					X	X	X		
17	Saaten-Union	Germany	140	X	X	X	X	X	X				X			
18	Sigma Semences de France	France	135	X	X	X	X	X	X				X			
19	DLF Trifollum	Denmark	130			X	X	X	X			X	X		X	
20	Barenbrug	Netherlands	125	X	X	X	X		X			X	X	X	X	
Total	(US$ Millions)		**7,796**													

Source: Calliez (1997).

Table A-4: **Major Animal Health Companies**
(Based on Estimated 1995 Global Sales of Animal Health & Nutrition Products)

Rank	Name	Country	Sales (US$ Million)
1	Hoffman-La Roche	Switzerland	1,440
2	Rhône-Poulenc	France	1,357
3	Pfizer	USA	1,250
4	Merck	USA	792
5	Bayer	Germany	754
6	Novartis	Switzerland	743
7	BASF	Germany	738
8=	Hoechst	Germany	512
8=	Eli Lilly	USA	512
10	Mallinckrodt	USA	454
11	American Home Products	USA	389
12	Pharmacia & Upjohn	USA	383
13	Degussa	Germany	355
14	Akzo Intervet	Netherlands	272
15	Solvay	Belgium	265
16	Virbac	France	243
17	Novus	USA	238
18	Boehringer Ingelheim	Germany	222
19	Sanofi	France	202
20	Schering-Plough	USA	190
21	Alpharma	USA	163
22	Takeda	Japan	157
23	Janssen	Belgium	145
24	Nippon Zenyaku	Japan	144
25	Tortuga	Brazil	134
Total	(US$ Million)		**12,054**

Source: Wood Mackenzie (1997).

B. NEWS AND EVENTS

UN and other organizations' news

Biodiversity indicators and implementation targets: Global Diversity Forum prepares for United Nations General Assembly review

Methods for assessing the status of biodiversity and how it changes over time in order to measure the effectiveness of the Convention on Biological Diversity (CBD) was the focus of the most recent session of the Global Biodiversity Forum (GBF). On the eve of the United Nations review of Agenda 21—an extensive programme for achieving sustainable development that encompasses among its many provisions the principles and objectives of the CBD—some 90 participants from 30 countries gathered at UN Headquarters in New York to discuss and compare tools for monitoring such elements of biodiversity as species and ecosystems and the impact of conservation efforts.

The sixth GBF was co-sponsored by Biodiversity Action Network (BIONET); the Center for International Environmental Law (CIEL); the Governments of Costa Rica, Denmark and Sweden; IUCN—The World Conservation Union; the UN Environment Programme (UNEP); World Resources Institute (WRI); Worldwatch Institute; and the World Wide Fund for Nature International (WWF).

Hundreds of indicators—a technical term for species or populations that serve as evidence of overall environmental conditions but also incorporating many other types of measurement—have been considered by parties to the Convention, international agencies, and non-governmental organizations in their efforts to facilitate compliance with the CBD's calls for identifying and monitoring the effectiveness of conservation and sustainable use of genetic resources. Such indicators are designed to measure the extent to which activities, processes and policies promote sustainable use of genetic resources in such areas as *in situ* and *ex situ* resource management, incentives promoting these goals, access to genetic resources, transfer of technology among parties and institutions, and financial mechanisms and processes.

A discussion draft developed for the GBF jointly by BIONET, WRI, Worldwatch Institute and the World Conservation Monitoring Centre (WCMC) provided a compilation of types of biodiversity measurements as well as reference points:

- **Benchmarks** measure current status and therefore represent a starting point from which changes may be monitored. Comparing the benchmarks taken at different points in time can indicate the impact of activities undertaken and the level of progress achieved during that period.
- **Thresholds** are pre-assigned, quantifiable levels at which conclusions can be drawn regarding the status of elements of biodiversity that signal the need for a change in activity or policy. For instance, when acreage of deforested land reaches a specific percentage of all forest area, measures to minimize or halt further erosion may be implemented.
- **Targets** are goals that provide the framework for policies, strategies and activities to be undertaken with the objective of achieving the goals, preferably within a certain period of time. An example might be planning to reduce annual forest loss to 10 per cent or less of overall forest area by 1999.

BIONET, the catalyst for GBF's focus on indicators and targets, compiled a preliminary bibliography of resources, including books, articles, papers, and Internet sites on these and related issues, and is currently preparing a more comprehensive listing. These measurement efforts will undoubtedly occupy scores of statisticians, field scientists and information systems managers worldwide as the CBD advances to further stages of implementation and its resulting assessment and evaluation.

The burgeoning field of biodiversity measurement and assessment continues to produce a wealth of strategies, approaches, tools, and analytic methodologies. While quantification—and methods of evaluating quality—are not new, such tools and practices have taken on an increased sense of importance among those following implementation of the Biodiversity Convention, particularly those responsible for translating the Convention into reality. Several questions arose during GBF discussion, however, regarding how indicators and targets designed for widely disparate areas can be combined to assess global effectiveness. Clearly, participants agreed, as databases, publications, and information clearing houses continue to develop and measurements are taken and analysed, refinements will be needed to deal with the magnitude of assessing the status and trends of biodiversity worldwide.

For further information, lists of resources and information sources, and copies of materials prepared for the Global Biodiversity Forum on targets and indicators, contact: Biodiversity Action Network, 1400 16th St. NW, Suite 502, Washington, DC 20036, USA. Tel.: +1-202-547-8902. Fax: +1-202-265-0222. E-mail: <bionet@igc.apc.org>.—CJ (Source: *DIVERSITY*, Vol. 13, No. 1, 1997)

Boosting seed supply

In large parts of the developing world, non-availability of seed is the single biggest constraint to smallholder agriculture. Improved varieties are available in many countries—but seed is not. Realizing the urgency of this need, the International Centre for Agricultural Research in the Dry Areas (ICARDA), ICRISAT, International Institute of Tropical Agriculture (IITA), and Deutsche Gesellschaft für Technische Zusammenarbeit (GTZ) organized a five-day conference on improvement of seed production and distribution held at Harare, Zimbabwe, March 1997. The conference gathered together about 70 seed specialists, donors and NGOs representing a diversity of nationalities, agencies and research institutions. Scientists from 18 countries, representatives of NGOs and such regional and international agencies and donors as the Belgian Agency for Development Cooperation, Food and Agriculture Organization of the United Nations (FAO), GRZ, the Bundesministerium für Wirtschaftliche und Entwicklung Zusammenarbeit (BMZ), SACCAR, SADC, USAID and the World Bank attended. Seed policies, sustainability of NGO programmes, the role of farmers' groups and cooperatives, and seed information systems were some of the topics

discussed by working groups. The conference culminated with the formulation of action plans for each of three regions—West Asia and North Africa (WANA), Western and Central Africa Region (WCA) and Southern and Eastern Africa Region (SEA). (Source: *SAT News,* July 1996/April 1997)

Cassava bacterial blight: a major threat to production

Cassava is the staple food of nearly 500 million people in Latin America, Africa and Asia, and crop losses can upset the sometimes delicate nutritional balance of millions. Bacterial blight is a major problem, as it is widespread, can reduce yields by 20 per cent to 100 per cent, and infects the cuttings that constitute the farmer's "seed". Orstom has been working on the problem since 1979; some studies also involve INRA in Toulouse and the CIAT in Colombia, which has 6,000 cassava genotypes in its collection.

Research strands include: epidemiology and the disease cycle; the population structure, pathogenic variability and genetic diversity of the bacterium; detection methods; plant-parasite relations; and resistance in the cassava plant, for which a full gene map has been drawn up. The research has produced many findings that point the way forward.

Work on the bacteria genome is leading to the idea of using modified, non-pathogenic mutants to control the disease, at least in industrial-scale plantations. Genetics work and molecular biology have also led to more efficient diagnosis methods. This will make it possible to certify healthy cassava germplasm. One particularity of the bacterium is that it lives both in the plant's vascular system and, in the dry season, on its leaf surfaces. Some of the plant's resistance mechanisms have been found, e.g. the development of intra-cellular structures called tyloses whose contents have bactericidal properties. This discovery may help to identify resistance markers, which would be very useful for varietal improvements.

In field trials, costly copper-based chemical pesticides have proven ineffective because bacterial populations build up again very rapidly. Biological control using natural enemies has also been unsatisfactory. Simple methods include quarantine of cuttings, producing young plants in forest zones (where Orstom has found the disease does not occur), weed control (since the bacterium can live on some weeds) and crop rotation.

So far, farmers have not adopted new varieties with any enthusiasm. Extension work needs to be developed more fully, and forthcoming varieties may prove more successful since work on host resistance now takes better account of variability in the bacterium. (Source: *Orstom Actualités,* 1997)

Regulatory issues

USDA amends regulations for GMOs

The Animal and Plant Health Inspection Service (APHIS) of the US Department of Agriculture is amending its regulations pertaining to genetically engineered plants introduced under USDA's notification and petition regulatory processes.

The amended regulations will allow a broader application of existing simplified procedures for requests for movement or field testing of genetically engineered plants. They will also streamline the determination of non-regulated status for plant varieties that closely resemble other varieties that have already been through the determination process. This will enable APHIS, when appropriate, to extend the existing determination of non-regulated status for new products that do not raise new risk issues.

For plants that are being evaluated in field tests, reporting requirements have been made more consistent. For example, for trees and other long-lived plants field data reports will only need to be provided upon the conclusion of the trial. However, applicants must apply to APHIS for yearly renewal to ensure appropriate measures are taken when plants become reproductively mature.

APHIS will also use appropriate guidelines to provide additional information to developers of regulated articles and other interested persons regarding procedures, methods, scientific principles, and other factors that could be considered for various aspects of its regulations. The first guidelines will provide information to help applicants on requests for extension of a determination of non-regulated status.

Contact: John Payne, Director, Biotechnology and Scientific Services, APHIS, 4700 River Road, Unit 98, Riverdale, MD, USA 20737-1237. Tel.: 301/734-7602; or visit the APHIS Web site at http://www.aphis.usda.gov. (Source: *The AgBiotech Bulletin,* June 1997)

Blunt pharming talk

Eva Sandberg—head of the microbiological department of the Danish Medicines Agency (Copenhagen), and a senior figure in European drug regulation—declared recently that pharming—the production of compounds in transgenic animals—is not, from a regulatory point of view, going to be the most rapid route to the market. Speaking at the 22nd European Society of Regulatory Affairs meeting in Amsterdam at the beginning of June 1997, she went on to say that in assessing new biological drugs, production in yeast or bacteria is preferred over production in mammalian cells. With transgenic animals and mammalian cells, there is, she says "always an additional risk of failure of good manufacturing practice", which, in the worst case, could result in virus-infected (or prion-infected) products. Sandberg, however, is enthusiastic about gene therapy—as long as vectors do not contain or rely on replicating viruses. (Source: *Nature Biotechnology,* Volume 15, July 1997)

Microbial biotech regulations set

The US Environmental Protection Agency is issuing regulations that establish a streamlined process for the screening of certain microbial biotechnology products to ensure that they are safely developed for commercial use in a broad range of industrial and environmental applications.

The regulations cover those microbial biotechnology products developed for industrial applications subject to EPA oversight under the Toxic Substances Control Act (TSCA). Other federal authorities regulate the development and introduction of biological pesticides, drugs and food additives.

Under these regulations, companies that manufacture or researchers who develop microbial biotechnology products are required to notify and obtain EPA review prior to the use of their products in commerce or testing in the environment.

The new rules tailor pre-existing screening requirements for new chemicals and establish a distinct programme for biotech products under section five of TSCA. EPA has been reviewing these products for 10 years under the authority of a policy statement issued in 1986 and under TSCA regulations originally written for new chemicals. (Source: *Chemical Manufacturing Reporter,* 7 April 1997)

New US regulatory framework emerges for genetics

The creation of a new Advisory Committee on Genetics and Public Policy (ACGPP) in the office of the US Health and Human Services Secretary was endorsed unanimously on 21 February 1997 by the US National Advisory Council for Human Genome Research (NACHGR), which reports to the US National Human Genome Research Institute (NHGRI). ACGPP will be independent of NHGRI for funding, with a mandate to discuss a wide range of current and emerging ethical, legal and social issues and to advise and shape government policy on genetics. The joint US National Institutes of Health (Bethesda, MD)/Department of Energy (DOE; Germantown, MD) Working Group on Ethical, Legal and Social Implications of Human Genome Research—known as the ELSI working group—is also to be restructured as a 12-member ELSI Research Evaluation Committee to advise Francis Collins, director of NHGRI, and his counterpart at the DOE on the quality and focus of extramural ELSI research. (Source: *Nature Biotechnology*, Volume 15, April 1997)

Task force finalizes genetic testing recommendations

The US Task Force on Genetic Testing, created by the US National Institutes of Health (Bethesda, MD)/Department of Energy (Germantown, MD) ELSO working group has finalized its recommendations on genetic testing—its final act before being disbanded. The recommendations propose the formation of a National Genetics Board (NGB) to provide expert guidance to institutional review boards (IRBs) on the validity and utility of genetic tests requiring high scrutiny (e.g., those tests with low predictive value and/or for conditions that have no treatment). In addition, to assure the proficiency of laboratories performing genetic tests, the task force suggests the establishment of a national accreditation programme which would be carried out under the auspices of the Health Care Financing Administration (HCFA). An issue on which the task force could not reach agreement is the role of the US Food and Drug Administration (FDA, Rockville, MD) in regulating genetic tests. One option is to set up a Genetics Advisory Panel that would help the FDA focus specifically on tests requiring stringent scrutiny. (Extracted from *Nature Biotechnology*, Volume 15, April 1997)

EC food regulations published

The Novel Food Regulation governing labelling of genetically engineered foods and food ingredients in Europe (Regulation No. 258/97) was finally published on 14 February 1997 in the L43 issue of the *Official Journal of the European Communities*. It will come into force in all European Union member countries on 15 May—90 days after publication. The regulation, particularly article 8, which states that genetically modified foods should be labelled if the modifications render a novel food or food ingredient no longer equivalent, has been criticized by industry and consumer groups alike for being subject to interpretation. Tanya El-Cherkeh, biotechnology specialist in the Food and Biotechnology unit of European Commission (Brussels) industrial directorate DGIII, however, defends the regulation, saying that the six points in article 8 are guidelines for submitting a product. "They aren't very specific requirements", she argues "because there should be a case by case discussion". (Source: *Nature Biotechnology*, Volume 15, April 1997)

Ethical issues

Europe/Japan face up to legal hurdles to cloning

As in the United States, human reproductive cloning will be banned in Europe and Japan if reports from ethical groups are translated into law. The Group of Advisors on the Ethical Implications of Biotechnology (GAEIB) sent its advice to the European Commission (EC, Brussels) on 30 May 1997, and two Japanese groups—the Committee for Basic Plans for Life Sciences and the Committee for Life Sciences—will report to the Japanese Government. While legislators are receptive to the advice, the translation of ethical opinions into law is far from straightforward.

GAEIB has advised the EC that all animal cloning, both reproductive and cell cloning should be permitted, as should the cloning of human parts for organ replacement and replacement skin. However, reproductive human cloning should be outlawed. "Instrumentalization [a term used by GAEIB, describing the use of humans as tools] and eugenics render any such acts ethically unacceptable."

The GAEIB report is a crucial document in the development of cloning rules in Europe. It was produced following a request from EC president Jacques Santer, who has said that the Commission will follow GAEIB's views on both animal and human cloning. However, the mechanism for forming legislation in Europe is currently unclear.

In Japan, not only is the legislative mechanism unclear, but its discussions are not as far forward. (Extracted from *Nature Biotechnology*, Volume 15, July 1997)

US bioethicists say continue human cloning moratorium

Having rushed to meet the 90-day deadline set by US President Bill Clinton, the members of the National Bioethics Advisory Commission (NBAC; Washington, DC) recommended in its report issued in June 1997 that the moratorium on federally sponsored human cloning efforts should continue. It also urged that a similar ban should be extended by legislation to the private sector. In both cases, however, it asked that legislation should allow the ban to lapse after three to five years, thereby permitting cloning issues to be re-examined formally.

The NBAC report—and similar recommendations in Europe and Japan was prompted by the cloning of Dolly the sheep by researchers at the Roslin Institute in Edinburgh. In accepting the Commission report, the US President called upon the private sector to continue observing a voluntary moratorium and promised to submit a bill to Congress soon that would achieve the full public-private ban that the Commission recommends. Meanwhile, several members of the US Congress are already drafting bills on human cloning. If enacted, any legislation would mark the first time that the US Government had issued such a blanket ban on a biomedical research and development activity. In earlier NBAC hearings, lawyers expressed the view that a ban might raise constitutional issues. (Extracted from *Nature Biotechnology*, Volume 15, July 1997)

Ethics of AZT studies in poorer countries attacked

Debate heated up at a congressional hearing on bioethics held on 8 May 1997 when the topic turned to US Government-funded studies in developing countries aimed at preventing the transmission of HIV from mothers to infants.

Public Citizen, a consumer-advocacy organization, has been waging a high-profile campaign in recent weeks to modify the trials, arguing that it is incredible they include as control subjects pregnant women who are given no treatment to prevent maternal transmission of HIV. But at the hearing, AIDS researchers and their sponsors vigorously defended the trials, which are under way in Africa, Thailand, and the Caribbean, testifying that they may answer critical questions for HIV-infected women in those countries. Several people called to testify also expressed dismay at the inflammatory rhetoric and the aura of an emerging crisis fostered by Public Citizen, noting that the studies were thoroughly debated before they were launched.

In February 1994, a large study of HIV-infected pregnant women in the United States and France, known as ACTG076, found that an intensive course of treatment with the anti-HIV drug AZT could prevent maternal transmission of HIV nearly 70 per cent of the time. Researchers quickly realized that the results would have little relevance in most developing countries, where the incidence of AIDS is rising the fastest. The reason is that most HIV-infected women in those countries cannot afford the treatment, which entails taking AZT during pregnancy, receiving an intravenous drip of the drug throughout labour, and feeding the infant AZT syrup for six weeks after birth. This realization got many investigators interested in testing cheaper prevention strategies, such as shorter drug regimens, vitamin supplements, or HIV-antibody injections. At the time, researchers debated whether it would be ethical to incorporate into the studies a control group that would receive only a placebo.

According to a widely held ethical precept, people who volunteer to take part in clinical trials should be given, at the very least, the standard of care in their country. Proponents of placebo-controlled trials argued that if the standard of care was no treatment at all, the use of placebos would be ethically justified. At a World Health Organization meeting in June 1994, AIDS researchers from around the world agreed, recommending that "placebo-controlled trials offer the best option for a rapid and scientifically valid assessment" of alternatives to ACTG076. (Extracted from *Science,* Vol. 276, 16 May 1997)

AIDS trials ethics questioned

Early in 1997, researchers running a state-of-the-art, clinical trial of anti-AIDS drugs abruptly called a halt to the study, which they felt could no longer be ethically justified. Patients in the "control" arm of the trial, who were being treated with a combination of two drugs, were getting sicker and dying faster than were those receiving a more powerful, triple-drug cocktail. Stopping a trial when a candidate therapy looks especially promising is not unusual. But the demise of this large study, known as ACTG320, added fresh urgency to a debate that has been simmering for years about how to get useful results from drug tests without risking patients' lives. It also highlighted how the recent advent of potent combination therapies has dramatically changed the ground rules for AIDS drug testing.

From the start of the AIDS epidemic, researchers have argued over how to test new therapies without putting patients in harm's way. The standard approach is to test candidate drugs against a placebo or a benchmark therapy, using a clinical measure, such as death rates, to evaluate effectiveness. When the first AIDS drugs went into trials more than a decade ago, researchers and AIDS activists agonized over whether it was appropriate, given the lethal nature of the disease, to test potential drugs against placebos. As more candidate therapies came along, they debated the propriety of using clinical measures such as mortality rather than more indirect, "surrogate" measures such as blood levels of critical immune-system cells, to judge effectiveness. The recent development of combination-drug treatments that reduce HIV in the blood to undetectable levels has only sharpened these issues. The central question now facing AIDS researchers and drug testers is whether it is unethical to run a trial that offers patients anything less than these new therapies. Trials in developing countries, where far fewer AIDS drugs are available, are also being criticized. (Extracted from *Science*, Vol. 276, 25 April 1997)

India fears patent and ethics abuses

One issue dominated a recent conference (Indian National Academy of Sciences Bioethics Symposium, 22-25 May, Goa) in India on ethical issues surrounding the human genome: the fear that pharmaceutical companies would exploit Indian human diversity and inventiveness at great cost to the poorest of the peoples.

Participants at the conference expressed concern about the difficulty of obtaining voluntary first-person informed consent, given the education of the majority of Indian people. It was suggested that random tests to check whether research subjects actually understood what they were consenting to should be introduced. Protecting the economic interests of genetic donors was also a concern.

There was general agreement, at least among the Indian participants, that transfer of genetic material abroad should only take place in exceptional circumstances, and only to laboratories operating under similar legal constraints. This closed, protectionist attitude towards genetic information is part of a wider and, in India, hotly debated topic—intellectual property rights. The United Nations Development Programme estimates that biological resources worth approximately $5.4 billion are being stolen from developing countries every year. Although India was a participant in the Uruguay Round of GATT concluded in 1996, the Indian Government has not yet ratified its intellectual property provisions. That, in effect, means both that India's own patents are not internationally recognized and that India does not recognize other nations' patents.

Some participants suggested that legislative changes would have no impact because there are not enough resources to enforce patent legislation in India. As an example of this laxity, they cited the wide flaunting of the ban on the use of amniocentesis and ultrasound for sex selection. Indeed, "genetic counselling" has become a euphemism for sex selection among certain service providers. (Extracted from *Nature Biotechnology,* Volume 15, July 1997)

Bioethical aspects of biotechnology in the agro-food sector—developing countries

The European Union is funding a project to examine bioethical issues resulting from the application of modern biotechnology in agriculture, fisheries and food. The report resulting from this study will be used in preparation for a Europe-wide conference proposed by the Parliamentary Assembly of the Council of Europe in a recommendation made in 1993, supported by the Committee of Ministers, to aid in determining the desirability of the drawing up of a European Convention covering the bioethical aspects of biotechnology in relation to Agriculture, Fisheries and Food.

Five working groups have been set up to examine the bioethics involved in agriculture relating to:

- Food (including animals and food processing);

- Industry (non-food biotechnology);
- Medicine;
- Environment; and
- Developing countries.

The brief given to each includes the examination of issues relating to both positive and negative implications of the technology, to include general ethics, patenting, regulation and safety, economic and political issues.

The groups have been asked to:

1. Review the existing research, any documents or other material in their respective areas;
2. Identify any deficiencies requiring further review and/or work;
3. Conduct the appropriate work if necessary;
4. Draw up a report of their findings.

The working group with responsibility for looking at the issues relating to developing countries would welcome ideas about the issues. We are a group based in Europe and may not appreciate the perception of modern biotechnology particularly of those in developing countries, or those in countries which have until recently had a "managed economy".

In order to allow a wide-ranging debate, we invite anyone to write to the organizers (e-mail preferred) to provide them with their ideas on the ethical issues associated with modern biotechnology within the agro-food area and the impact on developing countries. The organizers will attempt to produce a summary of the comments they receive, and send the summary to all who comment to them.

Send you e-mail to: babas@sheffield.ac.uk. Dr. Julian Kinderlerer, Department of Molecular Biology & Biotechnology, The University of Sheffield, P.O. Box 594, Sheffield, S10 2UH, England. (Source: *Australasian Biotechnology*, Vol. 7, No. 2, April 1997)

EuropaBio ethical code put up for consultation

The European association for bio-industries, EuropaBio, has published a draft code of ethics for consultation. If adopted by its 600 member firms, EuropaBio claims the code will commit firms to prioritizing environmental protection in the manufacture and use of biotechnology products.

The code, presented at the recent first annual European bio-industry congress in Amsterdam is seen as EuropaBio's response to recent polls which indicate that ethics rather than risk represent the greatest public concern about biotechnology.

Under the draft code, EuropaBio pledges to maintain dialogue on the ethical and societal implications of biotechnology. The congress was told progress had been made in setting up an independent panel to advise the industry on ethical issues. (Extracted from *European Chemical News*, 7-13 July 1997)

Bioethics convention

Almost 20 European countries have signed the first ever convention on bioethics, drafted by the Council of Europe in Strasbourg. It is intended to establish common standards for biomedical research. (Source: *Chemistry & Industry*, 21 April 1997)

General

Moral lesson for policy makers

Moral issues are the biggest barrier to public acceptance of biotechnology in the European Union, according to a new survey. Transplanting animal organs into humans (xenotransplants) and developing genetically modified animals for research were vetoed on moral grounds. The findings also challenge industry's assumption that greater public understanding of biotechnology will inevitably lead to wider support.

The survey, which polled 16,000 EU citizens across all 15 member States, contains important lessons for biotechnology policy makers, claims co-author George Gaskell of the London School of Economics. Most policy decisions are based on arguments about potential risks to people and the environment rather than moral issues, he says. Gaskell hopes that the findings will contribute to a broader public debate on how to regulate biotechnology.

Moral issues aside, the public is deeply ambivalent about biotechnology, the survey reveals. For example, people do not support genetically modified foods but do support genetically engineered pest-resistant crop plants because they are "useful". Usefulness, however, does not guarantee acceptance; the respondents agreed that genetically modified research animals and xenotransplants are useful but did not support them.

People are more knowledgeable about biotechnology than three years ago when the European Commission carried out a similar survey. But significantly, they are less supportive and less optimistic about the contribution that it can make to the quality of life.

The public also thinks that international bodies such as the United Nations and the World Health Organization should regulate biotechnology, and that environmental and consumer organizations and the medical profession are the most trustworthy sources of information. Governments, industry, the media, political parties and religious organizations are widely mistrusted. (Source: *Chemistry & Industry,* 7 March 1997)

Genetically modified food

Greenpeace is maintaining its campaign against genetically modified corn and soybeans, but there is little evidence of a knock-on effect on the technology licensors, Novartis and Monsanto.

Greenpeace's campaign has focused on Europe's three biggest food producers, Nestle, Unilever and Danone. The fourth-biggest, Kraft Jacobs Suchard (KJS), has said it will not use genetically engineered soybeans. On 21 March, KJS recalled 500 tonnes of Toblerone chocolate from sale in Switzerland after lecithin in it was found to be made with genetically engineered soybeans.

Some European governments have already imposed bans or labelling requirements on genetically engineered food products.

The Austrian Government has banned imports of Novartis' corn until early May 1997, although observers think the ban is unlikely to be extended because it clashes with European trade law.

Luxembourg has also imposed a ban, while the French, Danish, Dutch, Swiss and Spanish governments are bringing in food-labelling requirements for soyabeans, corn, or both.

Monsanto expects that around 8-10 million acres of the genetically engineered beans will be harvested in the US in 1997, accounting for around 15 per cent of the crop. Only 2 per cent of the 1996 crop was genetically engineered. The USA, Australia and Brazil are the main soybean producing countries.

More than 75 seed companies will have Monsanto licences for the gene technology in 1997. The beans have been approved for planting in Canada and Australia, while field trials are starting in Brazil. (Source: *European Chemical News*, 7-13 April 1997)

The Biotechnology Industry Organization (BIO) and SciQuest(sm) to form Internet Partnership

SciQuest and the Biotechnology Industry Organization (BIO) are to build a clearinghouse of biotech information, resources and services on the World Wide Web. The new site will educate the public about biotechnology, improve communications and collaboration throughout the industry, offer BIO membership information and develop a national programme for purchasing products and information. This new resource, to be located at BIO's existing site (http://www.bio.org), is scheduled for June 1997. (Source: *Australasian Biotechnology*, Vol. 7, No. 2, April 1997)

WTO overrides EU ban on BST-beef imports

A panel of the World Trade Organization has determined that the European Union's ban on hormone-treated beef is illegal, according to an article in the *New York Times*. The panel says that Europe's import ban on beef produced with growth-enhancing hormones is illegal because it has no scientific justification.

The decision could set an important precedent for attacking scores of other trade barriers based on health concerns. The article also says that it "marks an unprecedented use of international trade law to overturn internal domestic laws that have strong popular support. Unlike many import restrictions, the European ban on hormone-treated beef was not erected to protect local farmers but rather to assuage widespread popular angst among consumers over chemicals in food, and it applies equally to European and non-European farmers".

The USA and the EU both have an opportunity to make comments about the preliminary report, and a final version will be issued in the near term. The EU can then appeal to the World Trade Organization, but the Organization's rules require that the report be approved unless there is a unanimous vote against doing so.

Experts on both sides of the Atlantic have commented that they expect the Europeans to seek some sort of negotiated solution that would allow them to keep their ban intact. Under the rules of the World Trade Organization, a country can choose to maintain its restriction if it gives up something of comparable value, such as cutting tariffs on other products. (Source: *The AgBiotech Bulletin*, June 1997)

Human cloning ban urged by Germany and France

French President Jacques Chirac will press for a world-wide ban on human cloning following the recent cloning of a sheep by Scottish scientists. His concerns were echoed by German scientists who urged that human cloning be banned "absolutely, everywhere and forever".

While some US and British scientists defend the idea of cloning human cells for medical reasons, a German expert report called on the German Government to seek a world-wide ban.

An interim ban was urged in March by the British science journal *Nature*, which published the breakthrough results from Scotland. (Source: *The AgBiotech Bulletin*, June 1997)

ABIC '98 conference focuses on business of agriculture

The seeds of a second global agricultural biotechnology conference have been planted in Saskatoon, Canada. Building on the success of the inaugural 1996 conference, ABIC '98 (an acronym for Agricultural Biotechnology International Conference 1998) will be held from 9 to 12 June 1998. The conference theme, "Agbiotech: The Science of Success", focuses on strategies for the commercialization of agbiotech products. Twenty-two of the conference sessions deal directly with plant production innovations through biotechnology and related commercial activity.

ABIC '98 will also feature tours highlighting Saskatoon's agbiotech industry, over 50 expert presentations by 30-plus speakers, a 60-exhibit trade show, poster presentations and social events. Presentation topics include: international patterns and projections in agbiotech development; emerging market opportunities; hot technologies; strategies for building agbiotechnology businesses; and tips on entering the international marketplace.

Anyone interested in becoming a corporate sponsor can contact the ABIC '98 office c/o The Signature Group, 608 Duchess Street, Saskatoon, Saskatchewan, Canada S7K 0R1. Tel.: 306/934-1772; fax 306/664-6615; e-mail: sigantur@eagle.wbm.ca. (Source: *The AgBiotech Bulletin*, June 1997)

Engineered maize condemned

The European Parliament wants a suspension of sales of Novartis' genetically engineered maize and a reappraisal of the health and safety evidence, following a claim by Austrian authorities that they have come up with some worrying new scientific findings yet to be fully disclosed. The Parliament condemned the "irresponsibility" of the European Commission for clearing the crop despite some member States' opposition and before a regulation on novel foods had come into force.

At present, member States are free to import the maize, which is resistant to the European corn borer, but they cannot grow it until it has been registered as a new plant species. Austria and Luxembourg have forbidden imports, while France has issued a planting ban.

The Parliament is concerned that the arrival of the maize into the European market will disadvantage European producers and could force them to start growing the crop despite concerns over environmental and health risks.

Meanwhile, the Commission has adopted a draft directive that amends a previous regulation on labelling genetically modified organisms. It makes compulsory the labelling of raw materials resulting from genetic engineering—but not processed products—and requires data on these materials to be held in a register. The regulation does not apply to products already approved. (Extracted from *Chemistry & Industry*, 21 April 1997)

Novartis' agribusiness

With turnover in the crop protection sector of its agribusiness division up 8 per cent since the merger of Ciba and Sandoz in 1996, Novartis is confident about remaining number one in agrochemicals.

Continued investment in R&D is combined with the promise of further business in France and the USA, where the merger is yet to be fully completed. This, it is hoped, will keep the company in pole position.

In France, the sector companies were officially set up on 16 April 1997 while the merged organization will be launched in June. In the US, sales teams will be merged during the year, streamlining the company's turnover there.

Novartis' first financial results saw combined sales for the agribusiness of SwF 7.6 billion ($5.2 billion), with crop protection generating SwF 5.6 billion of this. R&D expenditure on agribusiness was Sw F675 million, equivalent to 8.9 per cent of sales.

Highlights from the crop protection sector include strong sales in corn herbicides in North America, and a promising start for the fungicide *Bion*, launched as a plant tonic in Germany. Novartis is hopeful for the continued success of *Bion*, which works by activating plants' defence mechanisms in the manner of immunization.

The seed treatment business, which is the smallest division of the agribusiness, saw the best growth rate, with double-digit sales increases.

Emerging products include the insecticide *Chess*, launched three years ago in Switzerland and set to launch Europe-wide over the next couple of years, pending registration in other countries, and the fungicide *Ridomil Gold,* launched in the US in 1996 and to be launched in other countries from this year onwards. *Ridomil Gold* consists of the active enantiomer of the fungicide *Ridomil,* reducing application volume by 38-50 per cent.

Products in the pipeline include the maize herbicide *Dual*, to be launched in all markets following the US and South Africa this year. Novartis also has an insecticide product in development for several crops which affects the salivary gland of sucking insects, preventing them from feeding. It does not harm beneficial insects.

Novartis clearly sees R&D as the pathway to continued success and plans to magnify the number of new substances which undergo biological screening for potential development each year from 15,000 to 100,000. This will be performed using miniature tests, synthesis robotics and the development of molecular libraries. It is hoped this extensive substance investigation will give Novartis exclusive access to some useful substances. (Extracted from *European Chemical News*, 28 April - 4 May 1997)

Bioprospecting deal

Hyseq, Inc. (Sunnyvale, CA) and Conservation International have established a partnership to leverage Hyseq's high-speed gene sequencing technology to support Conservation International's bioprospecting goals.

Conservation International is trying to make the global search for wild plants and organisms which may provide the basis for new drugs and foods, a tool for conservation as well.

Bioprospecting is the basis for partnerships that Conservation International is developing between the private sector and communities in biodiversity hotspots around the world.

Hyseq will contribute a percentage of any revenues resulting from the partnership to conservation efforts within the country where the project occurs. Conservation International will help structure agreements between local communities, governments and Hyseq, regarding the use of the genetic resources, promoting equitable sharing, community participation and technology transfer.

Conservation International has recently developed other programmes to bring innovative technology and resource optimization to bear in conserving tropical rain forests.

An example of the organization's success is a project in Suriname, on the north-eastern coast of South America. Conservation International has joined with local Surinamese, a Surinamese pharmaceutical company and US pharmaceutical experts. An ethnobotanically based biodiversity prospecting initiative identifies and screens tropical plants for potential medicinal uses on an interational scale. (Extracted from *Genetic Engineering News*, 1 April 1997)

Sharp reaction to cloning

The European Parliament is expected to call for a ban on the cloning of humans following the successful cloning of a sheep at Scotland's Roslin Institute. The Parliament will demand a statement from the European Commission as to its intentions in approaching this subject, especially in the area of genetic engineering research funding. A spokesperson for the Socialists, the largest grouping in the Parliament wanted the EU to ban human cloning now. This view has also been supported by the European Federation of Pharmaceutical Industries Association (EFBIA) who according to their President, Prof. Rolf Krebs, "are against cloning human beings and will back any initiative that addresses this specific concern".

There have also been calls for a moratorium on the cloning of animals, but agreement on this issue has not been unanimous amongst the various political grouping. Euro-MPs are also due to call for the creation of an international body to examine the ethical considerations raised by cloning and the implications of the technique for health and the competitiveness of industry and farming. (Source: *Irish Biotech News*, April 1997)

Europe's biotech sector to treble

Europe's biotechnology industry could treble in size by 2005. Turnover will grow from Ecu 42.5 billion ($48 billion) in 1995 to Ecu 100-150 billion by 2005, according to figures released by EuropaBio, the new European bioindustry organization, at its first congress in Amsterdam in June 1997.

The UK has the highest number of biotechnology companies with close to 200. Germany and France both have over 100, Sweden has 70 and the Netherlands 50.

Meanwhile, the US market for bio-engineered growth factors will grow rapidly over the next few years, according to Frost & Sullivan (F&S). The $2.7 billion market is estimated to expand to $5.4 billion by the year 2000, attracting new entrants and spurring medical technologies.

To date only blood growth factors have been approved, but later this year F&S expects to see the first FDA approvals for tissue growth factors. This additional sector will triple total market size between 1996 and 2003, it says. (Source: *European Chemical News*, 30 June - 6 July 1997)

New rules for GMOs

The European Commission has published new proposals for labelling genetically modified organisms (GMOs), but they will not affect seed products already on the market nor will they apply to food containing GMOs.

The proposal makes labelling or an "accompanying document" compulsory for new GMOs. Companies applying for authorization will have to submit "certain molecular data", which could include nucleotide sequences, to be included in a product register.

As well as soybeans and corn, 11 products awaiting approval will not be covered by the new rules. These include herbicide-tolerant oilseed rape varieties developed by Plant Genetic Systems and AgrEvo, and maize from Monsanto, AgrEvo and seed companies Pioneer and Northrup King. The Commission will invite these companies to label their products voluntarily. The proposals are a "transitional measure" until a revised directive is produced within the next few months.

Food products containing GMOs are covered by the "Novel Foods" directive. In 1996, revised regulations required only "live" foods such as tomatoes to be labelled.

European countries have imposed or are planning varying labelling requirements. (Source: *European Chemical News, 7-13 April 1997)*

Amersham merges with P&U unit

Amersham International is to merge its life sciences business with Pharmacia & Upjohn's biotechnology supply division. It creates the world's biggest research-based biotechnology supplier with sales of about £430 million.

Amersham and Pharmacia Biotech (APB) both supply reagents, systems and services for biomedical research. "By combining Amersham's strengths in sequencing, labelling and detection with Pharmacia Biotech's separation, instruments and software skills, the new APB has a unique opportunity," says Ron Long, APB chief executive and formerly Amersham's managing director. (Extracted from *Chemistry & Industry*, 16 June 1997)

Roche-Mannheim proposed merger

The proposed acquisition announced in May 1997 of Boehringer Mannheim (Mannheim, Germany) by Hoffmann-La Roche (Basel, Switzerland) for $11 billion surprised some observers. Boehringer Mannheim has $300 million in cash, a strong, eclectic pipeline of biotechnology drugs—20 per cent of Boehringer Mannheim's turnover is from genetically engineered products, much higher than the 5 per cent pharmaceutical turnover generally—and numerous R&D agreements. The sales of the combined companies take Roche from tenth to fourth in the global pharmaceutical league table.

Although the field of diagnostics is undergoing consolidation, it is also becoming revitalized, perhaps because of the growing number of companies exploiting the interface between diagnostics and therapeutics.

The new acquisition has also produced synergies. Boehringer Mannheim has two tests that determine the degree of tissue damage in heart attacks—Cardia T and Trop T—and both Boehringer Mannheim and Roche have thrombolytic plasminogen activator drugs, Rapilsyn/ Retavase and Activase, respectively.

Boehringer Mannheim Lab Diagnostics is the world leader in clinical chemistry, and a moderate player in immunoassays, considered a good synergistic fit with Roche and its PCR technology. Moreover, Boehringer Mannheim's investment in electrochemiluminescence for immunoassays, a technology licensed from Igen (Rockville, MD) will also provide a platform for integration with clinical chemistry, and again complements PCR.

In addition to paring diagnostics and therapeutics for near-term use, Roche recognizes the role that pharmacogenetics will play in the future in diagnosing and treating disease. Diagnosis by examining a patient's genotype will enable more successful treatment, as it will help determine which drugs work best in which individuals. With its combined portfolio of diagnostics, Roche-Boehringer Mannheim is well positioned to capitalize on the trend towards pharmacogenetic diagnosis. (Extracted from *Nature Biotechnology,* Volume 15, July 1997)

MRA agreement signals start of global harmonization

After years of negotiation, the European Commission and the US Food and Drug Administration seem to have finalized a Mutual Recognition Agreement (MRA) on pharmaceutical products and site inspections. However, the agreement depends on three more years of compromise and indecision.

Inspections of pharmaceutical (including bio-technological) production sites by drug authorities can be an expensive and time-consuming process for authorities and manufacturers alike. At present, all drugs in the USA must be produced at factories that FDA inspectors have approved. In Europe, as part of the move to create a single market, there is now mutual recognition of national inspections throughout the European Union. The US-EU MRA discussions over the last three years have been an attempt to extend mutual recognition.

MRAs in six areas of trade—of which pharmaceuticals is one—have received political attention at the highest level in both the US and Europe.

One of the issues that had stalled the discussions previously was the FDA's discomfort with full mutual recognition of inspections carried out by regulators in all the EU member States. Their concern was that while authorities in countries like the UK and Germany had comparable competences to those of the FDA, authorities in some of the southern European nations might not. That hurdle has been overcome by the adoption of a "transitional period" of three years, after which the FDA and the EC will draw up a list of the authorities that provide "appropriate" or "equivalent" levels of competence and that can therefore be included under the MRA.

During that transitional period, there will be joint inspections—from different European nations—within Europe in an attempt to try to raise standards to a uniform level. The FDA has requested the option to participate in those inspections, but the expectation is that it will not exercise that option very frequently.

The US-EU agreement does not go as far as that between the EU and Canada, the test of which was completed and agreed to just a week before the US-EU agreement. (Extracted from *Nature Biotechnology*, Volume 15, July 1997)

Public voice concerns

Europe's biotechnology industry has a major problem with public acceptability, compounded by a lack of public confidence in governments and industry.

According to the latest Eurobarometer survey on public attitudes, published in *Nature*, Europeans are uneasy about modern biotechnology. The survey, conducted in 1996, questioned around 16,000 people in 15 member States of the European Union.

The use of biotechnology in "traditional" medical applications such as the production of new medicines and vaccines is supported more than in agriculture and food biotechnology, while the use of transgenic animal biotechnologies for medical research and xenotransplantations is opposed.

Labelling of genetically modified foods is supported by 74 per cent and 60 per cent believe the public should be consulted about developments.

One concern is that public unease over biotechnology has increased compared with previous Eurobarometer surveys in 1993 and 1991. The report states that, "although the public's knowledge of relevant basic biology has increased, optimism about the contribution of biotechnology and genetic engineering to improve our way of life has actually declined".

The survey has also uncovered a marked lack of public confidence in national public bodies and parliaments. Only 10 per cent of those interviewed expressed confidence in the ability of these bodies to regulate biotechnology.

Around 45 per cent said the medical profession could be expected to tell the truth about biotechnology while 26 per cent expressed confidence in environmental organizations. Less than 2 per cent expressed confidence in the industry and less than 1 per cent felt politicians told the truth. (Source: *European Chemical News*, 7-13 July 1997)

Europe and the biotechnology gap

Europe's biotechnology industry is coming of age and is set to become a crucial part of the region's future.

The European biotechnology industry is now a mature industry with more than 700 firms. Although it has yet to make any money overall, its growth will be of great importance to the future of Europe. To assess where it is going, over 500 delegates met at EuropaBio '97, the first annual congress of the new bioindustry organization, held in Amsterdam in May 1997.

At the congress participants were made aware of two "gaps". A gap in the commercial exploitation of biotechnology opening up between Europe and the USA; and a gap between the technical progress of the industry and public acceptance.

The event was used to launch the report *Benchmarking the Competitiveness of Biotechnology in Europe,* which had been commissioned by EuropaBio. In the study, four scenarios for the growth of the biotechnology industry in Europe were presented; fast, steady, limited and failed. In the "fast" scenario, the industry would grow from Ecu 40 billion ($45 billion) in 1995 to Ecu 250 billion in 2005, with employment growing from 300,000 to 3 million over the same period. In the "failed" scenario, the industry would be almost halved to Ecu 25 billion by 2005. Which scenario will win out in the end will be decided by the environment in which biotechnology has to operate in the future.

According to the report: "Europe has made important progress in recent years. But it remains well behind the USA in virtually every measure of competitive performance and risks losing ground in the future. The USA lead is largely due to a significantly more supportive external business environment."

The report also acknowledges that biotechnology is now an integral part of the pharmaceutical industry, with biopharmaceuticals accounting for 13 per cent of all new drugs developed between 1990 and 1994 and 5 per cent of all global pharmaceutical sales. There were 770 biotech drugs in development at the end of 1995, with 63 per cent of these coming from the USA and 25 per cent from Europe. There were 206 gene therapy drugs in development at the end of 1995, with 70 per cent of these coming from the USA and 22 per cent from Europe.

The gap is even greater in agricultural biotechnology. Most R&D takes place in the USA and Canada; more products have been approved for use in the US and Japan than in Europe; and US farmers are already making great use of transgenic crops. The acreage of transgenic crops cultivated in Europe is negligible.

However, the latest report from Ernst & Young described 1996 as a tremendous year for the industry with encouraging signs for both job creation and continued expansion. Compared with the previous year, 1996 revealed a 60 per cent increase in job creation and a 23 per cent increase in the number of companies. Biotech companies raised a total of Ecu 1.6 billion in new equity in 1996 compared with Ecu 400 million in 1995.

The programme for changing the business environment for biotechnology will also involve winning support from the public. This could present a major problem for the industry, particularly in the light of the results of the latest Eurobarometer survey.

In response to this, EuropaBio has produced a *Draft Core Ethical Values* document. Among its notable general principles, EuropaBio confirms opposition to reproductive human cloning, and commits itself to dialogue with those concerned about ethical and societal implications of biotechnology. Other issues addressed include animal welfare, protection of medical information, alteration of human sperm, eggs and embryos, consumer information for food products, and conservation of genetic diversity.

The document is seen by EuropaBio as being just the first step in a permanent process through which it intends to engage in open dialogue on ethical questions raised by the use of modern biotechnologies. (Extracted from *European Chemical News*, 7-13 July 1997)

World environment

Shifting the tax burden from wages and profits onto pollution and resource depletion is a powerful tool for protecting the environment, according to a new report* from the Worldwatch Institute. The study concludes that tax shifting can create jobs and boost living standards without damaging industrial competitiveness or increasing the overall tax burden.

According to the report, 90 per cent of the world's $7.5 trillion annual tax burden is levied on work and investment, and less than 5 per cent is levied on environmentally damaging activities. Making polluters pay in full would raise more than $1 trillion a year worldwide allowing a 15 per cent tax cut on wages and investment, says the report.

This would reduce the cost of job creation and ease the plight of the working poor, claims the report's author, David Roodman. According to Roodman, European Commission figures show that an EU-wide shift to carbon taxes would allow 1.5 million jobs to be created.

Roodman says that Sweden, Denmark, Spain, the Netherlands and the UK have recently made tax shifts away from work and investment and towards environmentally damaging activities. The landfill tax in the UK, for example, shifted 0.2 per cent of the tax burden from income to the environment. Although the revenue shifts are too small to have a measurable impact on jobs or living standards, the trend is encouraging, he says.

Making polluters pay also stimulates the market to come up with solutions to pollution, creating money-making opportunities, Roodman explains. In the Netherlands, for example, taxes on heavy metal emissions turned Dutch companies into world leaders in water pollution technology and cut heavy metal contamination by up to 97 per cent.

However, Roodman concedes that energy-intensive industries like chemicals would suffer, but argues that others, like computer software and recycling, would gain in equal measure. But he believes that a nation's industry would not necessarily forfeit international competitiveness if tax shifts were applied unilaterally. The tax could be rebated on exports and an equivalent tax could be levied on imports to effectively level the global playing field, he says.

A spokesman for the US Chemical Manufacturers Association said that the US chemical industry is generally

*"Getting the signals right: tax reform to protect the environment and the economy", Worldwatch Institute, 1776 Massachusetts Avenue, NW Washington, DC 20036-1904.

opposed to environmental taxation and would be unlikely to support the report's conclusions. (Source: *Chemistry & Industry*, 19 May 1997)

Biopharmaceuticals set for change

Change is in store for the biopharmaceutical industry, according to a new study from Waltham, MA-based Decision Resources (DR). Pharmaceutical companies are expected to change their relationships with biotech companies as they become more familiar with and even begin to profit from new biotechnologies. Historically, the major drug companies have invested heavily in smaller, biotechnology-oriented companies. Such alliances have served both industries well as a mutually beneficial and economically feasible means to develop new technologies.

The biopharmaceutical industry has grown rapidly over the past 20 years. The development of the enabling technologies that facilitate the core biopharmaceutical technologies has advanced clinical trials, spurring growth and stability in the industry.

DR's report discusses the changing technological base of the biopharmaceutical industry as genomics, nucleic-acid-based therapeutics, and small-organic-molecule mimetics become accepted as biopharmaceuticals.

The report examines the coming changes, how they will shape the industry, and the opportunities they will present for smaller biopharmaceutical firms and the major drug companies. Also included are market and technology profiles of 20 companies; status and future direction of key technologies; timing, targeting, and structuring of deals; regulatory impacts and market size. (Source: *Chemical Manufacturing Reporter*, 7 April 1997)

C. COUNTRY NEWS

Austria

EC urges Austria to end modified maize ban

The European Commission (EC) is likely to issue a proposal by the end of June 1997 that Austria should end its ban on imports of genetically modified maize. The EC said that it would be acting "on scientific advice" by proposing an end to the ban which Austria imposed in December 1996 amidst concerns over health risks.

EC environment spokesman Peter Joergensen said three European Union scientific committees had not yet found any new information regarding the crop which might lead the EC to reverse its decision made in December 1996 to allow imports of the modified maize.

The EC has also approved two kinds of genetically modified oilseed rape by Plant Genetic Systems for the marketplace.

The approval follows a "favourable opinion" from the Regulatory Committee set up under directive 90/220/EEC on the deliberate release into the environment of genetically modified organisms.

Meanwhile, the Irish High Court has given the go-ahead to Monsanto to begin field trials on genetically modified sugar beet at a state research farm in County Carlow, despite objections by Genetic Concern, an Irish environmental lobby group, on public health grounds. (Source: *European Chemical News*, 16-22 June 1997)

Brazil

BIOLATINA 98

The Brazilian Association of Biotechnology Enterprises (ABRABI) will be convening BIOLATINA 98, the Latin American Meeting on Industrial Biotechnology, to take place in Rio de Janeiro on 20 to 23 October 1998. The meeting will focus on opportunities in the Latin American biotech markets and will offer a friendly environment for the setting up and financing of joint ventures between small high-tech companies in Latin America and those of other regions, with the emphasis on industrialized countries. More information on BIOLATINA 98, such as the programme and procedures for registration and space reservations at the exhibit hall can be found at www.abrabi.org/biolatina98, or at ABRABI—Brazilian Association of Biotechnology Enterprises, Dr. Antonio Paes de Carvalho, M.D., Ph.D., President, Polo Bio-Rio—Cidade Universitaria, Rio de Janeiro—RJ, Brazil 21.941-590. Tel.: (+55-21) 290-5839; Fax: (+55-21) 260-7920. E-mail: info@abrabi.org.br

Canada

Canadian biotech regulations

New regulations for biotechnology products under the Canadian Environmental Protection Act were published in *Canada Gazette Part II* on 5 March 1997. The regulations, a guideline to the regulations and a brochure can be seen on the Internet at: http://www.ec.gc.ca/ccebl/eng/biohome.html (English) http://www.ec.gc.ca/ccebl/fre/biohome.html (French).

Regulations covering the Environmental and Health Assessments of Novel Agricultural Products of Biotechnology under the *Seeds Act, Feeds Act, Fertilizers Act* and *Health of Animals Act* are now available on the Internet. Also, agreement in principle has been reached between Natural Resources Canada (Canada Forest Service) and Agriculture Canada that forest trees and seedlings with novel traits will be regulated under the *Seeds Act*. Check for the *Canada Gazette Part II* dated 8 January 1997 at http://www.agr.ca/fpi/agbiotec/home.html. (Source: *The AgBiotech Bulletin*, May 1997)

Biotechnology boom

Canada's biotechnology industry is growing at an unprecedented rate, according to a report by financial consultancy Ernst and Young.

The industry's revenue tripled from Can$ 353 million in 1993 to $1.1 billion in 1996, while the number of companies in core biotechnology business increased from 121 to 224 over the three-year period. Funding raised last year totalled over Can$ 1 billion, equal to total funding raised in the previous five years.

Of the 224 biotech companies included, 59 per cent were in the healthcare field and over 25 per cent were involved in agricultural end-products. However, Canada's complex regulatory process remained the major challenge to further development of the industry, the report concluded. (Source: *European Chemical News*, 7-13 April 1997)

Help for Cuban Biopharmaceuticals

Toronto-based York Medical Inc. has formed a novel partnership with the Cuban Government to develop and market Cuban biopharmaceuticals. An initial prospectus aims at raising between C$ 12 million and $16 million in a private placement.

York Medical, with backing from Yorkton Securities Inc., of Toronto, is providing the Cubans with product evaluation, out-licensing, clinical and regulatory expertise and access to capital markets they need to commercialize their research.

The Cuban products targeted by the venture include DiaCIM™ and TheraCIM™, products based on a humanized epidermal growth factor receptor, EGFr-3MAB, for diagnosing and treating breast, lung, head, and neck cancer, Udertan®, a natural product to prevent mastitis in cows; Diramic®, for diagnosing infection-causing bacteria and antibiotic susceptibility; and Dermofural®, a topical anti-bacterial and anti-fungal ointment. Another product, Heberkinasa™, is a recombinant streptokinase, which the company claims costs 40 per cent less to produce than conventional streptokinase. A Phase III clinical trial is planned to begin in the UK later this year. (Extracted from *Genetic Engineering News*, 15 April 1997)

China

US China pact yields new cancer vaccines

Researchers at the Sidney Kimmel Cancer Center and the People's Republic of China say they have developed a new method for creating vaccines against cancer.

In the two-step process, tumour cells removed from a patient are first modified in the laboratory with a combination of cytokines to enhance the expression of tumour antigens and immune activating molecules needed to generate the body's immune response.

Treated tumour cells are then armed with a hybrid bispecific monoclonal antibody.

The antibody recognizes an antigen on tumour cells and another that binds to a key immune activating molecule (CD28 antigen) expressed on T cells.

The finding is reported in the April 1997 issue of *Nature Medicine*.

Collaborators in the study are from the Shanghai Hospital and Shanghai Second Military Medical University (People's Republic of China), Case Western Reserve University School of Medicine and the University Hospitals of Cleveland. (Source: *McGraw Hill's Biotechnology Newswatch*, 7 April 1997)

Biotech key to self-sufficiency in China

China's vice minister of agriculture *Wan Baorui* says his country will rely on biotechnology, better management and more farm-sector foreign investment to ensure food self-sufficiency in the next three decades, according to a release by Agence France Press.

In a keynote address entitled "Food in a Borderless World" given at a symposium of the National Forum for Agriculture, *Wan Baorui* sought to ease fears among some food experts that China's growing appetite for grain might spark a future global food crisis. Stressing that agriculture was a top priority for his government in the post-Deng area, he said: "For a big country with a 1.2 billion population, a high degree of grain self-sufficiency is a must to guarantee development and social stability. Under normal circumstances, China will keep its self-sufficiency rate at no less than 95 per cent and net grain import no more than five per cent of total domestic consumption."

He stressed biotechnology offered great prospects for boosting crop yields, particularly on low-yielding land. The share of agri-science and technology in helping boost farm production is only 35 per cent, and it will reach about 50 per cent by the end of the century compared with 60 per cent now in developed countries. (Source: *The AgBiotech Bulletin*, June 1997)

Costa Rica

Indena, INBio enter collaboration

Milano-based extract specialist Indena SpA has signed a collaboration agreement with the Costa Rican Research Institute INBio (Instituto Nacional de Bioversidad).

The two will work together to identify plants with potential for pharmaceutical applications in the anti-microbial and anti-fungal areas.

INBio will identify a number of plants suspected of having the desired anti-fungal and anti-microbial therapeutic properties. It will then carry out a preliminary screening to select the 60 most promising species.

These candidates will be subjected to advanced pharmacological screenings to determine therapeutic activity levels. Indena will then extract active therapeutic substances from the leading candidates.

The partners are hoping to capitalize on Costa Rica's extensive biodiversity, which, according to claims, represents 4 per cent of the world's biological wealth. Roughly 25 per cent of the country's territory is comprised of protected wooded areas. Indena and INBio say that approximately 500,000 species of plants, animals and microorganisms exist within these state-protected tracts.

INBio is a privately funded research institute which was established in 1989 with the specific task of exploiting the country's biodiversity.

Indena is one of Europe's leading botanical extracts specialists and had 1995 sales of $150 million, a 47 per cent increase over the previous year.

As part of company history, Indena provided Bristol Meyers Squibb with the precursor to the anticancer agent Taxol several years ago, helping to quell US environmental concerns about the increasing shortage of Pacific yew bark needed to meet growing demand. (Extracted from *Chemical Market Reporter*, 7 July 1997)

European Union

EU enforces biotech rules

The European Commission has charged Germany, Luxembourg, Portugal and Spain with failure to adopt and report on national laws relating to all genetically engineered organisms. The cases will be heard by the European Court of Justice and may lead to substantial fines for the countries concerned.

The Commission says Portugal, Spain and Luxembourg have failed to implement national legislation under the 1994 directive setting out controls on the use and release of the organisms in the environment. It has accused Germany of failing to make adequate provision for emergency plans in the event of accidents.

The action comes at a time when the US is applying increasing pressure on the European Union (EU) on trading conditions involving genetically engineered products.

In the past month the commission has initiated more than 30 other cases involving noncompliance with environmental legislation. The Commission denies that the court proceedings represent a hardening of environmental enforcement in Europe. Austria faces three court proceedings for failing to adopt legislation relating to air quality. Transgressions include non-compliance with the EU's 1980 sulphur dioxide and particulates directive and the 1985 directive on nitrogen dioxide. (Source: *Chemical Week*, 16 July 1997)

EU to insist on product labelling

The European Commission has adopted a directive to make labelling compulsory for "all new products containing or consisting of genetically modified organisms (GMOs) notified for placing on the EU market".

The directive amends a controversial 1990 law (directive 90/220/EEC) on the release of GMOs into the environment. The EC has warned member States that this must be transposed into national law by 31 July.

The regulation is not retroactive and does not apply to current pending notifications to the Commission of GMO products. However, all those companies with notifications pending are invited to label their products on a voluntary basis. (Source: *European Chemical News*, 23-29 June 1997)

Public voice concerns

Europe's biotechnology industry has a major problem with public acceptability, compounded by a lack of public confidence in governments and industry.

According to the latest Eurobarometer survey on public attitudes, Europeans are uneasy about modern biotechnology. The survey, conducted in 1996, questioned around 16 000 people in 15 member states of the European Union.

The use of biotechnology in "traditional" medical applications such as the production of new medicines and vaccines is supported more than in agriculture and food biotechnology, while the use of transgenic animal biotechnologies for medical research and xenotransplantations is opposed.

Labelling of genetically modified foods is supported by 74 per cent and 60 per cent believe the public should be consulted about developments.

One concern is that public unease over biotechnology has increased compared with previous Eurobarometer surveys in 1993 and 1991. The report states that, "although the public's knowledge of relevant basic biology has increased, optimism about the contribution of biotechnology and genetic engineering to improve our way of life has actually declined".

The survey has also uncovered a marked lack of public confidence in national public bodies and parliaments. Only 10 per cent of those interviewed expressed confidence in the ability of these bodies to regulate biotechnology.

Around 45 per cent said the medical profession could be expected to tell the truth about biotechnology while 26 per cent expressed confidence in environmental organizations. Less than 2 per cent expressed confidence in the industry and less than 1 per cent felt politicians told the truth. (Source: *European Chemical News*, 7-13 July 1997)

European patent directive

The European Parliament is due to vote on the European patent directive—the outcome of which will have a major impact on the future of the European biotechnology industry.

The directive was voted through by the legal affairs committee in June 1997 with 64 amendments. The concern is that further amendments could be voted through (more than 300 amendments have been proposed), which could seriously weaken the directive.

The most important parts of the directive are Articles 3 and 9, which respectively, clarify the issue of patenting of human genes and ethical concerns around issues such as cloning, gene therapy and transgenic animals. The directive was originally rejected by the European Parliament in March 1995.

Industry has pushed for the adoption of the directive despite the fact that it is already covered by the European Patent Convention. It was felt the existing legislation could not adequately deal with new developments in biotechnology.

Should the directive be adopted as it stands it will be brought into force by 1999.

VFA, the industry association for Germany's research-oriented drugmakers, has warned that more European R&D will shift to the US and Japan if the revised biotechnology patent directive fails again to pass the European Parliament in the July vote. (Extracted from *European Chemical News*, 14-20 July 1997)

Germany

Biotech given a helping hand

Three pharmaceutical and chemical majors have teamed up with a consulting firm to promote biotechnology in the Rhine-Neckar region of Germany.

Abshagen Consulting has set up the company, Heidelberg Innovation Consulting, in Heidelberg. The other companies involved are BASF and its pharmaceutical subsidiary, Knoll, along with Boehringer Mannheim and Merck.

Heidelberg Innovation's purpose will be to support cooperation between the industrial and scientific sectors and to develop new products. A venture capital fund to provide aid to new biotech firms will also be established. (Source: *European Chemical News*, 7-13 April 1997)

Germany's herbal medicine industry

The global market for herbal medicines in 1996 was estimated at $14 billion, distributed in the following manner: Europe, $7 billion; Asia, $2,7 billion; Japan, $2.4 billion; North America, $1.6 billion; and the rest of the world, $0.3 billion.

Economically and technologically, Germany has the most developed herbal medicine industry and the single largest market ($3.5 billion). Consumers, who often reject conventional drugs with their potentially severe side effects, often prefer natural alternatives. In Germany, consumer attitudes fit into a medical establishment that accepts the use of herbal medicines (i.e., phytopharmaceuticals). Courses in the use of herbal medicines are a regular component of medical and pharmacy curriculae, and since 1993, this subject has been a regular component of the German medical examination. More than 70 per cent of general practitioners prescribe herbal medicines, most of which are reimbursable by the public health insurance system.

The German Medicines Act of 1978 allowed for the issuance of Standard Licenses for herbal products, subject to the publication of a monograph that provides qualitative and quantitative information about each product. These monographs are produced under the jurisdiction of a special body, known as Commission E, and provide information on indications, contraindications, side effects, interactions, dosages, manner of use and effects.

As of July 1988, there were 200 monographs, including 140 drug monographs. The overall focus in the German system is on individual herbs. This approach has now been accepted by the European Union.

The existence of a legal framework for herbal products has certain important consequences: they can be sold as drugs with both labels and inserts providing the necessary information; they can be prescribed by physicians; and they are reimbursable through medical insurance schemes.

In Germany, herbal medicines can be sold through *Apotheken* (which also sell prescription drugs), pharmacies (which sell OTC products and cosmetics), and natural food stores. In the future, this system is likely to undergo major changes, since Commission E has been disbanded and new EU regulations will require herbal medicines to be treated in the same way as chemical products or be sold only as a traditionally used drug.

In an environment in which herbal medicines are part of the established medical practice, half of these products are sold for self-treatment and the other half by medical prescription.

German market data provide an insight into those disease categories for which customers are most likely to use herbal remedies. The five top categories are anti-arteriosclerotics, gynaecologicals, cold/cough preparations, hypnotics/sedatives, and laxatives, some of which capture more of the market than their pharmaceutical counterparts.

The list of German herbal medicines shows the dominance of such prescribed products as those derived from the *Gingko biloba*, even though those are now decreasing in sales. Another major product over the past two years has been St. John's-wort (i.e., Hypercicum), which has been the most popular herbal antidepressant since 1995.

Such developments have attracted the attention of major European multinationals—and include companies such as Boehringer Ingelheim, Boehringer Mannheim and Bayer—that see the potential of what are called "green pharmaceuticals".

At present, most of the German companies are privately owned and have sales ranging from $20 million to over $100 million. These are a growing target for acquisition by both European and US multinationals. The latter are interested in establishing a foothold in this growing and profitable pharmaceutical business. (Extracted from *Genetic Engineering News*, 14-15 April 1997)

Hong Kong

Biotech in Hong Kong

Hong Kong differs markedly from its Asian counterparts, Taiwan, South Korea and Singapore. It lacks a comprehensive government policy to promote biotechnology and does not have a significant industrial base in either pharmaceuticals or agriculture. Hong Kong is still developing research and training capabilities in the biological sciences, and its major financial institutions have shown little interest in biotechnology.

The single major strength has been the biological research carried out at the three main universities: Hong Kong University (HKU), the Chinese University of Hong Kong (CUHK) and the Hong Kong University of Science and Technology (HKUST). The Royal Hong Kong Jockey Club invested $39 million into the Biotechnology Research Institute (for basic and applied research) at HKUST and the Hong Kong Institute of Biotechnology (for downstream research) at CUHK.

During the past three years, the Industry Department established three new programmes: the Industrial Support Fund (ISF), the Applied R&D Scheme and the Cooperative Applied R&D Scheme. The ISF has worked with the Biotechnology Committee of the Industry and Technology Development Council to approve 56 biotechnology projects. The project areas include diagnostics, food processing, agriculture, aquaculture, floriculture, development of vaccines, biopharmaceuticals, drug delivery technologies and traditional Chinese medicines (TCM). The three principal universities provide a good education in the biological sciences and in 1996 enrolled 1,000 under-graduates and over 250 graduate students. Employment opportunities for such students are uncertain.

The biggest problem facing Hong Kong is the lack of an industrial base in biotechnology. According to the Industry Department, there are 39 pharmaceutical companies (most of them involved in tableting, packaging and marketing). There may be as many as 100 companies dealing in TCM, mainly packaging and distributing products coming out of China.

In the food sector, there are 35 companies, 18 of which process Chinese food products; 16 fulfil the demand for Western food products. None of them has significant R&D activities.

The development and expansion of such companies require both technology and a larger market. Across the border, in Shenzhen, there are 20 biotech companies, some of which manufacture recombinant DNA products. Further afield, there are about the same number of biotech companies around Beijing and Shanghai.

All of this suggests that if biotechnology is to flourish in Hong Kong, it will do so through its linkages with the vast Chinese hinterland, which will provide both skilled manpower and growing markets.

Two studies have concentrated on trying to ascertain biotech's future in a Hong Kong under Chinese rule. The "Biotechnology Focus Study", carried out by the Industry Department and the State Science and Technology Commission of China, looked at the potential collaboration between Hong Kong and China. The "Made by Hong Kong (MbHK) Study" was undertaken by a group of researchers at MIT on contract to the Industry Department and the private sector.

The Focus Study emphasized TCM, generic drugs, drug delivery and human genomics. The human genomics area would focus on those genetic differences between Asian and Western populations and could result in diagnostic systems and biological therapeutic products for the Asian market. Both studies have focused on TCM and generic drugs as areas in which Hong Kong, in collaboration with China, would have a competitive advantage.

The studies recommended that Hong Kong should use TCM as a basis for new drug discovery with new TCM-based drugs becoming the basis for its pharmaceutical industry. Such a recommendation is based on a long history of TCM's efficacy for many diseases, the potential market size for China and Hong Kong, a large library of possible compounds, TCM as a major area of R&D in Hong Kong universities and on a base of knowledge.

Since Hong Kong is already a major centre for the trade in TCM, it should be possible to identify major supply sources in China.

While the recommendation focuses on the Chinese market, the situation as it relates to patent protection and regulatory approval of herbal products (in general) is unclear and rather volatile. Neither the US nor Western Europe has licensed TCM for sale as drugs.

Many Chinese pharmaceutical companies had been state-owned, and have continued to use processes and manufacturing facilities based on obsolete Chinese and Russian designs. Both production output and product quality are far from modern world standards, thus making it difficult to meet the demands of Chinese consumers. This also prevents the creation of an export business into the developing Asian market.

The MbHK report proposes that the Chinese pharmaceutical situation provides an opportunity for Hong Kong that would have three different components. One would involve the adaptation of existing Western manufacturing processes for antibiotics (the type of project envisioned for HKIB); another, the creation of modern generic companies that would sell high-quality products to China; and, finally, engineering companies that would transfer this manufacturing technology into China. Such opportunities are extremely attractive, but they are handicapped by the lack in Hong Kong of modern pharmaceutical manufacturing companies as well as the types of expertise required. For such an effort to succeed, a harmonization of manufacturing and drug licensing

standards and patent protection in Hong Kong and China are also required.

The future development of biotechnology in Hong Kong will be determined both by the new policies of the Special Administrative Region (SAR) and Beijing governments and the economic situation that it generates. Hong Kong has rapidly seen its manufacturing base shrink from being 23 per cent of GDP thirteen years ago to 9.3 per cent now. Much of this manufacturing has moved across the border into Guangdong and beyond. A good deal of the value added to the products from these Chinese factories came from the "Hong Kong hustle", which has been defined as a combination of management design, product development, marketing, logistics, telecommunications, quality control, testing and certification, financial services and component parts. There is increasing concern that the escalation of costs both in Hong Kong and the adjacent Chinese areas makes the current situation unsustainable.

New initiatives being considered include increased funding of R&D, expansion of elementary and secondary education, worker training, development of high-tech industrial parks (possibly in border areas), creation of start-up companies, establishment of a venture capital fund and creation of a NASDAQ-type stock exchange.

Much of this can be done by drawing from the $60 billion in foreign reserves left by the British administration. While such plans are attractive to foreign investors and the highly skilled professionals necessary to make it work, there are a number of crucial questions that can only be answered in the years to come.

Hong Kong has profited from the British rule of law. Whether the judiciary will continue to be independent, particularly in providing protection from arbitrary government action, implementing regulations in a fair and even-handed manner, and supporting the independent work of regulatory agencies is a concern. These issues centre on how much autonomy the SAR government will receive from the central government in Beijing.

The situation is further complicated by the fact that it is unclear which Chinese government entity will be responsible for Hong Kong.

The two biotechnology project areas, TCM and generic drugs, proposed in the two recent studies are embedded in the context of a close collaboration between companies and institutions in Hong Kong and China. The complexity of such projects as well as the need for significant financing is likely to require the creation of new companies (presumably in Hong Kong), technology from Western corporate partners (possibly American) and companies and institutions in China. Such efforts require downstream technology and entrepreneurial individuals. Neither of the two are in abundant supply in Hong Kong. (Extracted from *Genetic Engineering News*, July 1997)

India

India bans shrimp farming

India's Supreme Court has ordered all large commercial shrimp farms in five coastal states to close by the end of April 1997. That action has caused a political row since Indian shrimp farming is a US$ 500 million-a-year business. Court action was brought about by conservationists who have campaigned for years against shrimp farming in coastal waters. Activists claim that shrimp farmers contribute to wetland destruction, pollution of coastal waters, degradation of fisheries and land grabbing. Scientific studies have concluded that the environmental degradation caused by shrimp farming is actually costing India more than it is earning through shrimp exports.

Shrimp aquaculture requires large quantities of water. To raise one metric tonne of shrimp, 50 to 60 million litres of water are needed, about half of which is fresh water—a serious burden in regions where drinking water is scarce. Each kilogram of produce generates about 15,000 litres of effluent including toxic residues. This chemical stew is often released, untreated, into the ground water, leading to contamination of local communities' supplies. Shrimp production is also energy-intensive. Shrimps are fed three times their harvested weight, but convert only 17 per cent of this feed into edible flesh. Since the creatures are fed mostly with fish meal, shrimp farming encourages fishermen to hunt down the food chain to smaller fish.

In India, shrimp farming has been supported by the World Bank, FAO and the Asian Development Bank as a means of generating foreign exchange. Increasingly, the industry is run by transnational corporations who have little interest in providing jobs for local communities and who threaten to relocate if regulations become too strict.

Shrimp farming, as currently practised by the large commercial farms, is unsustainable. About 200,000 hectares of coastal lands are said to have been abandoned worldwide after producing shrimp for only four or five years. These lands may take 15 to 20 years to regenerate. But shrimps may also be produced in an ecologically and socially sustainable way or caught in the wild. Rather than calling for a general boycott of shrimps in rich countries, consumer organizations are therefore thinking of establishing guidelines on how to identify shrimps produced in sustainable ways. (Source: *D+C*, April 1997)

Transgenics tops research agenda

The Department of Biotechnology, a section of the Indian Government, will sanction a project at the Tamil Nadu Veterinary and Animal Sciences University to develop transgenic animals capable of producing biomolecules.

The three-year project involves the artificial introduction of genes into animals in the embryo stage. The first stage of the project will be the introduction of the beta casein gene in rabbit embryos to increase its production of the milk protein.

Other research includes the introduction of the human insulin-producing gene to goat embryos.

University researchers have also successfully cloned the gene responsible for the production of cellulose in the rumen (first of four stomach compartments in a cow or buffalo) and propose to use the gene to increase the cellulose-digesting capabilities of cows so that they can be fed paddy straw. Paddy straw contains a high level of cellulose and is therefore indigestible by normal cows. (Source: *McGraw Hill's Biotechnology Newswatch*, 2 June 1997)

Ireland

Biotech in Ireland

Today, Ireland enjoys the fastest-growing economy in the European Union. It expanded by 6 per cent in 1996, compared to an average EU growth of approximately 2 per cent. Growth of 5 per cent is forecast for 1997. Employment is increasing rapidly and interest rates are at their lowest levels since the 1960s.

Exports account for three quarters of the national output, a level that is unique in Europe. That success has been, in large measure, due to the contribution of high-tech overseas companies that have found Ireland to be a highly

competitive location from which to serve international markets.

Over the past two decades, more than 1,000 overseas companies have joined the strong base of local firms trading from Ireland—not just with Europe but worldwide.

The Irish Government has sought to create an environment that is attractive to multinational pharmaceutical, healthcare and biotechnology companies, while also taking measures to develop indigenous firms.

A national biotechnology programme was announced in June 1987 that it had as its objective the development of commercially oriented biotech research in Irish universities. This resulted in the creation in 1988 of BioResearch Ireland (BRI). BRI's policy has been clearly commercial from the outset. It established five centres of biotech in universities that provide a wide range of research and technical services to the food, diagnostic, agro-industry, pharmaceutical and other bioindustries.

BRI's overseas clients include biotech companies and organizations in Europe, the USA, Canada, South America and Japan. BRI also invests in products and technology with a view to licensing or sale of the resulting products. BRI now markets 12 products and has recently spun off an independent company offering quality analysis services to the pharmaceutical industry. Plans are also under way to expand BRI's GMP contract-manufacturing facility.

Pharmaceutical and medical product companies from around the world use Ireland as a base for developing, manufacturing and marketing a diverse range of products, from analgesics to disposable contact lenses. Between them, they generate $6 billion of exports every year. Thirteen of the world's top pharmaceutical companies and ten of the world's top 15 medical product companies have operations in Ireland. (Extracted from *Genetic Engineering News*, July 1997)

Irish biotechnology company update

The "Irish Biotechnology Sourcebook, 1997" has been published jointly by BioResearch Ireland (BRI) and the Centre for Innovation in Biotechnology in Northern Ireland. The new edition is a significant expansion and updating of BRI's successful 1994 edition, which only covered the Republic of Ireland. The new guide contains details on companies, consultants, support organizations, research projects and third level courses on biotechnology in both the Republic and Northern Ireland. Of the 140 companies listed, 33 per cent are involved in human/pharmaceutical research; 16 per cent are in the veterinary sector; 15 per cent in food and drink, and the remainder are involved in environmental, agriculture, plant breeding and instrumentation.

The sourcebook is available from BioResearch Ireland, Forbairt, Glasnevin, Dublin 9, Ireland. Fax: +353 1 837 0176, E-mail: breslind@biores-irl.ie. Price IR£ 50 (Europe), US$ 100 (worldwide). (Source: *Irish Biotech News*, April 1997)

BioResearch Ireland announces its first spin-off company

BioResearch Ireland has announced the formation of its first spin-off company Arqtech Laboratories. This new company evolved due to BioResearch Ireland's increasing success in the area of the detection of residual DNA in genetically engineered products and processes. This business was previously run by BRI's National Diagnostic Centre in Galway.

Arqtech Laboratories is currently providing impurity testing services to the biopharmaceutical industry. The main focus of the company is on testing genetically engineered pharmaceuticals for the presence of residual DNA and is also providing services to several multinational companies in Europe. (Source: *News Release*, 18 April 1997)

Italy

Gene Therapy Centre in JV with Boehringer Mannheim

Boehringer Mannheim and San Raffaele Hospital have inaugurated a new facility in Milan designed to provide a complete range of vectors used in gene therapy for cancer and other disease treatments. Molecular Medicine SpA (MOLMED, Inc.), a joint venture between the two parties, represents the first commercial venture of its kind to open in Italy.

The San Raffaele Biomedical Science Park was founded in 1993 and is the largest biomedical and biotechnological conglomerate operating in Italy. In addition to the San Raffaele Hospital, Italy's largest private medical centre, the Park includes the Department of Biological and Technological Research (DIBIT), the Telethon Institute for Genetics and Medicine (TIGEM), the San Raffaele-Telethon Institute for Gene Therapy of Genetic Disease (HSR-TIGET), various research departments of major international corporations such as Roche, Bayer, Schering-Plough, Primm, Charles-River and Sorin-Biomedica. Several other Italian academic institutes also have facilities there.

The new alliance will combine Boehringer Mannheim's biotechnology diagnostics's expertise companies with the clinical experience of San Raffaele Hospital for the conduct of controlled trials of genetic agents.

Italy's National Health Authority (Istituto Superiore di Sanità) has proposed new governmental regulations permitting the use of gene therapy procedures in clinical trials. This authority has drafted guidelines based on those established by the US FDA and the European Agency for Drug Evaluation (EMEA) for gene therapy-based clinical trials. (Extracted from *Genetic Engineering News*, 1 April 1997)

Japan

Biotic pesticide to be developed to prevent anthracnose

A "biotic pesticide to prevent anthrocnose" has been selected by the Japan Science and Technology Corporation (JST) as a theme for cooperative development with industry. The project is the result of research by Chief Researcher Seiju Ishikawa of the Plant Disease and Insect Section Tochigi Prefectural Agricultural Experiment Station. The development will be commissioned to Idemitsu Kosan Co., Ltd., with a goal of putting the biotic pesticide into production in three years. The budget for the project is 260 million yen.

Anthracnose generates a mass of salmon-pink spores and black spots on leaves, stems and fruits of a plant (e.g. strawberries, apples, peaches, watermelons) and withers the plant to death. In particular, in strawberries with anthrocnose, discrimination of a sound plant from a potentially infected one is difficult, and thus a potentially infected plant may be used as a seedling or mother plant. Thus, preventing the disease is difficult if it has arisen.

This biological agent, will prevent "anthracnose". It will protect the plants from the disease by inoculating them with a antagonistic fungus, a kind of mould, separated from the tissue of strawberries. It reportedly causes little

environmental contamination. For further information, contact the 2nd Division, Department of Contract R&D, JST; Tel.: 03-5214-8995.(Source: *STA Today*, Vol. 9, No. 6, June 97)

Eight crops OK'd by Health Ministry

Japan's Ministry of Health and Welfare has verified the safety of eight new crops produced with recombinant gene technology.

In addition to releasing application documents and gathering general sentiment about the issue, the committee will report to the Health and Welfare Minister.

This is the second verification of the safety of recombinant gene crops, following confirmation of other crops in July 1996. The verified crops include herbicide resistant corn, three types of potato and insect-proof cotton.

Last year, the safety of seven herbicide-resistant crops, including soya beans, was confirmed. Import of the crops has already begun. (Source: *McGraw Hill's Biotechnology Newswatch*, 7 April 1997)

MITI to support tissue, organ research

Starting in 1998, MITI's Agency of Industrial Science and Technology will support research into the production of human organs and tissues under artificial conditions using the patient's own cells.

The project—three-dimensional cellular structure module engineering—is aimed at artificially producing replacement modules by cultivating the specific cells in a way that will let them differentiate into the target organs or tissues.

If the module development is successful, it will be possible to perform organ transplantation without looking for donors. According to officials involved in the project, the module would also be used for producing substances such as cytokines, as well as for clinical testing of drugs instead of animal tests.

Under the plan, human cells of the target organ or tissue will be arranged in a three-dimentional matrix and cultivated by elaborately controlling the differentiation-inductive factors, growth stimulating factors and cell-contact factors of the cells so that they can develop into the organ or tissue performing the same functions as the target organ or tissue. (Source: *McGraw Hill's Biotechnology Newswatch*, 7 April 1997)

Korea, Republic of

Government to develop biotechnology industry

The government has selected the biotechnology industry as one of its strategic areas for extensive development. For this purpose, it will pour 210 billion won ($235 million) into the sector by the end of 2000, said officials at the Ministry of Trade, Industry and Energy (MOTIE). Of the total amount, about 14 billion won will be pumped into the development of basic technologies this year and an additional 24 billion won next year. The ministry plans to increase the share of domestic firms in the world market to 4 per cent, or $4 billion in terms of value, by the target year and further to 5.7 per cent by 2005. The biotech industry is expected to emerge as one of the most promising high-tech industries in the next century, a ministry official said. (Source: *Newsreview*, 19 July 1997)

Philippines

First-to-file system adopted

In an address to the APC Ministerial Meeting held recently at Subic Bay, the Philippines Secretary of Trade and Industry announced steps to be taken to strengthen intellectual property rights in the Philippines. Legislation has been introduced as a result of the TRIPs Agreement. In particular, the first-to-invent system of priority will be abandoned, and a first-to-file system will be adopted. This will conform Philippines Patent Law to the system operated in almost the rest of the world, and will greatly simplify determination of examination and determination of who should be granted the patent. This will leave the United States as the only country still retaining a first-to-invent system.

Other measures being taken to enhance intellectual property protection include the requirement for technology transfer arrangements to be evaluated by the BPTT; such agreements will simply be registered in the future. Enforcement of intellectual property rights will be made easier, and a presidential inter-agency committee on intellectual property rights has been established. Special courts for intellectual property rights have been designated, and criminal penalties for infringement have been increased. (Source: *Australasian Biotechnology*, Vol. 7, No. 2, April 1997)

Russia

ABS in Moscow alliance

American Biogenetic Sciences (ABS) Inc. has formed a strategic alliance with Moscow's Russian Academy of Sciences. Under the terms of the agreement, ABS receives the rights to develop and commercialize any diagnostic and therapeutic products generated within the alliance.

The Russian Academy of Sciences will receive the rights to use the ABS patented antigen-free technology to produce monoclonal antibodies (MAbs) with superior affinity and specificity.

In addition, the Russian Academy of Sciences will coordinate cooperative efforts between other Russian Institutions, including the Moscow Medical Academy, Russian State Medical University, Moscow Medical Dentistry Institute, Scientific Research Institute of General and Forensic Psychiatry, Scientific Research Institute of Genetics and the Scientific Research Institute of Immunology. (Source: *McGraw Hill's Biotechnology Newswatch*, 16 June 1997)

Russia steps into AIDS research arena

Russia is beginning to come to grips with a newly recognized health threat: AIDS. The Russian Government is expected to launch its first AIDS research programme, a $15 million effort to develop a vaccine against HIV.

Russia's public health has eroded since the end of the Soviet Union, with some infectious diseases becoming rampant. Government estimates put the number of HIV-infected Russians at several thousands, including about 1,000 cases of full-blown AIDS. However, the number is thought to be much higher.

To lead the new programme, approved by the lower house of parliament (the Duma) in the 1997 budget, Russia

has chosen two respected Mosow-based immunologists: Ram Petrov of the Institute of Bioorganic Chemistry and Rakhim Haitov, head of the Institute of Immunology. (Source: *Science*, Vol. 276, 4 April 1997)

Switzerland

Import of genetically altered soya beans

The Swiss Government will allow imports of genetically altered soya beans. The announcement came just days after some 500 tonnes of Switzerland's well-known Toblerone chocolate bars were recalled from Swiss stores for containing traces of genetically manipulated soya beans.

Chocosuisse, the organization of Swiss chocolate producers, called the recall absurd, and warned that if Switzerland maintained its ban on genetically modified soya beans, chocolate manufacturers would be forced to move elsewhere. In a bid to ease public concern, the Government has said any genetically modified soya beans must be labelled. They are used in food products ranging from chocolate to sauces to baby food. (Source: *The AgBiotech Bulletin*, May 1997)

Taiwan

Biotech panel set up

In efforts to promote its biotechnology industry, Taiwan's Ministry of Economic Affairs (MOEA) has established a biotechnology guidance panel to help increase the country's annual biotechnology production to about $3.63 billion by 2005 from the current $727 million.

The panel is responsible for policy promotion, regulations, assistance, technology transfer, R&D, personnel resources, intellectual property rights and marketing.

Establishing R&D systems is the first priority with MOEA's Industrial Development Bureau, setting the foundation by developing flowers, veterinary vaccines, and biological pesticides within the next three to five years.

An investment company, which is also provided for under the plan via government funds and manufacturers' capital, will be used to select overseas biotechnology firms for technology transfers into Taiwan, and marketing rights throughout the Asia-Pacific region will be obtained to expand the sales channels for Taiwanese biotechnology manufacturers. (Source: *McGraw Hill's Biotechnology Newswatch*, 2 June 1997)

United Kingdom

Spearheads strategy to maintain bioscience industry in pole position

The UK bioscience industry clearly leads the way in Europe. A recent industry report from Ernst and Young stated that the UK has as many biotech companies as France and Germany put together. In a move to maintain this competitive edge the Bioindustry Association has issued "A Charter for Bioindustry" highlighting six key issues to be addressed to ensure the current health and future growth of bioscience in the UK. The Charter sets out these issues in detail to help ensure the continuing prosperity of industry's bioscience sector and influence policy decisions both at the national and European levels.

The Charter focuses on six areas:

- Stimulating science teaching and research in universities;
- Effective and assured intellectual property protection for biological molecules;
- Regulation that is science based and commensurate with real risk;
- The implementation of an effective Orphan Drug Act;
- Policy measures to facilitate industrial R&D;
- Encouragement of risk-taking necessary to develop bioscience industry.

According to an industry report by Arthur Andersen it is predicted that UK biotechnology-dependent sales could be £9 billion by the year 2000, putting the bioscience industry on a par with the computer industry in terms of sales and contribution to the UK economy.

The public launch of this Charter follows nine months of discussion between the BIA, its members, leading industry figures, as well as government officials and Members of Parliament. The Charter will be distributed to BIA members, Government representatives and other relevant groups. The publication of the Charter follows the publication in June 1997 of a BIA-sponsored supplement to Nature Biotechnology, "Putting biotechnology to work" in collaboration with Macmillan Magazines Ltd.

For further information contact: Lisa Maher, Communications Manager, Bioindustry Association, 14/15 Belgrave Square, London SW1X 8PS, Tel.: 0171-2459911, Fax: 0171-2354759, E-mail: admin@bioindustry.org. (Source: *News Release*, 16 July 1997)

The IBIS project

An Internet Botanical Information Server (IBIS) is being developed at Kew as a means of recording, assimilating and disseminating information on plant systematics. IBIS will be an interactive tree-viewing system on the Internet that concurrently displays a "tree" at any taxonomic level together with information appropriate to the region selected. The user will navigate within the tree simply by "clicking" on a terminal branch to display a more detailed tree e.g. from a family tree to a genus tree. At the deepest level where tree terminals represent species, a good quality picture and various additional information will be displayed. Initially the tree will be based on the *rbcL* data of Dr. Mark Chase and co-workers, but it will eventually incorporate other sources of taxonomic evidence to produce a composite picture of angiosperm systematics. Contact: Dr. Tony Cox, Royal Botanical Gardens, Kew, UK, Tel.: 0181-332 5360, E-mail: tonycox@rbgkew.org.uk. (Source: *Kew Scientist*, April 1997)

Health and safety environment professionals

The UK Institute of Chemical Engineers (IChemE) and the Royal Society of Chemistry have published a register of well-qualified and experienced professionals in the areas of health, safety and the environment. "Health and safety environment professionals" lists members of the associations who have shown that they have in-depth knowledge and experience of their specialist work.

Copies of the register are available from Sue Barnett, IChemE, 165-189 Railway Terrace, Rugby, UK CV21 3HQ; Tel.: +44 1788 578214; Fax: +44 1788 560833. (Source: *Manufacturing Chemist*, July 1997)

Biotech in Scotland

The growing significance of Scotland as a leading-edge bioscience developer and a key player in the European biobusiness market is becoming evident.

Scotland is also home to 8 per cent of Europe's biotech companies, and biotechnology is growing faster than any other sector in the Scottish economy. Since 1993, the number of dedicated companies has increased from 23 to 43, while the number of biotech support companies has grown from 39 to 48. Scotland's main strength currently lies in pharmaceutical and biotechnology support. Key companies within this sector include subsidiaries of some of the world's leading contract research organizations.

However, there is also growth in pharmaceutical, diagnostics, environmental and agricultural biotechnology areas.

One of the key factors in the success of Scottish biotechnology is undoubtedly the country's traditionally strong research base in the biological sciences. Its 13 universities, which all have links to industry, produce 18 per cent of all biotechnology-related Ph.D's in the UK, providing a high-calibre recruitment pool for both new and established companies. In a recent survey by the Institute of Scientific Information (Philadelphia), the University of Dundee ranked first in the UK in both biology/biochemistry and molecular biology, while Edinburgh came up top in microbiology. Meanwhile, the veterinary schools at Edinburgh and Glasgow have a world-class reputation and feed into all sectors of the biotechnology industry.

There has always been support from both private venture capital and government for the Scottish biotech industry. Scottish Enterprise, a non-departmental government organization charged with economic development and training, set up a biotech group two years ago. The group has already supported several start-ups in areas as diverse as cancer and bioremediation. It also aims to improve the industry's infrastructure and internationalize it through the promotion of exports and direct foreign investment. A recent project is the co-funding of the Medical Research Council (MRC) Collaborative Research Centre (Edinburgh), which will commercialize MRC-supported research in human genetics, fertility, neurobiology and virology.

The Biotechnology Group is also building on Scotland's traditional strengths in education and training by funding business-oriented projects for final-year students at the Universities of Glasgow, Strathclyde and Paisley.

For more information on biotechnology in Scotland, contact Ian Leslie, Scottish Enterprise, 120 Bothwell St., Glasgow, Scotland G2 7JP; Tel.: 44-141-248-2700; Fax: 44-141-228-2412. (Extracted from *Genetic Engineering News*, 15 April 1997)

USA

EPA issues new requirements for biotech products

The US Environmental Protection Agency is issuing new regulations that establish a streamlined process for the screening of certain microbial biotechnology products to ensure that they are safely developed for commercial use in a broad range of industrial and environmental applications. The new regulations are being issued under the Toxic Substances Control Act (TSCA).

The action is designed to protect human health and the environment, while providing flexibility for the development of the emerging biotechnology for pollution prevention and environmental cleanup. The regulations establish a distinct programme for microbial biotechnology products; continues to focus the regulatory attention on microorganisms that are likely to display new traits or to exhibit less predictable behaviour in the environment; and provides full or partial exemptions from the notification and screening requirements for certain categories of new microorganisms for which EPA has acquired substantial assessment experience. (Source: *The AgBiotech Bulletin*, May 1997)

Phytoremediation activities

The US Environmental Protection Agency (EPA; Washington, DC) and the US Department of Defense (DoD; Arlington, VA) have joined forces to develop plant-based approaches for cleaning up soils and water at hazardous waste sites, and the EPA is now seeking industry partners to help develop and support this technology.

In May 1997, DoD and EPA officials gathered at the US naval air base at Fort Worth (TX) to show off plantings of cottonwood and other trees on a site containing ground water contaminated with trichloroethylene (TCE). The trees, ranging from saplings to maturer specimens with 4-inch diameter trunks, efficiently take up ground water and can decontaminate the TCE-containing plume.

But researchers on the project have yet to determine just how the cottonwood trees act on the TCE dissolved in the shallow aquifer beneath them. They expect some combination of passive uptake, entrapment, and transpiration, along with active metabolic degradation by tree enzymes and possibly also by microorganisms associated with the tree root systems. Besides tracking the fate of TCE, investigators will also assess the cost effectiveness of this approach for decontaminating ground water.

EPA is sponsoring similar phytoremediation-based projects in at least four US locations. Together with other federal agencies, such as the US Geological Survey (Reston, VA) and with industry, EPA is also supporting phytoremediation efforts through its Remediation Technology Development Forum. The forum operates by establishing "self-managed action teams", in which representatives from universities and industry pursue joint field work and are funded jointly by EPA and industry. (Extracted from *Nature Biotechnology*, Vol. 15, July 1997)

Amended biotech rules

In April 1997, following 11 years of delays, the US Environmental Protection Agency (EPA, Washington, DC) published final rules for reviewing "new" microorganisms developed for commercial purposes. When the US Department of Agriculture (USDA; Washington, DC) Animal and Plant Health Inspection Service (APHIS) issued more industry-friendly, simplified rules for introducing genetically engineered plants into open environments, environmental groups were perturbed.

EPA rules apply to the commercial use of "new" microorganisms formed by combining genetic material from organisms in different genera. Commercial uses of these microbes, ranging from the production of industrial enzymes and specialty chemicals to use as biofertilizers or in bioremediation, were previously subject to EPA oversight under the federal TSCA regulations. These earlier rules were invoked on the use of recombinant DNA. The "intergeneric" definitions reflect the agency's interest in environmental risk of microbes rather than the process through which they are formed.

The rules further deregulate intergeneric microorganisms used in contained fermentation applications. Also

exempt are projects in which investigators comply with the US National Institute of Health (Rockwille, MD) "Guidelines for Research Involving Recombinant DNA Molecules", and outdoor testing on 10 acres or less for projects involving two particular nitrogen-fixing microorganisms, *Bradyrhizobium japonicum and Rhizobium meliloti.*

The amended regulations simplify procedures for virtually all genetically engineered plants, expedite reviews, and adjust reporting requirements for field tests to make them more consistent. For instance, although annual renewal notices still need to be filed with APHIS, investigators need not furnish the agency with results of field trials on long-lived plant species such as trees until those trials are completed. The new rules also make it easier to classify plant varieties as "nonregulated" when new products raise no risk. (Extracted from *Nature Biotechnology*, Vol. 15, June 1997)

NIH steps up malaria research

The US Government is planning to intensify its attack on malaria, part of a broad initiative backed by the US National Institute of Health (NIH) along with European and African scientists. The National Institute of Allergy and Infectious Diseases, NIAID—the world's largest funder of antimalaria research—is taking several immediate steps. It is creating a shared repository of malaria research materials, boosting its malaria budget and paying to sequence the DNA of two new malaria parasite strains. In 1996, an international consortium began sequencing the deadliest strain, *Plasmodium falciparum*, and now NIAID is adding *P. vivax* and *P. berghei* to the list. NIAID's repository, meanwhile, will offer researchers high-quality, scarce reagents, which Fauci hopes will attract newcomers to the field. (Extracted from *Science*, Vol. 276, 13 June 1997)

D. RESEARCH

Research on human genes

Key protein found for brain's dopamine-producing neurons

A team led by Thomas Perlmann of the Ludwig Institute for Cancer Research and Lars Olson of the Karolinska Institute, both at Stockholm, reports that a molecule called Nurr1 plays a critical role during embryonic development in the formation of the group of dopamine-producing brain cells that are lost in Parkinson's disease. Nurr1 also appears to help keep those cells active throughout life.

Neuroscientists are intrigued by the discovery because it may help explain why that particular set of neurons degenerates in Parkinson's patients. The problem might, for example, result from a defect in Nurr1 activity. The finding also raises the tantalizing possibility that boosting or restoring Nurr1 activity in failing nerve cells may delay or prevent the onset of Parkinsonian symptoms. (Extracted from *Science*, Vol. 276, 11 April 1997)

Human artificial chromosomes

Researchers have succeeded in creating the first human artificial chromosomes (HACs) using de novo arrays of α-satellite DNA, telomeric DNA, and other genomic DNA fragments. Huntington Willard and colleagues at Case Western Reserve University and Athersys, Inc. (Cleveland, OH) report their findings in the April issue of *Nature Genetics*. Using a bottom-up combinatorial approach, they first constructed 90 kb concatemerized arrays of α-satellite sequence—important components of human centromeres—from chromosomes 17 or Y, incorporating a G418 selectable marker. These sequences were then transfected into the human fibrosarcoma cell line HT1080 in conjunction with genomic DNA sequences and telomeric DNA consisting of arrays of $(TTAGGG)_n$. Nine of 26 resulting G418-selected clones contained micro-chromosomes when analysed by fluorescence *in situ* hybridization; using appropriate α-satellite probes. One clone derived solely from α-satellite DNA and telomeric DNA, but lacking genomic sequences, also contained a microchromosome. Using chromosome-specific α-satellite and specific chromosome paints, Willard and colleagues demonstrated that some of the microchromosomes were not derived solely from transfected sequences; however, in (at least) one case, a complete de novo linear microchromosome was detected. Further analysis showed that the microchromosomes contained active centromeres (on the basis of centromere protein binding) and that they were maintained stably through multiple cell divisions. HACs have obvious potential in gene therapy, but "several key steps remain to be addressed before practical application", Willard cautions.

Meanwhile, there is a report from researchers at the Murdoch Institute in Melbourne, Australia, who say they have identified a new, simpler DNA element that can fulfil the function of a centromere, a key chromosome component. Having a stripped-down centromere could bring the day closer when genes are delivered to an organism via the stable vector of artificial chromosomes.

In addition to ordinary genes made up of DNA, an artificial chromosome requires at least two pieces of specialized DNA: telomeres, which cap the ends of DNA strands, and a centromere, which anchors the chromosome to protein fibres that pull chromosomes apart during cell division. But while scientists know the DNA sequence of telomeres, they do not know what makes for a working centromere, although it seems to include highly repetitive DNA stretches.

Molecular geneticist Andy Choo and his group at the Murdoch Institute, reporting in *Nature Genetics*, have identified a "neocentromere" that was found five years ago in cells taken from a retarded child. The child's chromosome 10 had fractured in two; one piece carried the original centromere, and the other carried what Choo says appears to be a "latent centromere". Its DNA—unlike that of ordinary centromeres—has no alpha satellite repeats.

That is exciting news, because one of the big drawbacks of working with repetitive DNA is that is notoriously difficult to clone. Says Choo, "We hope to use the special properties of the neocentromere to develop a more user-friendly way of making HACs". (Source: *Nature Biotechnology*, Vol. 15, May 1997 and *Science*, Vol. 276, 27 June 1997)

Small molecule regenerates nerve tissue

Researchers at Guilford Pharmaceuticals (Baltimore, MD) report a novel small molecule, GPI-1046, that stimulates nerve regeneration in vitro and in vivo with picomolar potency. The drug mediates its action by binding to cellular immunophilins—a family of proteins involved both in regulating T-cell responses and in stimulating nerve growth. On the basis of work with Solomon Snyder at Johns Hopkins University School of Medicine, Guilford researchers have developed a series of novel immunophilin ligands, including GPI-1046, that possess potent neurotrophic activity, but lack immunosuppressive activity. They found that GPI-1046 induces neurite outgrowth in neuronal cultures and protects greater than 80 per cent of nigral-striatal dopamine neurons in an MPTP mouse model of Parkinson's disease, producing regrowth of functional neurons up to one month after nerve lesioning. Guilford has two other immunophilin ligands that are up to 50-fold more potent than GPI-1046. (Source: *Nature Biotechnology*, Vol. 15, April 1997)

Human haemoglobin from transgenic plants

Scientists at the French research institute INSERM (Le Kremlin-Bicêtre) and at Biocem (University of Cézeaux, Aubière, France) have come up with a useful alternative production system for human haemoglobin-based blood substitutes. In a scientific correspondence to *Nature* (**386**:29-30, 1997), Michael Marden and colleagues report the successful overexpression of the α- and β-subunits of human haemoglobin, HbA, in transgenic tobacco plants, obtaining a fully functional complex haemoglobin molecule, as measures by flash photolysis. Haemoglobin is currently derived from outdated human blood, but supplies are limited and blood-type matching to recipients is required. Marden

believes HbA expression in plants has several advantages over recombinant expression in yeast or bacteria. Ongoing research will test HbA expression in plants other than tobacco to see if higher yields are possible, with simpler purification and sterilization steps. (Source: *Nature Biotechnology*, Vol. 15, April 1997)

Chimeric protein cytotoxic against KS tumours

A chimeric protein composed of interleukin (IL)-13 and a truncated form of *Pseudomonas* exotoxin A has been shown to be highly toxic to five AIDS-associated Kaposi's sarcoma (AIDS-KS) derived cell lines. Raj Puri and colleagues report these findings in a recent issue of *Clinical Cancer Research* (3:151-156, 1997). The chimeric protein, IL13-PE38QQR, was toxic at very low concentrations to all AIDS-KS derived cell cultures tested, but showed no cytotoxicity to other cell lines of lymphoid or bone-marrow origin expressing low levels of IL-13 receptor. Moreover, IL13-PE38QQR inhibited tumour growth in a human adenocarcinoma xenograft model in mice. Puri hopes the chimeric protein "will be more effective in treating Kaposi's sarcoma (and maybe cancer in general) than interferon-α, which has seen only limited success as it requires a relatively intact immune system". (Source: *Nature Biotechnology*, Vol. 15, April 1997)

Double first

One of the first groups to synthesize the cancer therapy *Taxol* has managed to produce artificial versions of two more naturally occurring compounds that show promise in treating cancer.

Kyriacou Nicolaou and his team at the Scripps Research Institute in La Jolla, CA have made epothilones A and B. These compounds are produced naturally by the mycobacterium *Sorangium cellulosum* and have generated intense scientific interest since their discovery.

Like *Taxol*, epothilones stabilize the tiny tubes called microtubules which make up the microscopic skeleton found inside cells. This helps the cell maintain its defences against the onslaught of cancer cells. But epothilones even work in cells that are resistant to *Taxol*.

The Scripps team reports the first solid-phase synthesis of epothilone A, the total synthesis of epothilone B and the production of a small library of epothilones that could be screened for compounds of pharmaceutical interest. (Source: *Chemistry & Industry*, 19 May 1997)

Gene linked to autism

Autism is a complex and cruel puzzle. Although it is known to be largely genetic in origin, researchers have been unable to pin down its mechanisms, in part because so few people —five to ten in 10,000—are afflicted.

One part of the puzzle now may be falling into place. Researchers have found what appears to be the first link between autism and a specific gene: one that regulates serotonin, a key brain chemical. A team led by child and adolescent psychiatrist Ed Cook, of the University of Chicago Medical Center, has found, from a study of 86 autistic children and their parents, that autistic children are significantly more likely to have a shortened form of the serotonin transporter gene. This gene codes for a protein that reabsorbs serotonin into the neuron that has released it; the shortened version would be expected to make more serotonin available for receptors.

Oddly, it is a shortage of brain serotonin that has long been suspected of playing a role in autism. The most powerful evidence comes from the fact that antidepressant drugs such as fluoxetine (Prozac), which increase the availability of serotonin, often suppress autism symptoms such as repetitive and ritualistic behaviours associated with aggression or anxiety.

Cook, who cautions that his results are preliminary, says that, in any case, the short version of the gene, which occurs in 16 per cent of the general population, would need to act in concert with others, yet unidentified, to lead to autism. (Source: *Science*, Vol. 276, 9 May 1997)

New yeast discovery hints at improved cancer treatment

A research team from Acacia Biosciences, Inc. (Richmond, CA) and the University of California, Berkeley reports that they have discovered an enzyme that triggers the activity of the *ras* oncogene. When they removed the enzyme from cancer-like cells in the yeast *Saccharomyces cerevisiae*, the cells returned to a near-normal state. This could be an opening to an improved new form of cancer chemotherapy, according to the scientists.

Matthew Ashby, Ph.D., director of biology at Acacia and colleagues Jasper Rine and Victor Boyartchuk found the potential therapeutic enzyme after a seven-year hunt at UC Berkeley.

What the researchers actually found is a gene that encodes a protease enzyme that is involved in processing *ras*. *Ras* transmits signals for cells to divide, differentiate or remain quiescent. To do this *ras* must undergo three C-terminal processing steps.

Ras has long been the focus of "frantic" investigation due to its assumed role in a wide range of difficult-to-treat cancers, including colon, lung, pancreas and liver cancer. *Ras* is the second most prevalent oncogene in humans.

In oncogenic forms of *ras*, the mechanism that controls cell division is locked into an "on" position causing the non-stop cell proliferation characteristic of cancer. The newly discovered protease enzyme, Rce 1, helps *ras* to settle near the cell membrane and begin transmitting these signals.

Although a long way from human tests, the yeast experiments suggest that the right drug could reverse uncontrolled cell division and simultaneously have no effect on healthy cells. This is a far cry from standard chemotherapy.

The goal now, says Dr. Ashby, is to use the finding to learn how to block *ras'* harmful activities and at the same time preserve its necessary functions.

So far, yeast is the only eukaryote with a completely sequenced genome. It was recently discovered that its 12 million units of DNA carry the code for 6,000 genes, but what most of these genes do is still a mystery. Far less is known about the human genome, which is thought to contain perhaps 70,000 genes. (Extracted from *Genetic Engineering News*, 15 April 1997)

First lymphatic growth factor identified

Vascular endothelial growth factors (VEGFs) regulate vascular permeability and angio-genesis. Now, a group from Finland has shown that VEGF-C, a ligand for VEGF receptors 2 and 3, specifically induces proliferation of the lymphatic vascular system. Kari Alitalo and colleagues have cloned VEGF-C behind the human keratin promoter, K14, and expressed it in the skin of transgenic mice. Histologic examination of the connective tissue of the dermis using electron and light microscopy revealed large, dilated vessels, with no red cells and a thin endothelial layer. Antibodies to collagen type IV, type XVIII, and laminin—proteins characteristically present in blood vessels—gave little or no

staining, whereas antibodies against desmoplakins I and II, which are specifically expressed in the lymphatics, stained positively. Fluorescent staining of the skin with dextran-FITC revealed that the lymphatic vessels of VEGF-C transgenic mice were twice the diameter of control mice. According to Alitalo, VEGF-C induction of endothelial proliferation leads specifically to hyperplasia of lymphatic vessels, without evidence of sprouting of new blood vessels. He believes recombinant VEGF-C could be of use in treating lymphedema due to parasitic infections or surgery of the groin. "It may also enable treatment of lymphangiomas and enhanced delivery of chemotherapeutic agents to tumours, which often have very high internal pressures due to the absence of lymphatic vessels." Alitalo cautions, however, that more needs to be known about the role of these factors in lymphatic metastatic spread. VEGF-C tagged paramagnetic, radioactive, or electron-dense markers may also be useful as an imaging system for the lymphatic system. (Source: *Nature Biotechnology*, Vol. 15, July 1997)

Stress proteins and human ageing

Researchers at the University of New England have discovered that stress not only contributes to the human body's well-being, but also may hold some of the secrets to human ageing. According to the Head of the Department of Molecular and Cellular Biology, Associate Professor Ken Watson, all living cells, when placed under stress, produce specific proteins that perform essential "housekeeping functions". He added that these stress proteins not only acted as molecular "chaperones" in targeting proteins to specific parts of the cell, but also were vital for the removal and repair of damaged proteins.

During studies to explore potential links between stress proteins and ageing, Dr. Watson, in association with UNE biologist Dr. Graham Lloyd Jones and postgraduate student Sunil Reddy, compared stress protein levels in 40 individuals aged between 13 and 94. The researchers subjected lymphocytes that had been isolated from participants' blood samples to mild heat stress. It was noted that cells from younger individuals produced stress proteins much more readily when subject to stress than those from older individuals.

Dr. Watson said the studies offered a new approach to understanding the extremely complex process of human ageing. While acknowledging that there are numerous other factors involved in the ageing process, the research was one of the first attempts to examine linkages between stress proteins in animal models and ageing. The research group is now considering collaborating with pharmaceutical companies to explore ways of prompting the human body to synthesize stress proteins when it becomes less inclined to do so naturally. Medical breakthroughs over the past 50 years have contributed to the world's population steadily growing older. Around six per cent of the population is currently aged over 65, with estimates that this figure will climb to around 20 per cent by the year 2050. (Source: *Australasian Biotechnology*, Vol. 7, Number 2, April 1997)

Map marks the X chromosome

Molecular biologists edged closer to their goal of sequencing the human genome last month with the release of the best physical map yet of the X chromosome.

David Schlessinger of the Washington University in St. Louis, MO and his colleagues have placed molecular landmarks at about every 75,000 base pairs along the chromosome's DNA, three times as many as were on earlier versions of the X map, exceeding the goal, set in 1990 by the Human Genome Project, of landmarks at every 100,000 base pairs. The map will help sequencers find their way along the chromosome's 160 million base pairs.

The 2,100 landmarks are tiny bits of known DNA sequences called sequence-tagged sites. As scientists report in the March 1997 issue of *Genome Research*, the map has several surprises. It shows that the genes are not spread out evenly along the chromosome but are instead clustered into five distinct regions. There is also a section some 20 million base-pairs long where recombination—in which genes are swapped between two copies of the same chromosome during egg or sperm formation—does not seem to occur. Scientists had assumed that the nearer two genes are to each other, the less likely they are to swap places. Now, it appears that process is also affected by the particular sequence of base pairs.

More genetic road markers have to be planted before geneticists gear up for a nucleotide-by-nucleotide sequencing offensive. (Source: *Science*, Vol. 276, 4 April 1997)

Tumour suppressor gene

Identification of a tumour suppressor gene is shedding some light on how tumours might become more aggressive. Researchers from Columbia University (NY) and a collaboration between the M.D. Anderson Cancer Center (Houston, TX) and Myriad Genetics (Salt Lake City, UT) have both identified a gene involved in the progression of brain tumours to a more fatal form of cancer. The gene—named *PTEN* by the Columbia group and *MMAC1* by the M.D. Anderson group—is located on chromosome 10 and was found to be mutated or missing in the majority of glioblastoma multiforme cancers (a usually fatal brain cancer), as well as in some breast, prostate, kidney and skin cancers. In addition to being comparable to the protein tyrosine phosphatases (regulatory enzymes long suspected of playing a role in tumour suppression), *PTEN/MMAC1* sequence's similarity to the tensins—proteins that connect cell cytoskeleton to the external environment—suggests the protein may help prevent malignancy by anchoring cells within a tissue, and by preventing a cell from division when in contact with neighbouring cells.

Drug development is likely to focus on mimicking *PTEN/MMAC1* activity either by dephosphorylating (as yet unidentified) *PTEN/MMAC1* substrates or by blocking substrate phosphorylation by a putative *PTEN/MMAC1* antagonist protein tyrosine kinase. Both groups have filed patent applications for the potentially lucrative rights to *PTEN/MMAC*. (Source: *Nature Biotechnology*, Vol. 15, May 1997)

A cholera toxin effective in drug delivery

Alessio Fasano and Sergio Uzzau at the University of Maryland School of Medicine (Baltimore, MD) have used a toxin produced by the cholera pathogen for the successful oral delivery of insulin. Zonula occludens toxin (Zot)—a native noncytotoxic protein distinct from cholera toxin—has been shown to reversibly open tight junctions—the dynamic structures between gut epithelial cells that determine permeability. On binding to its receptor, Zot triggers a signalling cascade involving a modification of the cellular cytoskeleton, strategically localized to regulate the direct pathway from the intestine to the bloodstream. The resulting contraction of actin filaments alters gut permeability within 20 minutes, temporarily opening the junctions wide enough for macromolecules to pass through. When insulin was administered orally together with Zot to diabetic rats, regulation of blood glucose was comparable to that in rats

injected directly with insulin. Past attempts to alter gut permeability using surfactants and calcium chelators irreversibly forced tight junctions open, often resulting in fever, dehydration, and post-treatment histological changes—side-effects that so far are absent from Zot studies. Diarrhoea is avoided because Zot receptors are absent from the colon—permeability is altered only in the small intestine. Although this technology allows uptake of drugs not normally absorbed through the small intestine, it is not restricted to intestinal epithelium. Phase I trials in human diabetics are anticipated within the next year. (Source: *Nature Biotechnology*, Vol. 15, May 1997)

Engineered superantigen for efficient tumour killing

A fusion protein composed of the Fab portion of a tumour-reactive antibody and the bacterial superantigen staphylococcal enterotoxin A (SEA) engineered with a point mutation to reduce systemic toxicity has been shown to have potent anti-tumour effects in a mouse model. Working on the assumption that SEA's major histocompatibility class (MHC) II binding site is responsible for toxicity, Mikael Dohlsten and colleagues from the Lund Research Centre of Pharmacia & Upjohn (Sweden) have introduced an Asp227→Ala mutation into the carboxyl terminus and then cloned and expressed it as a fusion protein (Fab-SEA D227A) in *Escherichia coli*. Mice transgenic for human T-cell receptor V_β chains—which, unlike normal mice, are susceptible to superantigen-induced toxic shock—were seeded with tumours and injected intravenously with Fab-SEA D227A. Treatment with the toxin resulted in considerable tumour reduction. Fab-SEA D227A was less toxic than wild type, correlating with a 100-fold decrease in serum levels of interleukin-6 and tumour necrosis factor (TNF)-α and considerably lower numbers of cells producing TNF-α and interferon (IFN)-γ in mice spleens; in contrast, these same animals showed high levels of TNF-α and IFN-γ production at tumour-affected sites. (Source: *Nature Biotechnology*, Vol. 15, May 1997)

Sonodynamic therapy for selective destruction of tumour tissues

Prof. R. Nishigaki and a research team of the School of Pharmaceutical Sciences, Toho University, and Hitachi, Ltd., have developed a potential sonodynamic therapy to selectively destroy tumour tissues using ultrasound and drugs such as porphyrins.

Ultrasound waves are irradiated on the drug accumulated in the afflicted part to activate and generate active oxygen to destroy tumour tissues. Compared with photodynamic therapy using laser light, this new sonodynamic therapy enables selective healing using ultrasound, and is also applicable to destroying tumour tissues deep inside the body.

Porphyrins or chlorine derivatives display greater retention and remain longer in tumour tissues than in other types of tissues. When ultrasound or laser beam is irradiated on the accumulated drug, the drug and then its surrounding oxygen is activated and singlet oxygen is generated that destroys tumour tissues.

Porphyrins are carried by low-density lipoproteins (LDL) and captured by cells through the medium of LDL receptors. Tumour cells have a larger number of LDL receptors than other cells, so porphyrins are believed to be accumulated specifically inside the tumour. Photodynamic therapy using laser beam and porfimer sodium (Photofrin, Lederle Co.) in combination has already been used clinically, but the disadvantage is that the laser beam fails to penetrate deep into the body, and is therefore applied only to treating lung cancer near the bronchus and some digestive system cancers. In contrast, the sonodynamic therapy is advantageous in that the ultrasonic wave penetrates deep inside the body.

In experiments, tumour tissues were transplanted into mouse and rat kidney, and when the tumour grew to a diameter of about 3 mm, a gallium-porphyrin (ATX70, Toyo Hakka Co.) was injected, after which focused ultrasound was irradiated.

The ATX70 levels in the tumour tissues in the kidney of the mouse and rat rose to 2.5-3 times that of a normal kidney tissue within 24 hrs after the injection, indicating that ATX70 is concentrated inside the tumour. Only focused ultrasound and ATX70 in combination achieved a considerable tumour suppression effect, and observations of the afflicted kidneys fully corroborated the destruction of tumour tissues only at the irradiated parts.

Further details from Toho University, School of Pharmaceutical Sciences, 2-2-1, Miyama, Funabashi City, Chiba; Pref. 274; Japan. Tel.: +81-474-72-2578; Fax: +81-474-72-2595; E-mail: nishigak@phar.tohu-u.ac.jp. (Source: *JETRO*, April 1997)

Common asthma gene isolated, cloned by Sequana in two years

Sequana Therapeutics in conjunction with their strategic alliance with Boehringer Ingelheim, has isolated and cloned a common susceptibility gene responsible for asthma—a breakthrough that company executives said took only about two and one-hall years and validates its technology platform.

According to Sequana, the newly discovered gene is found in 10 to 20 per cent of those suffering from asthma, and up to 10 per cent in the general population, unlike the first, and less common, asthma gene, which was discovered in 1994 by William Cookson and colleagues at the Wellcome Trust Centre for Human Genetic Diseases in Oxford, UK. Cookson's gene encodes for part of the receptor for immunoglobulin E, a type of antibody that triggers a number of allergic responses, including asthma and atopic dermatitis.

To discover the location of the gene, the company employed advanced DNA analysis technologies, positional cloning, and population studies in conjunction with data provided by Toronto's Samuel Lunenfeld Institute of the Mt. Sinai Hospital, as well as from the residents of the small South Atlantic island, Tristan da Cunha, where 30 per cent have asthma. (Extracted from *McGraw Hill's Biotechnology Newswatch*, 2 June 1997)

Structure of mutant leptin resolved

The X-ray crystallographic structure—at 2.4 Å resolution—of a form of the human *obese* gene protein, leptin, has been determined. Faming Zhang and colleagues at Eli Lilly & Company (Indianapolis, IN) have used heavy-atom derivatives combined with solvent flattening to determine the crystal structure of leptin-E100, a form of leptin containing a Trp—>Glu substitution at position 100. Leptin-E100 has similar biological activity, dramatically improved solubility, and enhanced propensity to form crystals, compared with wild-type human leptin, which aggregates extensively and cannot be readily crystallized. The structure consists of four antiparallel α-helices connected by two long crossover links and one short loop arranged in a lefthand twisted helical bundle. Despite the absence of any sequence similarity, the leptin four-helix bundle is strikingly similar to the structure of long-chain cytokine family members (e.g. granulocyte colony-

stimulating factor and human growth hormone). The Lilly team is studying the leptin-E100 structure to garner crucial information about the protein's stability and solubility: "We can use the high-resolution structure to make mutants with better surface properties," says Zhang. In the long-term, this should enable crystallization of the leptin-receptor complex and ultimately the rational design of drug agonists with enhanced specificity and affinity. (Source: *Nature Biotechnology*, Vol. 15, June 1997)

Mechanism of IFN-resistant hepatitis elucidated

Recently reported findings (*Virology* **230**:217-227, 1997) indicate that the high proportion of hepatitis C patients who are nonresponsive to interferon (IFN)-α therapy may be due to viral inactivation of an IFN-induced cellular dsRNA-dependent protein kinase (PKR), which blocks protein synthesis and viral replication within infected cells. Michael Katze and colleagues report that the viral non-structural protein, NS5A, may be the prime culprit involved in this inactivation. Using bacterially expressed recombinant fusion proteins, they show that a region in PKR, stretching from amino acid residue 244 to residue 551, is both necessary and sufficient to specifically interact with NS5A in vitro. Using the yeast two-hybrid system, they went on to show that this interaction can be mapped to a region in NS5A, which they termed the IFN sensitivity determining region. This interaction results in an inhibition of the PKR kinase activity, establishing viral infection. Katze and his colleagues believe NS5A is a potential target for hepatitis C therapeutics: "If a compound can be identified that inhibits or prevents the association of NS5A with PKR without affecting PKR's function, the IFN response could be restored," he says. (Source: *Nature Biotechnology*, Vol. 15, June 1997)

Endocrine cancer

Scientists at the US National Institutes of Health (NIH; Bethesda, MD) have reported the cloning of a gene involved in endocrine cancers (*Science*, **276**:404-407, 18 April). The gene is linked to multiple endocrine neoplasia-type I (*MEN1*), a hereditary cancer syndrome estimated to occur in between 1 in 10,000 and 1 in 100,000 people worldwide, causing tumours of the parathyroids, enteropancreatic tissues, and anterior pituitary gland. Most MEN1 tumours are nonmestastisizing, but can cause severe effects because of their secretion of such endocrine substances as insulin and growth hormone. During the search for MEN1, which began nine years ago when a segment of chromosome 11 was linked to endocrine cancers, the NIH researchers sorted through over 30 candidate genes before finding the culprit; the MEN1 mutations—found in 14 of the 15 unrelated cancer patients studied—would probably result in dysfunction of the protein product, menin, suggesting that MEN1 is a tumour-suppressor gene.

Interestingly, sequence analysis shows that menin bears little resemblance to any known protein. "The sequence has been searched exhaustively and nothing has come up. It's still unclear what role [menin] plays in normal cell biology," says the study's lead author Settara Chandrasekharappa. Because the predicted menin sequence is so unusual, researchers believe that further studies on MEN1 may expose new oncogenesis mechanisms. In addition, MEN1 is expressed throughout the body, suggesting that it may be involved in other types of cancer. (Source: *Nature Biotechnology*, Vol. 15, June 1997)

Mouse multiple sclerosis model attenuated by IL-4

A T-cell line engineered ex vivo to express the immunosuppressive cytokine interleukin (IL)-4 has been shown to ameliorate disease symptoms in a mouse model of multiple sclerosis. Gerry Fathman and colleagues at the Stanford University School of Medicine, CA have shown that local delivery of IL-4 using T-cells that home in the central nervous system (CNS) can both delay the onset of experimental autoimmune encephalitis (EAE) and lessen the symptoms. The authors compared the therapeutic efficacy of an MBP-specific T-cell hybridoma transduced with a retrovirus expressing IL-4, the same T-cell line without the IL-4 transgene, and IL-4 transduced T-cells unable to recognize the CNS. Ten days after induction of EAE, only those animals receiving the CNS-homing T-cells transduced with IL-4 showed significant amelioration of symptoms. According to Michael Shaw, a collaborator on the paper, "local delivery of therapeutic agents bypasses many of the problems associated with systemic administration". He envisages that the approach could be applied to other inflammatory autoimmune diseases such as rheumatoid arthritis and diabetes. (Source: *Nature Biotechnology*, Vol. 15, July 1997)

New type of DNA-free inheritance in yeast is spread by a BSE mechanism

Researchers at the University of Chicago's Howard Hughes Medical Institute have found that a protein molecule able to transmit a genetic trait without DNA or RNA in yeast is able to string itself together into long fibres much like those found in the brain in BSE and human Creutzfeldt-Jakob diseases.

Scientists have suspected that in the neurodegenerative diseases of mammals such as sheep scrapie, mad cow disease (or bovine spongiform encephalopathy) and the kuru disease of the Papua New Guinea tribes, a normal protein in the brain can somehow become twisted and then corrupt other, healthy molecules of the same protein to do likewise, a process much like the seeding of a crystal. The improperly folded protein molecules seem to spin themselves together into fibres, which grow as other molecules are recruited.

The infectious protein particles are called prions, and their existence has been hotly debated for 30 years, since researchers showed that diseased brain tissue remained infectious even after treatment with radiation that would have destroyed any DNA or RNA.

In 1996, the Chicago team led by Susan Lindquist, Ph.D., professor of molecular genetics and cell biology, showed that prion-like proteins exist in yeast. In the mammalian brain, whose cells do not divide, prions pass between cells and function as infectious agents; in yeast, they produce heritable changes in metabolism from one generation to the next as the cells divide. The change is easy to see, because in one case the cells are red and in the other white.

Lindquist's group focused on a yeast protein called sup35, part of the normal yeast machinery for making all the other proteins in the cell. In certain strains which appear to have identical DNA to normal strains the sup35 protein does not work. They showed that the defective trait can be propagated by this faulty protein, without any DNA or RNA serving as the genetic blueprint. They now show that even in the test tube, the purified yeast protein can knit together into fibres that have the same staining properties and molecular

architecture as the amyloid plaques seen at autopsy in the brains of animals and humans that have died of transmissible spongiform encephalopathies. They also show that the formation of fibres from normal protein molecules is greatly speeded up by the presence of defective ones.

Lindquist said that the ability of certain proteins to confer heritable properties by changing their shape may underlie other unexplained genetic phenomena. A similar protein misfolding that is not infectious seems to cause Alzheimer's disease. (Source: *Australasian Biotechnology*, Vol. 7, Number 3, June 1997)

Research on animal genes

Electroporation for creating transgenic fish

Prof. F. Takashima and co-workers at Tokyo University of Fisheries have developed an efficient method for taking advantage of electroporation to create transgenic fish. The method dehydrates the sperm of fish, a foreign gene is implanted by electroporation, and the transgenic sperm are used to fertilize eggs of the species.

Genetic engineering is extensively used for breeding agricultural produce and horticultural plants, and is now beginning to be applied to fisheries. For instance, a growth hormone gene was transferred into fish to encourage faster growth. Conventional transgenic fish technologies include the microinjection of a foreign gene, and a genic bath process in which sperm and eggs are put in a liquid containing a target gene. Unfortunately, the conventional approaches afford too low a rate of hatched transgenic fish. microinjection uses a very fine glass pipette to transfer a foreign gene into a fertilized egg of a fish. The process has difficulty in locating the egg nucleus in the microscope view because the nucleus is small compared with the cytoplasm. Another problem is that the egg envelope (chorion) is a hard barrier against the fine tip of the micropipette. Manipulation of fish eggs individually is thus difficult work.

The new method is superior to the conventional electroporation methods for breeding transgenic fish fingerlings.

Further details from: Tokyo University of Fisheries; Department of Aquatic Biosciences; 4-5-7, Kounan, Minato-ku, Tokyo 108, Japan. Tel.: +81-3-5463-0534; Fax: +81-3-5463-0552. (Source: *JETRO*, February 1997)

Transgenic cows produce human protein

PPL Therapeutics (Blacksburg, VA and Edinburgh, UK), in collaboration with Wyeth-Ayerst (Philadelphia, PA), has announced the first ever expression data for the production of human protein in the milk of transgenic cows. For PPL's first transgenic cow, Rosie, born last year, each litre of milk contained 2.4 g of the human protein α-lactalbumin, compared with 2.5-2.7 g found in human milk. PPL manager, Julian Cooper, expects that α-lactalbumin "might have important physiological benefits" and be "of use in general nutrition products". Furthermore, the transgenic milk is more nutritionally balanced than bovine milk, and could, for example, be given to babies or the elderly with special nutrition or digestive needs, he says. PPL reports that 15 transgenic founder cattle have now been born. Their second transgenic cow product will be a phenylalanine-free form of α-lactalbumin for use as a nutritional supplement in people suffering from phenylketonuria—a debilitating disease in which phenylalanine cannot be broken down. Cattle transgenic for phenylalanine are expected to reach sexual maturity in the coming months. (Source: *Nature Biotechnology*, Vol. 15, March 1997)

Mouse gene of nerve cell apoptosis inducer enzyme CPP32

A joint team of researchers at Tokyo Metropolitan Institute of Medical Science and Howard Hughes Medical Institute at Yale University has identified a probable gene of the enzyme inducing the apoptosis (i.e. programmed death) of mice brain and nerve cells. Called CPP-32, the enzyme is homologous in the gene sequence to interleukin-1 converting enzyme (ICE) protease, which in turn is homologous with nematode (*Caenorhabditis elegans*) cell death protease CED-3. The research team demonstrated CPP32-deficient mice have disorders in the nerve system.

Apoptosis is critical to the normal development of organs and tissues, because morphogenesis and functions hinge on the apoptosis of cells programmed in genes. For example, in the maturing immune system of vertebrate animals, the thymic tissue undergoes an apoptotic phase in which autoimmune cells kill themselves to achieve immunological self-tolerance. Inducers of thymic apoptosis are well studied, but biologists have been unsuccessful in determining what gene triggers apoptosis of brains and nerve cells, and the translation protein from the gene. ICE-knockout mice were studied, but showed no noticeable disorder in the nerve system.

The joint research team bred CPP32 knockout mice. As with the ICE, the CPP32 enzyme is a protease with cysteine at the active centre. Production of CPP32 knockout mice needs no more than the conventional vector method in which a genomic fragment encoding the motif is replaced by the neomycin resistance gene.

Homozygous (CPP33-/3) mice presented a high lethality in the embryonic period, and no baby mouse had a life longer than three weeks. Anatomy revealed that the short-lived mutant mice had nothing anomalous in any tissues (e.g. liver and thymus) except the nerve system, where many ectopic cells were present. These additional cells obscured the flow of cerebral fluid resulting in very swollen brains. Their retina had a neuroepithelium protruding so much that it compressed the lens. Some investigations strongly suggested the aberrant cells should have died because of apoptosis. The implication is that the mutant mice had no gene causing nerve cell apoptosis, which should be CPP32.

Some physicians argue that brain atrophying dementia such as Alzheimer's disease is caused by the unprogrammed apoptosis of crucial nerve cells. If cell suicide is really prompted by the CPP32 enzyme, the disease may be prevented by an inhibitor of the enzyme.

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Mouse withdrawal genes

Trying to pinpoint some of the many genes involved in human alcoholism has so far been an unsuccessful endeavour, but scientists are finding some clues in mice that they say should help them figure out where to look in humans.

A team at Oregon Health Sciences University in Portland, OR has identified several chromosome regions in mice associated with alcohol-induced withdrawal symptoms. One of these regions sports genes for GABA receptors, which soak up central nervous system depressants such as Valium. Because alcohol and other central nervous system depressants are believed to occupy many of the same niches

in the brain, it suggests that GABA-receptor genes could be implicated in risk for alcohol dependence. The researchers found "very strong evidence" that three regions—on chromosomes 1, 4, and 11—are associated with withdrawal susceptibility.

Locating alcohol-related gene regions in mice "is a very exciting development", says geneticist David Goldman of the US National Institute on Alcohol Abuse and Alcoholism, because most mouse genes have their counterparts in the human genome. The fact that two of the mouse loci are also associated with withdrawal from pentobarbital, another central nervous system depressant, makes for "a very interesting convergence" between mouse and man. (Source: *Science*, Vol. 276, 23 May 1997)

Circadian clock gene identified and cloned in mammals

Scientists affiliated with the US National Science Foundation's (NSF) Center for Biological Timing have identified and cloned a gene for the biological clock in a mouse, the first such gene to be identified at the molecular level in a mammal. The identification of the "Clock" gene was proven by restoring a functioning biological clock in a line of mutant mice which had lost normal circadian rhythms. The researchers accomplished this by inserting DNA for the gene into developing embryos, which not only grew to have normal biological clocks, but incorporated them into their own genetic material, passing them on to their descendants. Fruit flies and fungi were until now the only organisms in which clock genes had been cloned and identified at the molecular level. (Source: *The AgBiotech Bulletin*, June 1997)

Dolly—the science behind the sensation

In the 27 February 1997 issue of *Nature*, Ian Wilmut's group at the Roslin Institute in Edinburgh (http://www.ri.bbsrc.ac.uk) report the first successful birth of a mammal after transfer of a nucleus from an adult tissue to an enucleated egg. This remarkable achievement follows their report a year ago (*Nature*, 7 March 1996) of the birth of lambs after transfer of nuclei from cultured embryo-derived cells. In the latest study, the researchers established three new cell lines derived from a Poll Dorset 9-day old embryo, a Black Welsh 26-day foetus and the mammary gland of a 6-year old Finn Dorset ewe in the last trimester of pregnancy. Nuclei were recovered from quiescent cells at passages 3 to 8 and introduced into enucleated eggs. Induction of quiescence was shown in the 1996 report to be important for "reprogramming" the nucleus to allow successful development.

Lambs were born to surrogate mothers from embryos reconstructed with nuclei derived from all of the cell types. Of the embryos reconstructed with a nucleus from mammary tissue, less than 12 per cent were able to develop to a transferable stage, and only about 3 per cent of these transferred embryos resulted in a live birth. A high rate of foetal loss was observed, but this is not unexpected for the development of any new technology.

Of the eight lambs born in the study, one died minutes after birth, but all displayed the morphological characteristics and, more importantly, the polymorphic genetic loci of the breed used as the nucleus donor. However, it is important to point out that the one "cloned" sheep from the mammary-derived nucleus was likely not to be a true clone of the donor ewe. Because the genetic makeup of a cell consists of DNA not only from the nucleus but also from the cytoplasmic mitochondria, a true clone would need to have mitochondria from the donor ewe as well as the nucleus.

Although the technology for cloning animals by embryo splitting has been available for a few years, the method does not allow performance testing of the animal prior to cloning. The real potential benefit of the technological breakthrough of Wilmut's group is the ability to clone animals with proven performance. For agriculture, this could mean the replication of a limited number of superior animals from an elite herd. Caution must be exercised with this technology to avoid excessively narrowing the genetic base of domesticated species, which would increase potential susceptibility to disease.

Reproduced from *ISB News Report*, March 1997.

Further information: Eric A. Wong, Department of Animal and Poultry Sciences, Virginia Tech. (ewong@vt.edu). (Source: *Australasian Biotechnology*, Vol. 7, Number 2, April 1997)

DNA vaccine protects chimps against HIV

Using an innovative DNA-based vaccine, a team led by University of Pennsylvania scientists has protected chimpanzees against massive doses of HIV. The vaccine uses HIV genes rather than proteins produced by the virus, as is the case with most virus vaccines. Two immunized chimps and a control chimp were exposed to 250 times the amount of virus sufficient for infection, using an HIV strain different from the one used to prepare the vaccine. The control chimp contracted the disease, but the scientists did not detect the virus in the two immunized chimps over 48 weeks. The researchers say the vaccine's effectiveness is unprecedented in a primate species. (Source: *Business Week*, 12 May 1997)

Research on plant genes

Expansins ripe for research

Expansins—proteins known to induce extension in plant cell walls—have now been implicated in the ripening of tomatoes, melons, and strawberries. According to Jocelyn Rose at the University of California at Davis, contrary to earlier belief, pectin metabolism is not the principal cause of fruit softening. Instead, she believes expansins play an integral role. Rose and her colleagues reached this conclusion after cloning an expansion (*LeExp1*) from tomato. Using northern blot analyses, they found that expression of *LeExp1* is abundant in maturing fruit, abolished in mature green fruit exposed to an inhibitor of ethylene action (2,4-norbornadiene), and markedly decreased in overripe fruit. By studying transgenic tomatoes expressing antisense RNA to an enzyme involved in ethylene biosynthesis, the authors also demonstrated that *LeExp1* expression is induced six hours after exposure to exogenous ethylene. Further analysis of the ripening pathway involving *LeExp1* expression was carried out in three ripening mutants. (Source: *Nature Biotechnology*, Vol. 15, July 1997)

Thermoplastic polymer from cotton fibres

Scientists at Agracetus, a unit of Monsanto in Middletown, WI (USA), have engineered cotton fibres that express a natural thermoplastic polymer by introducing into cotton seed bacterial genes that code for enzymes involved in the synthesis of poly-hydroxy-burtyate (PHB). The hybrid fibres have improved thermal properties, including slower rates of heat uptake and dissipation and higher heat capacity.

Bacteria synthesize PHB from acetyl co-enzyme A in a multistep process that requires three enzymes: B-keto-

thiolase, acetoacetyl coenzyme A reductase and poly-hydroxy-alkanoate syntheses. Cotton plants contain the starting material and thiolase, but lack the other two enzymes.

To endow the plants with the missing pair of enzymes and to track their expression, molecular biologists Maliyakal E. John and Greg Keller cloned the genes for the enzymes along with the gene for a marker protein. To localize PHB synthesis, they included a cotton promoter that turns on the reductase gene only in the fibres. They then coated the clones onto gold microparticles and "shot" them into germinating cotton seeds, using a technique called particle bombardment.

The scientists used a device called a gene gun that fires the microparticles at high velocity towards the target tissue. When a particle lodges in a cell, the cell takes up the DNA by some unknown mechanism, leaving the gold particle alone. In practice, 5,000 to 10,000 germinating seeds are bombarded to produce 10 to 20 transgenic plants.

Plantlets that express the marker protein are grown to maturity. Transformed plants pass along recombinant genes to their progeny.

The cotton experiment netted eight transgenic plants carrying all the recombinant genes. Because PHB is synthesized in the hallow of the fibres, it does not interfere with the architecture of their cellulosic cell walls which retain their structural integrity as the growing fibres elongate. Confining synthesis of PHB to the fibres is said to avoid the stunting effects on the growth and seed production observed in a weedlike transgenic plant crossbred to synthesize PHB.

So far, the team has produced only minute amounts of engineered fibres, with only small improvements in thermal properties. However, the recombinant feat represents an important step towards producing new-generation fibres for the textile industry, by showing that it is feasible to imbue cotton fibres with new traits. The work also validates the utility of particle bombardment in genetic engineering. (Source: *Tech Monitor*, May-June 1997)

Effectiveness of gene isolation confirmed

The system to obtain beneficial genes using transposons, the so-called "jumping genes", which has been developed by the Dutch research centre for Plant Breeding and Reproduction Research (CPRO-DLO) has been shown to be effective and widely applicable for both fundamental and practical research. Using this method, CPRO-DLO has already obtained many plant genes, including three which are responsible for male fertility. Post-graduate research has confirmed the effectiveness of the system.

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Large DNA molecules transferred to plants

A report in the *Proceedings of the National Academy of Sciences USA* says that scientists at Cornell University (Ithaca, NY) have developed a technique that enables scientists to produce transgenic plants with inserts of large DNA. Using a newly constructed plasmid vector, a 150 kilobase human DNA fragment was transferred into plant cells—some 10 times the normal DNA size transferred using conventional approaches.

The key is the methodical development of a unique vector called BIBAC (Binary Bacterial Artificial Chromosome). The BIBAC vector can multiply in both *E. coli* and *Agrobacterium*, and also has additional copies of the virG and virE genes whose products help in the efficient transfer of DNA from *Agrobacterium* to plant cells. Now that the size barrier for plant DNA transfer is broken, scientists can seek to alter quality and yield traits that are controlled by multiple genes. (Source: *The AgBiotech Bulletin*, May 1997)

All's fair in larvae war

The maize plant has developed an intriguing method of fighting off caterpillars. It emits a cocktail of gases which attract a parasitic wasp that spells the end for the leaf-hungry pests. Scientists have now isolated, identified and synthesized the chemical trigger for this volatile alarm signal.

The plant only emits the alarm when the oral secretions of the beet armyworm caterpillar contact its damaged tissue; physical injury to the plant has no effect, the researchers explain. Until now, a signal molecule in the secretions has remained elusive.

The team from the US Department of Agriculture in Gainesville, the Virginia Military Institute in Lexington (VA) and the Chalmers University of Technology in Goteburg, Sweden have shown that the signal is a fatty acid-based molecule which they have called volicitin—*N*-(17-hydroxylinolenoyl)-L-glutamine. It induces maize seedlings to release the same chemical cocktail of terpenoids and indole as when it is damaged by feeding caterpillars.

But why should a caterpillar make a chemical that betrays its presence and lead ultimately to an unpleasant death? (The wasps lay their eggs in the caterpillar and the emerging young devour their host). The team speculates that volicitin has a hormonal or digestive role in the caterpillar, but says further research is needed to answer the question.

Volicitin joins an "ever-growing family" of fatty acid-based biological regulators. It has structural features in common with a variety of molecules such as the primary amines that induce sleep in mammals, the acids that are involved in defence gene signalling in plants and the lactones that regulate social interactions in bacteria. (Source: *Chemistry & Industry*, 19 May 1997)

Transgenic potatoes

Australia's first harvest of revolutionary non-browning potatoes took place near Adelaide recently. CSIRO researchers have turned off the gene which causes potatoes to turn brown when they are cut or bruised. By inserting the gene back-to-front, or by slightly altering the structure of the gene, the potatoes no longer turn brown. CSIRO has patented the technology worldwide. The same technology can also be applied to other fruit and vegetables. Researchers say the technology can potentially deliver significant savings for potato processors. (Source: *Australasian Biotechnology*, Vol. 7, Number 3, June 1997)

Researchers find pathways for nitrogen fixation

The pathway in legumes that control the formation of nitrogen-packed nodules on roots has been identified by researchers at Texas A&M University (Corpus Christi, TX). The finding could help scientists better understand how to manipulate the growth of such unique plant organs which are vital to the Earth's ecological health.

Dr. Doug Cook, Texas Agricultural Experiment Station plant pathologist, and graduate student R. Varma Penmetsa have identified a genetic pathway that can potentially be manipulated to increase nodulation in crop legumes, such as alfalfa. "This gene (SKL1) tells us ethylene is used to regulate nodulation on the plant root," Cook said. "The

inability to recognize ethylene leads to a large increase in the number of nodules."

Cook noted that the field of biotechnology has long held a goal of figuring out how to regulate increased nitrogen fixation. However altering the process for practical purposes in field crops will not necessarily be simple. "Ethylene affects other systems in plants such as insect and disease resistance, so genetic engineering of ethylene recognition may have undesired consequences. Still, it identifies a target which may help us to engineer increased nodulation, potentially improving the benefit of legumes."

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Plastic from poplars

Researcher Eun-woon Roh of the National Forestry Breed Research Institute of Korea's Ministry of Agriculture and Forestry has genetically engineered aspen trees to produce plastic. The trees, which were transformed to express genes from a soil bacterium, have been grown in the laboratory and will now be tested by industrial partners.

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Engineering maize into chemicals

Researchers from Argonne National Laboratory, Argonne, IL, and three other US Dept. of Energy laboratories have developed a new process to convert maize into a cost-efficient source of commercial chemicals. Incorporated into polymers and solvents, the chemicals would be used in such things as clothing, fibres, paints, inks and food additives. The process first makes succinic acid by fermenting glucose sugar from maize, then separates and purifies the acid, and finally converts it chemically into 1, 2-butanediol, tetrahydrofuran, N-methyl pyrrolidone, and other chemicals used to make a wide assortment of products. (Source: *Industry Week*, 17 March 1997)

Tobacco gene encoding wound-induced protein kinase

Y. Ohashi and colleagues at the National Institute of Agrobiological Resources have isolated a gene governing the initial defensive response of tobacco cells to wounding. The gene isolation has partly elucidated the problem of how the plant organization copes with wounding, and may eventually lead to creating disease-resistant plants and developing anti-inflammatory drugs for humans.

When a plant is attacked by a pathogen, the infected cells kill themselves and the pathogen together to keep the disease from spreading further. The detritus of the dead cells results in "local lesions". Lesion formation in turn signals molecule production such as jasmonic acid and salicylic acid and salicylic acid for self-defence of the plant. In a normal plant, jasmonic acid activates a set of genes to enhance the plant resistance to wounding, and salicylic acid causes a similar effect against pathogens.

The research team focused on the initial signal transduction pathways in the tobacco plant response to attack, and successfully isolated the gene playing the key role. The gene confers production of a mitogen-activated protein (MAP) kinase homolog, which they named WIPK (wound-induced protein kinase). Northern hybridization analyses demonstrated that the gene transcripts are absent in leaves of an intact tobacco plant, but appear as early as one minute after damage to the plant, peaking within one hour, and then vanishing rapidly.

Experiments were conducted with a normal tobacco plant and transgenic plant cells containing transferred WIPK gene, and proved that when wounding the normal plant produces jasmonic acid, but not salicylic acid. In contrast, the wounding transgenic plant produces little jasmonic acid but salicylic acid instead. The transgenic plant seems to have the endogenous WIPK gene silenced by the inserted foreign gene.

Naturally, such a damaged transgenic tobacco plant proved to be more resistant to pathogens than before. The implication is that the WIPK gene regulates the switching between signal transduction pathways that were mediated by wound bioactive substances.

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Research on viral genes

Kaposi's sarcoma—associated herpes virus

For decades, researchers have been pursuing a trail of early clues suggesting that viruses might be culprits in human cancers. Only in a few malignancies have scientists been able to finger a viral suspect, however. Now, a group of researchers may have detected viral fingerprints on another cancer, a bone marrow tumour called multiple myeloma. But the group has found that in this case, the virus may contribute to tumour growth in a novel way, working behind the scenes like a cellular puppet master.

A research team led by oncologists James Berenson and Matthew Rettig of the Veterans Affairs West Los Angeles Medical Center in California reports linking multiple myeloma to Kaposi's sarcoma—associated herpes virus. KSHV is already under suspicion as the cause of Kaposi's sarcoma, a cancer that afflicts many AIDS patients. But unlike the malignant cells of Kaposi's and all the other cancers thought to be caused by viruses, multiple myeloma cells—derived from the bone marrow's antibody-producing plasma cells—do not seem to carry the virus. Instead, the Los Angeles team has found evidence that KSHV is lurking in adjacent dendritic cells, a subset of macrophages found in the bone marrow microenvironment.

In those cells, the virus appears to crank out its own version of a human protein called interleukin-6 (Il-6) that is known to stimulate myeloma cell growth. This, the researchers propose, is what propels the runaway growth of myeloma tumours.

The finding could steer researchers to new therapies for multiple myeloma, which strikes 13,000 people every year in the United States alone and usually kills its victims within three years. Drugs to block Il-6 might be one therapeutic avenue, and Berenson also suggests that it might be possible to devise therapies that specifically target the virus-infected dendritic cells themselves.

Attacking the virus with drugs or a vaccine might also stave off full-blown multiple myeloma in the estimated one million people who have been diagnosed with an apparent precursor condition called monoclonal gammopathy of undetermined significance (MGUS). Others who might benefit are AIDS patients, especially homosexual men, who have a high risk of becoming infected with KSHV and

getting Kaposi's sarcoma. (Extracted from *Science*, Vol. 276, 20 June 1997)

Modified cold viruses

A new system that used modified cold viruses to treat cancers of the head and neck has produced promising early clinical data. The virus is injected directly into the tumour, where it seeks out cells with a common cancer-causing mutation. It then reproduces inside them and bursts out, killing the cells and releasing new viruses, which start the cycle over again. The system, developed by Onyx Pharmaceuticals of Richmond, CA, was described at a recent meeting of the American Society of Clinical Oncology. (Source: *Chemistry & Industry*, 2 June 1997)

AIDS research

The major focus of basic AIDS research over the past 18 months can be summed up in one word: chemokines. The discovery that HIV hijacks the cell surface receptors for these immune system signalling molecules to force entry into its target cells has revolutionized the field and opened new avenues toward possible therapies. Now, research suggests that HIV may have yet another port of entry into some cells. The findings implicate a common virus as a possible accomplice of HIV, helping the AIDS virus infect some types of cells and wreak havoc on the immune system.

A team led by Marc Alizon at the Institut Cochin in Paris, France in collaboration with Michel Seman at the University of Paris, reports that HIV may use a protein called US28 to enter some types of cells. US28 is produced by cytomegalovirus (CMV)—a member of the herpes virus family that has long been a leading suspect as an AIDS cofactor. The protein is expressed in cells experimentally infected with CMV, and it had previously been shown to act as a receptor for the same chemokines that bind to CCR5, the chemokine receptor used by HIV strains that dominate during the early phases of infection.

Although the evidence supporting a cofactor role for CMV is contradictory and controversial, researchers say that if these new results hold up, they would imply a tighter symbiotic relationship between HIV and CMV than previously imagined.

To determine whether US28 might act as HIV's accomplice, the French group inserted the US28 gene into a human laboratory cell line that HIV does not normally infect. Alizon's group then exposed these cells, which express the US28 protein on their surfaces, to various HIV strains. They also tested whether these modified cells fused with a second cell line engineered to carry proteins from HIV's outer viral coat. In these and related experiments, Alizon's team found that US28-bearing cells were easily infected by HIV strains that normally use the human chemokine receptor CCR5, and somewhat less easily by strains that use another human receptor, CXCR4.

These findings are being greeted with surprise. Over the past year, several labs working on chemokine receptors had conducted experiments similar to those of the Alizon team to test whether US28 helps HIV enter cells. However, it is not yet clear whether the French group's results, which are restricted to laboratory cell lines, are relevant to HIV-infected people. (Extracted from *Science*, Vol. 276, 20 June 1997)

Research on bacterial genes

Salmonella bacteria used to hunt and attack cancer cells

Salmonella, a dangerous and sometimes deadly bacteria, can be trained to attack cancers while bypassing normal tissues, said Yale University (New Haven, CT) researchers.

The researchers cut out three genes, making the bacteria lose their taste for everything but malignant tumour cells, said parasite expert David Bermudes, a Yale University researcher currently working with Vion Pharmaceuticals, Inc., a New Haven, CT-based company inventing anticancer therapies based on *Salmonella* and other bacteria.

By deleting some genes and adding others, the scientists hope *Salmonella* may be turned into an effective vehicle to shuttle DNA into tumours in cancer-curing gene therapies.

So far, the Yale research team has added genes for herpes simplex virus thymidine kinase, which resulted in the phosphorylation of the prodrug ganciclovir, and suppressed tumour growth in mice.

They have also experimented with adding a cytosine deaminase gene under the control of a strong promoter, which converted nontoxic compound 5-fluorocytosine to the potent cancer killer 5-fluorouracil.

The advantage to *Salmonella* as a gene delivery system is its natural talent for finding and growing in certain cells. This ability to get inside cells, grow and then kill them is what makes unaltered *Salmonella*, what scientists call the "wild-type" bacteria, such dangerous pathogens.

Salmonella can also thrive with or without oxygen, which could be important in cancer treatment. The haphazard manner in which cancer cells grow often leads to oxygen-starved regions in the tumour, something that has thwarted many therapies.

The scientists hope to try their tamed *Salmonella* in humans in 1998. (Extracted from *McGraw Hill's Biotechnology Newswatch*, 21 April 1997)

Bacteria help to build honeycombs

Bacteria have inspired Bath University (UK) scientists to develop a novel approach to building honeycombed inorganic structures. Because the researchers can define the size, shape and arrangement of the pores, the structures have potential importance in catalysis, separation technology and biomaterials engineering.

The team led by Steve Mann constructed an organized array of regularly sized straight channels made from silica that were 0.5 μm in width. The channels formed around close-packed threads of a bacterium called *Bacillus subtilis* which were later removed. The framework contains a second level of porosity because the silica walls of the channel are also honeycombed.

The bacterial thread swells in water without losing its structural integrity, and contracts to its original dimensions when dried. The researchers used this property to infiltrate the spaces between the filaments—which ranged from 100-200 nm—with silica-based nanoparticles.

When the team dried threads that had been dipped in a silica solution, they found that an ordered silica framework formed around them. Heating to 600° C removed most of the bacteria and left white brittle fibres composed of amorphous, or non-crystalline, silica.

"The approach illustrates how biological assemblies could be used to process inorganic material," says Mann. He suggests that these structures could be used as templates for microscale assembly of ordered porous ceramic materials, or as membranes for filtering particles such as colloids or viruses.

These materials, whose honeycombed structure resembles bone, could also find use as porous coatings for medical implants. "Silica is bioactive and stimulates repair around implants," Mann says. (Source: *Chemistry & Industry*, 3 February 1997)

Biological source of solar energy studied

When converting light into usable energy, today's solar cells have nothing on the purple, photosynthetic bacterium *Rhodopseudomonas acidophila* that lurks in polluted ponds. Scientists at the University of Glasgow (UK) have figured out the molecular architecture of the bacterium's own solar "antennae" and how they work, raising the prospect of more efficient commercial technology to harness the sun's power even in parts of the world with relatively low light levels.

"*R. acidophila* converts 90-95 per cent of photons (light) into energy, so what we have is a blueprint for capturing light very effectively," said Neil Isaacs, whose team of crystallographers unraveled the structure of the bacterial complexes of protein and pigment that harvest light. Their structural studies have developed into thinking about commercial exploitation.

Obstacles include *R. acidophila* being tuned to absorb light in the green and near infra-red parts of the spectrum. While this is ideal for a pond-dweller lurking in the murk below a raft of green algae, a commercial solar cell must respond to a wider band of wavelengths. Developing bacteria that do this is one possible answer. Preliminary studies have suggested that it is possible to bind the light harvesting complexes to surfaces.

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Recombinant E.coli absorbs phosphate

In a joint project with Ebara Research, a team of scientists led by Professor Hisao Otake from Hiroshima University (Japan), has modified *Escherichia coli* by gene recombination so that the bacteria can adsorb and accumulate phosphate and polyphosphate effectively. The team used the genes Pst from *Escherichia coli* and PPK from *Klebsiella aerogenes*.

The research group now plans to modify *Pseudomonas putida* and *Klebsiella aerogenes* which are more suitable for waste water treatment than *E coli*.

The group intends to provide transgenic micro-organisms that are suitable for waste water treatment within the next three years. (Source: *McGraw Hill's Biotechnology Newswatch*, 17 February 1997)

Food biotechnology

A pip-destroying gene that could be used to boost the nutritional value of fruit has been discovered by Australian and Japanese scientists. They are planning to use the gene to channel energy away from seed production, producing new varieties of fruit that are both bigger and easier to eat.

The gene, called SDLS-2, switches off seed development at a very early stage. Team leader Anna Koltunow of the Commonwealth Science and Industry Research Organization's horticulture division at Adelaide, South Australia thinks that its natural function is to eliminate weakling seeds during development. The research team, which includes scientists from the National Institute of Agrobiological Research in Tsukuba, Japan, has boosted the gene to switch off seed development completely. They did this by strengthening a region of the gene called the promoter which determines the gene's activity.

Researchers have already used the modified gene to switch off seed production in tobacco plants. They are now testing it on a weed called *Arabidopsis*, a close relative of the citrus family. If the tests work then the team will engineer the gene into popular varieties of citrus fruit.

Before any genetically engineered seedless varieties reach the market they will have to gain regulatory approval. Ironically, the Australia/New Zealand Food Authority's recent proposal to severely restrict genetically modified food products could mean that any new fruits will never be tasted in their country of origin.

After citrus fruits, the team has its eye on grapes. Theoretically, they say, the gene could de-pip any fruit for which a gene delivery system were available. (Source: *Chemistry & Industry*, 17 March 1997)

Research instrumentation

Multiphoton imaging

Armed with a battery of lasers, photodetectors, and computers, plus a novel crew of powerful and adaptable fluorescent reagents, microscopists are literally bringing to light live cells, tissues, and even whole organisms. With a technique called multiphoton imaging, which gently excites fluorescence from cellular components without killing the cells, researchers are following fertilized zebrafish egg cells as they mature to larvae, seeing nerve cells exchange signals deep in the brains of live rats, and viewing organelles communicating in hard-to-image plant cells. "Every time we turn around, we find a new application," says multiphoton-imaging pioneer Watt Webb at Cornell University in Ithaca, NY.

Others are pushing the frontiers of inner space with a version of a technique that astronomers are using to probe outer space: interferometry. Interference microscopes use two interacting beams of light to tease apart tiny cellular structures with a resolution of less than 100 nanometres—sharp enough to see cytoskeletal proteins pushing forward migrant cells and clusters of genes lined up on separate chromosomes. And a few pioneers are now combining a variety of these cutting-edge technologies into a single instrument: a microscopist's dream machine that will allow researchers to pick and choose imaging modes, and even interact with their specimens, without moving their samples from under the instrument's lens.

The driving force behind this small revolution is molecular biology itself. Until recently, biologists generally had to infer what is happening from electron micrographs of thin, specially prepared specimens or by tagging molecules with fluorescent dyes and flooding specimens with light. But traditional fluorescence imaging, like electron microscopy, often limits observations to dead tissue. Many dyes and cellular proteins fluoresce only when they are zapped by short-wavelength, high-energy photons, which can be highly damaging to living cells. And because the entire specimen is illuminated, photons bouncing off other cellular components can greatly reduce the contrast of the image. Researchers have partially solved the contrast problems with the so-called confocal microscope, a device that illuminates only one section of the specimen and has a pinhole in front of the photodetectors to block out much of the stray light. But

multiphoton microscopy tackles both the contrast and the photodamage problems.

The key to this technique is the use of special pulsed lasers to fire precisely focused bursts of lower energy photons at the sample. If two or three photons strike the target molecule almost simultaneously, they produce the same effect as one photon with two or three times the energy. This double or triple punch lights up proteins that have been tagged with special dyes, and it can make some proteins fluoresce on their own. The lower energy of the individual photons cuts down collateral damage, allowing the cell to be kept alive for hours instead of minutes. And the tight focus of the laser beam—compared with bathing the entire specimen with light—greatly reduces effects of light scatter.

Neuroscientists also are using multiphoton imaging to look at previously unseen processes.

While interference and multimodal imaging devices are still in the development stages, multiphoton technology is now commercially available. But it comes at a high price. The Cornell Research Foundation has patented the technology and licensed it exclusively to BioRad Microscience Ltd., at Hemel Hempstead, UK, which is selling the complete instruments for anywhere from $300,000 to $450,000. About $100,000 of that stems from the cost of the laser, while the rest of the major costs are based on meeting European codes for the instrument. Even with that price tag and BioRad's decision not to sublicense, many researchers are optimistic that multiphoton imaging will become widespread. (Extracted from *Science*, Vol. 276, 27 June 1997)

Critters enjoy a glowing success

Scientists in Tennessee have invented a "living" silicon chip which they say could be used to detect pollution, diagnose diseases or even warn of terrorist attacks.

The prototype device, developed at the University of Tennessee and the Oak Ridge National Laboratory, is an ordinary silicon chip coated on one side with bacteria that have been genetically engineered to light up when they sense the chemical naphthalene, an ingredient of crude oil. The light is picked up by a tiny optical device on the chip and relayed to a central computer.

The bacteria, *Pseudomonas fluorescens HK44*, are trapped in a clear polymer that is porous to naphthalene. When the chemical seeps in, the bacteria turn on their naphthalene digester genes. They then inadvertently light up because the digester genes have been connected to a light-emitting gene from a luminous marine bacterium, similar to the gene that makes fireflies glow.

The prototype, which has earned the nickname "critters on a chip", is about 2 mm square and half a mm thick. Similar chips could be produced using existing techniques for less than $1 each, the researchers claim.

However, the team concedes that a few improvements are needed before the chips can be developed commercially. One of the biggest problems is that the bacteria usually die within days. Mike Simpson of the Oak Ridge National Laboratory thinks they could be kept alive using a "microflow" of nutrients.

The researchers say the next stage is to engineer bacteria that can sense commercially important chemicals. According to Simpson, the most likely targets are organic pollutants and heavy metals, but he says that detecting medically important molecules or nerve gases like sarin, used in the Tokyo subway terrorist attack, is a possibility.

In the longer term, the scientists want to attach wireless transmitters to the optical detectors so that the chips can send signals from remote places like groundwater sources or the interiors of chemical vats. Simpson also wants to increase the chip's sensitivity by improving the optical sensors and by increasing the intensity of the blue-green glow. (Source: *Chemistry & Industry*, 5 May 1997)

Infra-red spectroscopy basis of cervical cancer test, biotech firm

A decades-old technique widely used to quality check industrial chemicals has been updated as a cervical cancer screen that may turn out to be more accurate than the current standard, the Pap smear.

The technique, known as infra-red spectroscopy, analyses chemical composition based on light absorption properties. It can distinguish cancer from cells that are healthy or in a pre-cancerous state because every "molecule has its own fingerprint", said Max Diem, a professor of physical chemistry at Hunter College of the City University of New York. The technique may be able to find cancer at an earlier, more curable stage, he says. It may also be less prone to error than Pap tests, which rely on the eyes and minds of laboratory technicians, who must be able to pick abnormal cells from hundreds of thousands of normal ones. (Extracted from *McGraw Hill's Biotechnology Newswatch*, 5 May 1997)

Lasers to screen cells

Researchers at Sandia National Laboratory at Albuquerque, NM, have found a new way to examine cells with lasers. The technique, which incorporates the cells as de facto lenses, will potentially allow scientists to do lightning-fast screening of cells—as well as monitor what goes on inside them, says the system's developer, physicist Paul Gourley.

The technique is different from laser spectroscopy, in which cells reveal themselves by the ways they absorb or reflect light. In Gourley's system, cells are sandwiched between two reflective surfaces that form an "optical cavity". Here, the cells act as lenses that change the laser's output according to their shapes and refractivity.

Because the data files consist of one-dimensional light spectra and not images, they are small enough to be analysed rapidly. In initial experiments, the system has successfully distinguished normal from sickled red blood cells and cancerous from non-cancerous cells. Automated, it could potentially analyse tens of thousands of cells per second, says Gourley.

Researchers also can observe cellular activity in real time with the aid of a camera that records the effect as patterns in the laser beam, rather than as spectra. Gourley says the system could allow scientists to watch what is going on in the nuclei of cells involved in diseases such as cancer and lupus, where programmed cell death (apoptosis) fails to take place. (Source: *Science*, Vol. 276, 9 May 1997)

Biolog identifies over a thousand organisms

Don Whitley Scientific's Biolog System uses microplates to identify rapidly and accurately over 1,100 species and groups of bacteria and yeasts.

Microplates are supplied pre-prepared, each well containing one of 95 different carbon-based substrates. There are test panels for Gram negatives, Gram positives, lactic acid bacteria and yeasts. Simply inoculate with a standardized suspension of organisms, incubate and read the results.

Three models are available. The Microstation incorporates IBM compatible software to automatically read the plates and interpret the results; displaying biotype patterns, species information, and useful statistics.

More modestly priced, the Microlog 1 and Microlog 2 are manual versions. Results are read by eye and manually keyed into a PC for interpretation.

Contact: Don Whitley, Shipley, W. Yorks, UK; Tel.: +44 1274 595728; Fax: +44 1274 531197. (Source: *Manufacturing Chemist*, June 1997)

Carbon monoxide and the heme oxygenases

A new range of reagents from AFFINITI Research Products Ltd. (Exeter, UK) will help researchers to answer questions on how widespread is carbon monoxide as a physiological second messenger and neurotransmitter or what role do the heme oxygenases play in the pathophysiology of stress.

The catabolism of heme to biliverdin with the release of iron and carbon monoxide (CO) is mediated by the enzyme heme oxygenase (HO). Two distinct forms of heme oxygenase (HO-1—inducible; HO-2—constitutive) have been characterized from mammals and are now the subject of intense research activity following the identification of CO as a second messenger molecule and putative neurotransmitter.

Using the synthetic peptide approach to antiserum production, polyclonal antisera wholly specific to each HO isoform have been generated and characterized for use in Western blotting and immunohistochemical applications. In addition to antisera, AFFINITI's HO range also includes HO-enriched microsomal preparations of several rat tissues which serve as positive control lysates for Western blotting. Complete abolition of antiserum reactivity may be obtained when preadsorption with the synthetic peptides used to generate the antisera is carried out. Both peptides are offered for use as negative controls and as solid-phase ligands. Finally, a large range of HO substrates, inducers and inhibitors, including several porphyrin compounds is available.

Further details from Dr. Ian M. Varndell, AFFINITI Research Products Ltd., Mamhead Castel, Mamhead, Exeter, EX6 8HD, UK. Tel.: (+44/0) 1626 891010; Fax: (+44/0) 1626 891090; E-mail: affiniti@affiniti-res.com

New sensations in biosensor design

Two papers published in *Nature* report new types of biosensor. In the first, researchers at the University of Tübingen (Germany) led by Wolfgang Göpel describe a gas sensor that can discriminate different enantiomers of achiral compound. The device consists of a sensor surface coated with enantioselective polymers coupled to two types of transducer—one using a piezoelectric mechanism to detect analyte binding, the other using reflectometric interference spectroscopy. Using enantiomers of the amino acid derivative *N*-trifluoracetyl-alanin methyl ester or ethyl and methyl lactates, Göspel and colleagues demonstrated that sensors coated with *R*-polymer binds *R*-analyte more strongly than sensors coated with *S*-polymer and vice versa. They also showed that the enantiomeric composition of various mixtures of analyte could be determined quantitatively using unprocessed signals. Göpel believes the device could eventually supersede gas chromatography for analysing enantiomeric purity of drugs or anaesthetics. In another paper, an Australian group, headed by Bruce Cornell, have devised an ingenious sensor comprising a gold electrode onto which is tethered a lipid membrane incorporating gramicidin ion-channels linked to antibodies. Ion flux through the mobile gramicidin ion channels ceases when they are prevented from dimerizing as a result of binding of the antibody to the analyte. In this way, membrane conductance can be used to detect the presence of many different types of analyte, including proteins, viruses, antibodies, DNA, and drugs. (Source: *Nature Biotechnology*, Vol. 15, July 1997)

Device to detect airborne biological warfare agents

Gene-chip technology may soon allow rapid detection of airborne biological warfare agents. In May 1997, the US Defense Advanced Research Projects Agency (DARPA) announced the selection of a consortium of Canadian research groups in a project to develop an early warning system based on ID Biomedical Corporation's (British Columbia) cycling-probe technology (CPT)—a process whereby constructed DNA probes recognize and bind complementary DNA fragments from specific bacteria and viruses. Enzyme cleavage of the bound probe frees the agent DNA to bind more probe in subsequent cycles, which are repeated until there is enough cleaved probe for fluorescence or chemiluminescence detection. According to ID Biomedical vice president of R&D Robert Bryan, CPT will be incorporated on a thumbnail-sized microchip, allowing detection in a small, portable box. (Source: *Nature Biotechnology*, Vol.15, July 1997)

Building the virtual laboratory

The following list of Internet sites provides the tools one needs to set up a virtual laboratory

Equipment		
www.pbio.com	PerSeptive Biosystems (Framingham, MA)	Manufactures the Expedite 8900 Nucleic Acid Synthesis System which has a 3.5 minute cycle time with simultaneous dual column synthesis. With an optional multiple oligomer synthesis system (MOSS), a single operator can run up to 16 unattended synthesis runs.
www.perkin-elmer.com	PE Applied Biosystems (Foster City, CA)	ABI 3948 Nucleic Acid Synthesis and Purification System provides fully automated synthesis, cleavage, deprotection, purification, and quantification of 48 primer-length oligos in 24 hours.
Primer design and synthesis		
www.biosyn.com	Bio-Synthesis (Lewisville, TX)	This company uses 2-column machines that can produce a 20-mer in a little over 1 hour. If run around the clock, each machine can produce about 32 oligos a day.
www.lifetech.com	Life Technologies (Gaithersburg, MD)	This company uses a proprietary parallel array synthesis system that combines the high coupling efficiency of the phosphoramidite chemistry with 96-well technology. 96 oligonucleotides, up to 75 bases in length, can be synthesized simultaneously. This high-throughput system is monitored by inhouse software that tracks an order from the time it is received by customer service, through manufacturing, quality control, and finally to shipping.
www.genosys.com	Genosys Biotechnologies (The Woodlands, TX)	Automation and online ordering are part of this company's high-throughput facility which allows researchers to submit orders for large numbers of oligonucleotides directly into their synthesis instrumentation through the Internet.
www.natbio.com	NBI/Genovus (Plymouth, MN)	One of the original primer design programs to be marketed, OLIGO is now updated to automate the process of searching a target sequence: after setting user-definable parameters, the program automatically selects those oligos that meet the search criteria and downloads them into a primer database that can be used to generate an online order to an oligonucleotide facility.
www.premierbiosoft.com	PREMIER Biosoft International (Palo Alto, CA)	Offers a consulting service to tailor its program, PRIMER Premier, for user-specific applications. One modification automatically launches a homology search (BLAST) of the entire GenBank database to determine whether the primers that have been selected will be susceptible to false priming of other known sequences. After performing the analysis, the program can then generate a file containing a list of suitable primers formatted for automatic downloading to your favorite oligonucleotide synthesis facility.
www.operon.com	Operon Technologies (Alameda, CA)	Offers a custom synthetic gene service for sequences ranging from 100 to 15,000 base pairs, delivering 10 mg of the lyophilized DNA cloned in a standard plasmid vector. Since the gene is synthesized from scratch, the user has the option of optimizing codon usage for expression in any host organism as well as removing or inserting restriction sites, altering the base composition of the gene, or removing potential secondary structures.
www.ncbi.nlm.nih.gov/UniGene/	NCBI, NIH (Bethesda, MD)	A catalogue of over 55,000 different sets (or clusters) of ESTs that are being used for transcript mapping. Using this resource, clusters of ESTs that have been localized to specific chromosome regions can be identified or the database can be searched for a specific gene that has been localized.
www.resgen.com	Research Genetics (Huntsville, AL)	This company has prepared PCR primers (GenePairs) for each transcript on the Human Genome Map. If you are in a hurry to clone the gene, the company also sells a CEPH YAC clone containing the gene.

(Source: *Nature Biotechnology*, Vol. 15, July 1997)

General

Scientists study bioluminescence

Researchers at Southampton Oceanography Centre (UK) have been studying the physiology of marine organisms which produce their own light and how this bioluminescence has a role in the ecology of the deep oceans, according to a spokesperson.

The scientists now know that luminescence is widespread in the oceans and contributes to the success of many marine species.

Underwater studies on ostracods—small crustaceans abundant in coastal and deep waters—have shown that males of the *Vargula* group use light displays to identify themselves to willing females. Some other organisms may use luminescence as an alarm mechanism to distract a potential predator. It may also serve as a warning to other creatures or act as a form of camouflage by matching down-welling light from the upper ocean. (Source: *Sea Technology*, May 1997)

Genome study on diabetes in Africa

US and African researchers are beginning an unusual effort to link up laboratories on two continents in the first attempt to trace the genetic source of diabetes among black Americans to its possible roots among the people of West Africa. Adult-onset (type II) diabetes is of particular concern, because it affects about one in 25 African Americans, taking a heavier toll than among white Americans.

Researchers are looking for clues to inherited factors in Africa because intermarriage with other racial groups is less common there; thus, it may be easier to pick out uniquely African genes that contribute to the disease. Also, West Africans consume fewer calories than do Americans and are less likely to be overweight, a factor that confounds studies of diabetes in the United States.

The new project, sponsored by the National Human Genome Research Institute (NHGRI) and Howard University in Washington, D.C., involves two competitively selected hospitals in Ghana and three in Nigeria. Physicians and scientists there hope to find 75 pairs of siblings, both with type II diabetes. They will draw blood from the subjects and ship it to Howard and NHGRI for genetic analysis. If all goes well, the project will later expand to include 400 sibling pairs. (Source: *Science*, Vol. 276, 11 April 1997)

Drug delivery

Californian scientists believe they could have hit on a novel way of delivering complex cocktails of drugs to specific parts of the body, such as tumours and wounds, at a pre-programmed time.

Synthetic, bubble-like structures called vesicles are already used as drug delivery systems. They are made from a double layer of fatty molecules called lipids which enclose an empty space. When the space is filled with a drug, they form a protective capsule to transport the drug into the body.

The vesicles used today deliver drugs "passively", by constantly releasing very small amounts, explains Joseph Zasadzinski of the University of California at Santa Barbara. But his team's novel vesicles should target and release a drug at a specific time and place.

Zasadzinski's team has designed a structure which can keep the drug inside "quite a bit longer" than one vesicle membrane. The structures, called vesosomes, consist of an outer lipid layer than encloses a cluster of smaller vesicles. "Two layers, like two heads, are probably better than one in keeping all the drug from leaking out before it gets to a tumour or wound," says Zasadzinski.

Each interior vesicle or compartment in the vesosome package could hold a different drug inside, Zasadzinski believes. The vesosome could then deliver a cocktail of drugs rather than a single one.

It should also be possible to make each interior vesicle out of a different membrane; the outside layer already has a different lipid composition.

"The biggest benefit of vesosomes over ordinary vesicles is that we can tailor the release rate of a wide variety of drugs or other small molecules by our choice of membranes", says Zasadzinski.

To make a vesosome, the team exploits molecular self-assembly. They make a cluster of vesicles using a "molecular glue" made from biotin (vitamin H) and a bacterial protein called streptavidin; four biotin molecules stick very tightly to each streptavidin. When they attach two biotin molecules to one vesicle and two to another vesicle, and then add streptavidin, the four biotin molecules glue themselves and their vesicles to the streptavidin, making a cluster.

The outer lipid membrane starts life as a group of vesicles in the shape of a cylinder. The cylinder unrolls spontaneously around the vesicle cluster, attached by biotin-streptavidin links.

The efficiency of the vesosome reaction is around 5-15 per cent. This is good enough to show the technique works, but not high enough for economical drug delivery. But the team is working on separation techniques to remove unattached vesicles and more efficient binding techniques which it hopes will raise the efficiency to the 50 per cent range. The next step is to test vesosomes in animal trials. (Source: *Chemistry & Industry*, 5 May 1997)

TIGR releases EST data publicly

The Institute for Genomic Research (TIGR; Rockville, MD) is about to release the Human Gene Index, a publicly accessible database containing all currently known human genes. According to Anthony Kerlavage, director of bioinformatics at TIGR, the database contains more than 600,000 expressed sequence tags (ESTs), collected from worldwide sequencing efforts. The data in the TIGR database have been subject to rigorous quality control, eliminating low-quality sequences, vector sequence, and ESTs below ~50bp. Another unique feature is that, where possible, ESTs have been combined with full-length sequences and assembled into contigs called tentative human consensus sequences (THCs); alternatively spliced forms of genes are also represented. To date, 63,000 THCs have been lodged in the database, which will be freely available over the World Wide Web (http://www.tigr.org). Clones from a variety of tissue cDNA libraries will also be obtainable through links to the American Type Culture Collection (Rockville, MD). In another move, TIGR is depositing over 100,000 of its ESTs and all its THCs in GenBank, with links to further information in the TIGR relational database.

These data originate from the controversial Human Genome Sciences (HGS; Rockville, MD) TIGR EST database set up in 1992. At the time, HGS and TIGR were criticized widely for "locking up" sequence data from the public domain—in September 1994, Merck (Whitehouse Station, NJ) set up The Merck Gene Index as an alternative. TIGR also hopes to extend its Expressed Gene Anatomy Database to incorporate more microbial sequence data within the next year. (Source: *Nature Biotechnology*, Vol. 15, May 1997)

Telomerase seen as universal sign of cell's malignant transformation

An enzyme that plays a role in turning normal cells into malignant ones may be the key to developing easy, early cancer screening tests, said researchers at the annual meeting of the American Association for Cancer Research. The enzyme, called telomerase, has been found in most cancers, and scientists in hundreds of laboratories around the world are investigating it as a way to distinguish benign from malignant disease. Telomerase can be found in most tissue samples, such as urine, biopsy specimens and blood.

Telomerase activity has been seen in about 85 per cent of all tumours, but not in most normal cells. Therefore, researchers believe it will be a valuable marker, especially in such diseases as pancreatic and ovarian cancer, in which the diagnosis often comes after the point where there is anything doctors can do to help.

In addition, scientists are examining the enzyme as a way to find out if cancer therapy, such as surgery, radiation or chemotherapy, has really cleared out the cancer, or if some malignant cells are lingering after treatment.

In one of the many studies reported at the AACR meeting, scientists from Hiroshima University School of Medicine in Japan detected telomerase in 13 of 31 pancreas cell samples taken from patients prior to surgery. Of those, doctors discovered that 12 of the 13 were malignant when surgery was performed. In another study, conducted by Louis Dubeau of the Kenneth Norris Jr. Comprehensive Cancer Center, Los Angeles, CA, a telomerase test was able to find ovarian cancer in 10 cases that conventional tests missed.

Telomerase research is a relatively new field, but one that is growing. (Source: *McGraw Hill's Biotechnology Newswatch*, 21 April 1997)

Sequenced human genome

Gene mappers gathering for their annual meeting at Cold Spring Harbor Laboratory in New York reported that they are moving beyond mapping—identifying molecular landmarks along DNA's linear array—into sequencing pieces of the human genome. Fifteen participants presented new data. According to Eric Green of the National Human Genome Research Institute in Bethesda, MD, those data represent most of the human gene sequencing under way in the world. All together, the work totals about 52.4 million bases of the 3-billion-base genome. The researchers predict that by next May, their output will have quadrupled. That will leave 93 per cent of the genome to be sequenced by 2005, the scheduled completion date of the Human Genome Project.

Group	*Total bases finished and in GenBank by May 1997**	*New sequence expected by May 1998**
Sanger Centre (United Kingdom)	18.3	35.0
Washington University (St. Louis)	5.7	25.0
U.S. Department of Energy	4.0	16.0
University of Oklahoma	3.4	6.5
The Institute for Genomic Research	3.3	11.0
Baylor College of Medicine (Houston)	3.0	15.0
University of Tokyo (Japan)	3.0	5.0
Whitehead Institute	3.0	20.0
Institute of Molecular Biology (Jena, Germany)	2.4	6.0
PE-Applied Biosystems Inc.	2.2	4.0
University of Texas SW Medical Center	1.8	5.0
University of Washington	1.4	4.2
Genome Therapeutics Corp.	0.6	5.0
Albert Einstein College of Medicine (NYC)	0.3	?
Stanford University	0	6.0
Total	**52.4**	**163.7**

*Millions of bases.

(Source: *Science*, Vol. 276, 6 June 1997)

IBM Deep Blue to drug development

Scientists who created IBM's Deep Blue computer claim its ultimate purpose is to prevent human suffering.

Drug development will be the first major application for computers based on the Deep Blue massive parallel processing technology, said IBM officials at a press conference held while the computer was being pitted against world chess superstar Garry Kasparov. While Deep Blue's chess performance was breathtaking, IBM said that the computer is really a trial for a technology aimed at drug development, data mining and other scientific applications. More powerful versions of Deep Blue are already in development and these computers will be able to significantly speed up the production of drugs for cancer and other serious illnesses. Today, finding, testing and bringing a drug to market takes about 12 years. The new developments could cut the time in half.

IBM and Tokyo's Institute of Physical and Chemical Research are expected to have a cousin of Deep Blue ready for sale to pharmaceutical companies in early 1999. Like Deep Blue, the system will consist of a basic machine, the IBM RS/6000 SP, already on the market. It is at the heart of the Lawrence Livermore National Laboratory's $93 million effort to build the world's fastest supercomputer, which will keep tabs on the nation's nuclear stockpile, according to IBM. Lloyd's of London also has one for calculating its premiums.

What has made Deep Blue into such a formidable adversary are 512 specialized processors, which each analyse a different aspect of the chess problem. By contrast, the average desktop PC has one or two processors.

The drug seeking machine will have 5,000 specialized processors, all geared to analysing how atoms interact, improving a process that now takes weeks to examine thousands of atoms to one that can analyse a million overnight. (Extracted from *McGraw Hill's Biotechnology Newswatch*, 19 May 1997)

Protein yields catalytic key to telomerase

A protein similar to the one that allows the AIDS virus to thrive appears to play a crucial role in the immortalization of cells that leads to cancer, said an international team of researchers.

Even though the protein was isolated from common baker's yeast and a single celled pond dwelling creature called *Euplotes*, the finding is considered a breakthrough in the search for more precise diagnostics and more potent treatments for cancer in humans, investigators say. Efforts are already underway to find the human version of the protein.

The newly found protein, a form of reverse transcriptase, is "the heart" of telomerase, the "immortalizing enzyme" that lets cancer cells run rampant.

When activated, as it is in most cancers, telomerase prevents cells from going through the normal aging process marked by the progressive shortening of DNA sequences at the tail ends of chromosomes, which are known as telomeres.

The protein appears to be the key to rebuilding telomeres, which allow cells to live on and replicate past their normal lifespan, eventually becoming an out-of-control malignant growth.

For almost a decade, scientists have known that telomerase has the "very unusual" property of having both an RNA component and a protein.

The scientists proved the importance of the chromosome-replication role of the protein by tinkering with it in yeast. Slight changes, as small as a single amino acid, were enough to inactivate telomerase.

The next step will be to find the protein in humans. It is likely that scientists will find an equivalent protein, because it was the same in organisms that are far apart on the evolutionary scale.

Geron, a biotechnology company investigating telomerase as a target for cancer diagnosis and therapy, has licensed the University of Colorado patent on the discovery. (Extracted from *McGraw Hill's Biotechnology Newswatch*, 5 May 1997)

Parasite's food route under attack

A novel strategy for treating malaria promises hope for the 200-300 million people who are infected every year. It targets the parasite responsible for the most fatal form of the disease. In one part of its life cycle, the parasite *Plasmodium falciparum* invades the red blood cells of its host, the mosquito. Once ensconced there, it imports nutrients and exports waste by a largely unknown method.

Now US scientists have found that the parasite develops a network of tiny tubes which extends from its outer membrane to the edge of the blood cell. They believe this is how the nutrients travel from outside the host cell into the parasite.

The researchers suggest that they could use this route to deliver specific antimalarial drugs, which resembled nutrients, to the parasite. Or they could design drugs to disrupt the network, killing the parasite by starvation. According to team member Sabine Lauer of Stanford University School of Medicine, they have found a drug that blocks the network but it would not work in human malaria cases because it is inactivated by human enzymes.

The team found that the network grows after the first 30 to 33 hours following infection. Preventing the tubes from forming blocked the accumulation of important nutrients such as adenosine, glutamate and orotic acid by 60-80 per cent. (Source: *Chemistry & Industry*, 19 May 1997)

Non-parenteral vaccines

An ever-growing number of companies are employing oral, intranasal and other non-parenteral routes of administration for new vaccines. They have set their sights on the worldwide vaccine market, estimated at more than $4 billion.

A key force behind this trend is the belief that vaccines that induce mucosal immune responses (i.e. those characterized by secretory IgA antibody production) will provide better protection against infections that begin at the mucosal surfaces of the body than do injected vaccines that stimulate primarily systemic immune responses. An estimated 80-90 per cent of all infections enter the body via the mucosal tissue that lines the gastrointestinal, respiratory and urogenital tracts and the surfaces of the eye and inner ear.

Another factor driving the development of oral and other non-injected vaccines is the need for vaccines that are both more user-friendly and easier to administer, in order to increase patient compliance rates, make mass immunization more feasible and reduce treatment costs. Some experts also believe mucosal routes can lower the incidence of adverse reactions associated with injected vaccines.

In the last two years, several collaborations have been formed between the major vaccine manufacturers and smaller companies that possess technology for non-injected vaccine delivery and mucosal immunization. These technologies promise to overcome some of the possible

shortcomings of non-injected vaccines. Larger or multiple doses may be required to get the same degree of immunity that is generated with injected vaccines and to stimulate immunity in several mucosal sites. Other pitfalls include the tendency for mucosal immunity to face more quickly than systemic immunity and the need to protect oral vaccines from the acidic environment of the stomach. (Extracted from *Genetic Engineering News*, 15 June 1997)

E. APPLICATIONS

Pharmaceutical and medical applications

Study finds three-drug AIDS cocktail better than two

New data from the largest-ever AIDS study show that using a three-drug cocktail—the protease inhibitor INVIRASE® (saquinavir mesylate) and the nucleoside analogues AZT and HIVID®—delays time to disease progression or death by 50 per cent compared to the two-drug combination of AZT and HIVID. The global study, which took place in 22 countries, enrolled 3,485 people who have never been treated with antiretroviral therapy. (Source: *Genetic Engineering News*, 19 July 1997).

Fungus strain gives new drugs

The data, which come from an international clinical endpoint study (Hoffmann-La Roche trial SV 14604), show that three-drug therapy with a protease inhibitor is clinically superior to the standard two-drug regimen. However, a significant number of people with HIV and AIDS are still being treated with just two nucleoside analogues, according to Roche.

A team of biochemists from California has invented a new class of antibiotics which could help patients and doctors struggling against antibiotic-resistant infections.

The new antibiotics are based on erythromycin, a common antibiotic. Early tests show that the new compounds kill bacteria with as much vigour as erythromycin. The compounds will have to be clinically tested before they can be used to fight infections.

The researchers made the antibiotics by altering the biochemistry of the erythromycin-producing fungus *Streptomyces*. Normally, *Streptomyces* makes erythromycin by tinkering with a chemical called 6-dEB, which is built up from several small precursor units by an enzyme called DEBS.

DEBS, however, is not particularly fussy. When the normal precursor molecules are not around, the enzyme will work with all kinds of precursor units to form strange molecules that are similar but not identical to 6-dEB.

The researchers decided to cut off the supply of normal precursor by modifying a strain of *Streptomyces* so that it was unable to produce the normal precursor. They then fed the fungus unusual precursor molecules with extra aromatic rings, carbon chains and hydroxyl groups. As expected, the mutant strain churned out all kinds of strange versions of 6-dEB. The team then took these and fed them to another strain of *Streptomyces*, which turned them into the novel antibiotics.

According to the researchers, this is the first time that novel, erythromycin-like molecules have been produced by a method useful to the antibiotic fermentation industry. Other methods of producing erythromycin-like antibiotics have been tried without success, they claim. Some molecules were too complex to be synthesized from scratch using chemical techniques, and modifying ordinary erythromycin is very labour intensive. (Source: *Chemistry and Industry*, 21 July 1997)

Cinnamon inhibits H. pylori

Ohta's Isan researchers in Japan have discovered that cinnamon, used as an ingredient in gastric medication, is effective in inhibiting the propagation of *Helicobacter pylori*, the cause of many stomach and duodenal ulcers and stomach cancer.

The recent discovery may open new paths towards the development of preventative agents and treatment for gastritis and gastric ulcers, through inhibition of the bacteria. (Source: *McGraw Hill's Biotechnology Newswatch*, 7 April 1997)

Thalidomide prompts tumour responses

In trials supported by the National Cancer Institute (NCI) and co-sponsored by EntreMed and Bristol-Myers Squibb Co., thalidomide prompted a 50 per cent biological response in brain cancer patients and a 60 per cent response to treatment in Kaposi's sarcoma in Phase II trials.

Dr. Howard A. Fine, a leading neuro-oncologist based at the Dana-Farber Cancer Institute in Boston (MA), served as principal investigator of the brain cancer trials. In this trial, all patients have recurring tumours and have already received radiation treatment and many had received chemotherapy. A total of 32 patients with progressive glioblastoma multiformae and anaplastic gliomas were evaluated in the study, and Fine noted a 50 per cent response to those who received thalidomide treatment for at least two months. This includes 12 patients whose disease stabilized; two whose tumours were reduced by 50 per cent; and two whose tumour size was substantially reduced (less than a 50 per cent reduction).

NCI's Lauri Welles and Robert Yarchoan served as investigators for the Kaposi's sarcoma Phase II trial. Welles has shown that three of the five patients who received thalidomide achieved greater than 50 per cent reduction in the number of lesions associated with the disease. (Source: *McGraw Hill's Biotechnology Newswatch*, 2 June 1997)

Complex vaccine may overcome quick change talents of HIV

AIDS researchers report they have developed a way to shut down the rapidly changing part of the AIDS virus which has frustrated attempts to develop a vaccine for the disease that destroys a person's immune system.

Scientists have long attempted to attack HIV—the virus that causes AIDS—by aiming vaccine antibodies at the envelope glycoprotein (gp120) of HIV. But gp120 can rapidly change its composition, rendering impotent attacks by immunogens. The scientists claim they have had success in the laboratory in being able to design synthetic antibodies to bind to the sites the AIDS virus attempts to change most often. That ability to thwart the speed at which the AIDS virus changes itself—the moving target—could give future AIDS vaccines a chance to prevent infection.

Maria Carlos, D.V.M., of the medical microbiology and immunology department of the School of Medicine at the University of California, Davis, and her colleagues created a complex antibody that binds to the five most frequent sites where the HIV tends to change format.

Five synthetic constructs were designed, synthesized and tested individually as a complete vaccine preparation. The complete vaccine consists of a complex representing each one of five hypervariable epitopes.

Researchers now need to see if the vaccine cocktail can prevent infections, possibly in animal models before human testing can begin. (Extracted from *McGraw Hill's Biotechnology Newswatch*, 19 May 1997)

Vaccine effective in laboratory against airborne black death

US Army medical researchers say they have developed a vaccine that protects laboratory animals against pneumonic plague.

Pneumonic plague still crops up but prompt treatment can save patients. Current licensed vaccines are effective against bubonic plague—spread by infected flea bites, but is considered so ineffective against airborne plague that international health officials did not inoculate people with it in India in 1994 during the last large suspected pneumonic plague outbreak.

Although outbreaks of bubonic and pneumonic plague are rare in developed countries, there are still a few cases that occur each year. Pneumonic plague can be fatal if not treated within the first few days. While antibiotics can kill off the organism, damage already done to organs such as the lungs can be fatal.

George Anderson of the US Army Medical Research Institute of Infectious Diseases has demonstrated that his vaccine—an acellular fusion of *Y. pestis* proteins—protects laboratory mice from pneumonic plague.

The new vaccine is said to cause fewer side effects than the whole-cell bubonic vaccine; and the new vaccine requires just one inoculation for a year's protection. A booster shot after one year is likely to be needed. The current bubonic vaccine involves a series of three shots and a six-month booster.

Anderson is working with officials of the Food and Drug Administration to develop a surrogate marker that would prove the vaccine works since a field trial of a pneumonic plague vaccine is impractical.

Anderson suggested that if the vaccine demonstrates an immune response in monkeys and then the monkeys survive challenge with the airborne plague virus, it might be possible to use the immune response indications as proof that the vaccine works. That is, he said, if the vaccinated humans show the same immunologic response as the monkeys. Anderson said he believes that marker would be sufficient for FDA licensure.

Plague most frequently occurs in Africa, Madagascar, Viet Nam, Russia and part of South America. (Extracted from *McGraw Hill's Biotechnology Newswatch*, 19 May 1997)

Cancer therapy

A chemical derived from the bark of a South African willow tree could become a potent new weapon against cancer, according to researchers at the UK charity Cancer Research Campaign. The chemical, called combretastatin, kills tumours by cutting off their blood supply. The scientists say it could be effective against 90 per cent of all cancers.

The research team, led by Dai Chaplin of the Mount Vernon Hospital in Northwood, Middlesex, tested the chemical by injecting it into laboratory mice suffering from breast cancer. They found that the chemical reduced blood flow to tumours by 93 per cent, with the effect beginning within 20 minutes. Twenty-four hours after a single dose, 95 per cent of the cancer cells were dead because of lack of oxygen and nutrients.

The surviving cells lay round the rim of the tumour, where they are served by normal blood vessels. According to Chaplin, these cells would have to be killed by conventional methods such as chemotherapy or radiation.

Combretastatin has the added advantage of being highly selective, attacking the blood vessels that feed tumours but leaving healthy vessels alone, the researchers claim. Exactly how this happens remains a mystery, as does the exact mechanism by which the chemical attacks the vessels to shut down blood flow. They speculate that combretastatin could cause cells lining the blood vessels to change shape or come loose, blocking the flow of blood.

Chaplin says that shutting off a tumour's blood supply is an unusual but efficient anti-cancer strategy. Most cancer drugs attack individual tumour cells directly, but knocking out a single cell in a tumour blood vessel wall can kill 1,000 tumour cells at a time, he says. Combretastatin is not the first circulation-inhibiting chemical to be tested on tumours, but it is proving much less toxic that its predecessors, the team notes.

Professor Gordon McVie, Director General of the Cancer Research Campaign, says that he expects human trials to start in 18 months. He adds that the chemical could be effective against all 200-plus varieties of solid tumour—an exciting prospect given that different kinds of cancer usually respond to treatment in different ways.

Combretastatin was discovered in the bark of the African bush willow *Combretum caffrum* by Bob Pettit of Arizona State University, who specializes in searching for cancer cures in the natural world. Pettit, who owns the rights to the chemical, has strong links with the Cancer Research Campaign and asked Chaplin to undertake research and clinical trials. According to McVie, Petit's discovery reflects a resurgent interest in natural compounds following a period where designing molecules in the laboratory was all the rage. (Source: *Chemistry and Industry*, 2 June 1997)

Demeter compounds found active against resistant bacteria

A study conducted by Demeter Biotechnologies has shown that some of its Peptidyl Membrane Interactive Molecules (PMIMs) were effective in killing a number of micro-organisms which have demonstrated resistance to current antibiotics.

The study confirmed that Demeter PMIMs were active against multiple strains of both methicillin-resistant *Staphylococcus aureus* and vancomycin-resistant enterococci.

The lead PMIM in the study demonstrated minimum inhibitory concentrations at levels 10 to 20 times below the level cytotoxic to healthy liver cells.

There are around 60,000 deaths a year in the US alone from hospital-acquired infections, and nearly 40 per cent of hospital-acquired *Staphylococcus* infections are resistant to all antibiotics except vancomycin.

In other studies, PMIMs have demonstrated efficacy against common bacterial and fungal pathogens, including *Pseudomonas aeruginosa, Enterococcus faecalis, Streptococcus mitis* and *Candida albicans*.

Richard Ekstrom, President of Demeter Biotechnologies said, "With the emergence of multi-drug resistant bacteria, it will be necessary for companies to develop new classes of anti-infective drugs to replace current antibiotics, many of which are no longer effective against the more resistant bacteria". (Source: *Manufacturing Chemist*, July 1997)

A cheaper, quicker way to monitor glucose

The world's 100 million diabetics may soon have a better way to monitor their glucose levels, thanks to a polymer developed by Frances Arnold and her colleagues at the California Institute of Technology. Unlike current enzyme-based sensors, the polymer could be implanted in the patient and used to monitor glucose levels continuously.

The polymer, methylene bisacrylamide, contains cavities, made by molecular imprinting, which trap the glucose. Within each cavity is a copper complex, Cu(II) triazacyclononane, which binds to hydroxyl groups on the glucose molecules, releasing a proton. The more protons there are, the more acidic the solution becomes, so high acidity corresponds to high glucose levels in the blood.

Arnold has shown that the polymer responds to glucose in porcine plasma, but has yet to test it in human plasma. The next challenge is to couple the polymer to a proton detection mechanism, such as a pH meter.

The binding reaction between glucose and the copper complex is rapid and readily reversible. It should therefore be suitable for continuous monitoring.

Arnold's polymer is the first non-biological replacement for existing glucose sensors based on the enzyme glucose oxidase. According to Arnold, the polymer should be easier and cheaper to make than enzyme-based sensors, which could be important in the third world where the incidence of diabetes is increasing. It is also more stable and less likely to generate an immune response, so it should be suitable for implantation, she says. (Source: *Chemistry and Industry*, 5 May 1997)

Vaccines

Immunizations often need repeating three or more times before they become effective, but getting people to have their booster vaccinations can be difficult, especially in inner city areas and in third world countries. But now researchers at Genentech have designed a vaccine that is released over time, mimicking the effect of an original injection and subsequent booster shots.

The team enclosed the active part of the vaccine—the antigen—in a tiny polymer sphere which gradually degrades. The antigen stimulates the immune system to produce antibodies which protect against the disease.

The researchers used polymers of varying lengths in their vaccine. The longer polymers degrade more slowly, and take more time to release the antigen. The result is that the microsphere releases antigen in two separate bursts, between one and six months apart.

The key to making the vaccine is to use very low temperatures, which helps antigen stability as well as enhancing microencapsulation, explains Genentech's Jeffrey Cleland. The team chose a polymer called PLGA for the sphere which is used in biodegradable sutures.

Animal tests of two vaccines, one against HIV and other against malaria, in PLGA spheres indicate that the vaccines invoke similar or increased immune responses compared with repeated immunizations, reports Cleland. He believes this approach should work for other vaccine formulations, such as tetanus, diphtheria, herpes and hepatitis. (Source: *Chemistry and Industry*, 5 May 1997)

Wine appeal

Frequent, moderate consumption of red wine can help prevent breast cancer, according to Roy Williams of Old Dominion University in Norfolk, VA.

Both red and white wines contain the phytoestrogen *trans*-resveratrol (TR). Phytoestrogens are compounds produced by plants which can disrupt the way the sex hormone oestrogen works. Because of this oestrogenic activity, phytoestrogens can affect hormone-dependent cancers such as breast and prostate cancer.

Trans-resveratrol's structure is similar to several well-known anti-oestrogenic agents, such as diethylstibesterol (DES) and the breast cancer drug *Tamoxifen*. Because of this structural similarity, Williams' laboratory decided to test TR's oestrogenic activity in human breast cancer cells in culture.

Williams found that TR effectively binds to oestrogen receptors in human breast cancer cells, preventing a natural oestrogen, known as oestrodiol, from binding. At relatively high doses (20 μg/ml) of TR, the breast cancer cells die off as they are deprived of the oestrodiol they need to survive.

Unfortunately, wine only contains low levels of TR, typically 1-5 mg/l. Williams concludes that more research is needed to determine how much TR is absorbed from moderate wine consumption and how much TR is needed to give oestrogenic activity.

Similar phytoestrogens are also found in soy products. Since the Japanese eat large amounts of these products, this may help explain the low incidence of breast cancer in Japanese women and prostate cancer in Japanese men. (Source: *Chemistry and Industry*, 5 May 1997)

Promising results for HIV vaccine tests

A vaccine against HIV has produced promising results in trials with chimpanzees. The news coincides with the publication of results which show that a three-drug cocktail can effectively eliminate the virus from the bloodstream.

The vaccine is being developed jointly by the US company Apollon, the University of Pennsylvania and the Coulston Foundation in New Mexico.

A vaccine against HIV has been notoriously difficult to develop because the virus mutates so rapidly. This has led some researchers to concentrate on other therapeutic routes to control the disease, most notably the use of nucleoside analogues and protease inhibitors. However, only a vaccine could offer complete prevention.

The efficacy of combination therapies has been successfully demonstrated in a paper published recently in the journal *Science*. Researchers at the University of Minnesota found that a three-drug cocktail of AZT, 3TC and the protease inhibitor ritonavir eliminated the virus from the bloodstream over a period of six months. (Source: *European Chemical News*, 19-25 May 1997)

Gene vaccine safe for humans

A new type of vaccine that helps the immune system fight off cancer has been tested on humans for the first time. Researchers at Johns Hopkins University in Baltimore (MD) say that the genetically engineered vaccine is safe and effective, but warn that it will be a long time before it is widely available.

The therapy involves injecting a human gene called GM-CSF into cancer patients. GM-CSF triggers off immune system assaults on cancers but is not normally expressed at tumour sites. Scientists have known that GM-CSF is a potential tumour therapy for some time, but the Johns Hopkins group is the first to complete human trials.

The scientists made the vaccine by inserting the gene into surgically removed cancer cells, then re-injecting them. The cells were irradiated to stop their growth and prevent them from developing into new tumours.

The researchers tested the vaccine on 18 patients with advanced kidney cancer. They claim that the injections

boosted the activity of the patients' tumour-destroying white blood cells. A second group of kidney cancer patients who did not receive the gene did not show increased white cell activity.

The researchers claim that the study proves the vaccine is safe. It caused only minor side effects like skin rashes, a normal result of immune activation.

The results are promising enough to continue the clinical trials. The John Hopkins team is currently undertaking studies on pancreas and prostate cancer. Meanwhile, biotechnology company Somatix Therapy, which has bought the rights to the vaccine, will begin new trials on kidney cancer in Japan later this year. It believes that the vaccine can eventually become a routine part of cancer therapy. (Source: *Chemistry and Industry*, 21 April 1997)

Risk from metals at work

Exposure to manganese or copper in the workplace could cause Parkinson's disease, according to a new study from a Detroit hospital. People exposed to the metals for more than 20 years have a "significantly increased association" with Parkinson's, the study claims.

The researchers, from the Henry Ford Hospital, also found that people exposed to combinations of lead and copper, lead and iron, or iron and copper for more than 20 years are more likely to get Parkinson's than those exposed to only one of the metals. But the study indicates that exposure to mercury, zinc, iron and lead on their own does not cause Parkinson's.

A Health and Safety Executive spokesperson in the UK said that all the metals implicated are commonly used in manufacturing industry.

The researchers asked 144 non-demented Parkinson's sufferers and 464 healthy people to provide detailed employment histories including their job titles, the duration of their employment and the tools, machinery and protective measures they used. An industrial hygienist, who did not meet the subjects, then estimated how much manganese, copper, lead, iron, zinc and mercury they would have swallowed, inhaled and absorbed at work.

The team says that the biological mechanisms accounting for the toxicity of the metals are unknown, but recommends follow-up studies into the prevalence of Parkinson's among workers from particularly risky industries. (Source: *Chemistry and Industry*, 21 April 1997)

Livestock applications

Conference reports on giant clam farming

At the Seventh Annual Conference for Shellfish Growers, sponsored by the Washington Sea Grant Program, aquaculturists reported on their experimental attempts to farm North America's largest burrowing clam, the geoduck.

A Pacific Northwest native, wild geoducks can reach lengths of 21 centimetres, weights of more than 3.25 kilograms, and ages of more than 140 years. Aquaculturists speaking at the Conference estimated that cultured geoducks planted in Puget Sound beaches can grow to a harvestable weight of about one kilogram in three to four years. Don Dahman of Dahman's Shellfish Co., noted that geoducks can be planted on intertidal grounds not being used for other crops such as Pacific oysters or manila clams. Price is another incentive to grow geoducks, which are prized in Asian markets. During 1996 some commercial harvesters received about $5/pound for geoducks.

Pacific Northwest aquaculturists are building on the work of Washington Department of Fish and Wildlife (WDF&W) biologists, who spent more than a decade developing geoduck rearing techniques. The agency's initial goal was to replace geoducks harvested by commercial divers. In Washington State, divers harvest about 2-3 million pounds of geoducks annually from subtidal leases co-managed by WDF&W and the Washington State Department of Natural Resources.

As aquaculturists are beginning to show interest in commercial geoduck production, biologists have become concerned that cross-breeding between wild and cultured geoducks could change the population genetics of wild geoduck stocks. To minimize the impact of cultured stocks, grant researchers Beattie and William Hershberger of the Washington School of Fisheries are studying the feasibility of growing a triploid geoduck. Triploid organisms, which have three sets of chromosomes per cell instead of the usual two, are often sterile. Triploid geoducks may also grow more quickly than non-triploids. The triploid geoduck project builds on previous research to produce triploid Pacific oysters, which are now cultured throughout the west coast.

The availability of seed is the limiting factor in geoduck farming at present. To grow geoducks, aquaculturists must purchase broodstock from divers, taking care to select mature clams in good condition. After the broodstock spawn, the geoduck larvae are fed a diet of cultured algae in hatchery tanks. (Source: *Sea Technology*, May 1997)

Australians mass produce embryo clones

Australian researchers have created more than 400 cattle clones from embryos, a first step towards mass-producing identical farm animals, according to a report in the *New Scientist*.

Although the Australian clones are not the result of the same technology used to make Dolly, the Scottish lamb cloned from an adult sheep, Alan Trounson of Monash University in Clayton, Victoria, says that the Australian team might be able to use the newer Scottish techniques to clone hundreds of genetically identical adult animals.

The researchers currently produce the calf embryos using standard test-tube technology, letting them grow into a ball of cells known as a blastocyst. They then separate cells out and fuse them with eggs that have had their nucleus removed. The resulting embryos are grown and separated again and again to create a whole line of little clones—470 at last count.

The Australian researchers say they want to use their technology to create a reliable herd of prize cattle. Currently farmers will breed from one prize bull over and over again, but offspring vary in quality depending on the mothers. Cloning would allow for guaranteed elite livestock. (Source: *The AgBiotech Bulletin*, May 1997)

Plant-grown vaccines protect animals

An article in *Nature Biotechnology* (March 1997) confirms that plant-based vaccines can protect animals against infection. It reports that researchers Kristian Dalsgaard and colleagues from the Danish Veterinary Institute for Virus Research have demonstrated that a vaccine produced in cowpea plants protects mink against the mink enteritis virus (MEV). MEV belongs to a group of viruses that causes disease in mink, cats and dogs.

The researchers fused a small segment coding for the epitope of MEV into the coat protein gene of cowpea mosaic virus. The engineered plant virus with the mink virus

epitope "piggybacked" onto the coat protein multiplied in infected cowpea plants. Scientists were able to recover abundant amounts of chimeric virus from the plants and injected small amounts into minks. All the immunized mink resisted a subsequent inoculation of MEV while most of those not immunized quickly succumbed to the disease.

The research supports the prospect of commercial production in plants of edible vaccines against infectious human and animal diseases. Such vaccines are considerably cheaper, can be produced anywhere, and do not require refrigerated transport and storage. As well, they are potentially safer as they consist of subunits of the pathogen rather than whole organisms which are used in many conventional vaccines. (Source: *The AgBiotech Bulletin*, May 1997)

Natural gum

As anyone who has ever tried pulling mussels off a rock will appreciate, the glue used by shellfish is strong. According to Sigma, a company supplying laboratories with biochemicals and reagents, the adhesive secreted by *Mytilus edulis* is as good as epoxy resins, and it is waterproof. The company, which includes the natural adhesive in its list of supplies, points to its advantages as a non-toxic glue for possible use in medicine. Broken bones, teeth and open wounds might be easier to fix with the biocompatible glue.

The glue, according to Sigma, is a protein of molecular weight 130,000 comprised of about 80 repeating sequences of hexa and decapeptides.

The adhesive can bond to almost any type of solid surface, including glass, and the natural product is of great interest because it cures in a watery environment. (Source: *Technology Ireland*, May 1997)

Newcastle disease

Chicken farmers have a hard time avoiding Newcastle disease, and in an effort to improve resistance, Dr. Agbede, a researcher from the University of Dschang, Cameroon, has gone back to the home of the wild *Gallus domesticus* ancestor. In Java he collected eggs, raising chickens and inoculating each generation with a harmless (attenuated) form of the viral disease. Breeding from chickens with a high immunological response led to increased resistance, a discovery which could lead to improved breeds. (Source: *Technology Ireland*, May 1997)

Monoclonal antibodies produced in transgenic goat's milk

Genzyme Transgenics Corp. has announced it has successfully demonstrated high-level expression of a therapeutic monoclonal antibody in the milk of transgenic goats. Monoclonal antibodies are proteins that can find and attach to specific cell targets.

It may not be cost-effective or even feasible to make such antibodies in commercial quantities using mammalian cell culture, the current method of producing monoclonal antibodies. Genzyme Transgenics believes transgenic technology offers a cost-effective method of producing the high volumes that may be required to meet the needs of potential commercialization.

The new expression results and verification of binding quality came as part of the company's collaboration with Bristol-Myers Squibb. BR96-doxorubicin, a conjugation of the BR96 monoclonal antibody with the anti-cancer drug doxorubicin, is being developed by Bristol-Myers Squibb for potential cancer therapies. Genzyme Transgenics is developing transgenic goats that will produce BR96 in high volumes. Genzyme Transgenics has already produced several goats that have the gene for the BR96 antibody. The level of the target monoclonal in milk was 14 grams per litre, more than 10 times the expression levels achieved in cell culture for comparable antibodies. (Source: *The AgBiotech Bulletin*, April 1997)

Agricultural applications

Antifreeze gene from white pine may help shield crops from frost

Canadian forest scientists think they may have inadvertently found a plant antifreeze gene that could have wide application in agriculture.

Abul Ekramoddoullah, an immunochemist with the Canadian Forest Service in Victoria, British Columbia, was trying to understand the natural history of a pest called white pine blister rust when he stumbled on an unusual protein.

What was odd was that "samples (of white pine) collected late in the season had more of this protein. If we sampled some trees in the summer months we did not see this protein".

But because it seemed to have little to do with the blister rust problem, the unusual 18-kilodalton protein was "put on the back burner". It was only later when the research team realized that the protein might have something to do with regulation of defences.

Ekramoddoullah said the research team noticed a significant correlation in white pine between levels of the protein and ability to resist damage from cold, which was their first clue they might have a vegetable antifreeze gene.

Antifreeze genes would be of great importance to agriculture, especially for crops that are now raised in areas with short and variable growing seasons.

Sequence data show that the protein is very water soluble, opening up the possibility of other uses, including allowing organs destined for transplant to be stored for longer periods. (Extracted from *McGraw Hill's Biotechnology Newswatch*, 7 July 1997)

Sweet potato with edible leafstalk

Japan's National Agriculture Research Centre of the Ministry of Agriculture, Forestry and Fisheries has developed a new sweet potato cultivar of which both the storage root and the petiole part are edible, enabling the sweet potato plant to be utilized as a green vegetable in summer. The petiole part can be cooked without peeling off the skin, is delicious and highly nutritious, and is available in adequate yield.

The new sweet potato cultivar is called *Elegant Summer* and was developed by crossing breeding lines with long and thick petiole parts. The petiole part is eaten in Asian countries such as the Philippines, Viet Nam and Thailand, and in some parts of Japan as a summer vegetable. However, with a conventional cultivar, the yield of the petiole is rather small, and the surface skin has to be peeled prior to cooking.

Elegant Summer's petiole has no hairs on its surface and has a good greenish appearance, and contrary to other cultivars, is not bitter, can be cooked without peeling the surface skin, and features a good texture, colour and taste. It can be eaten raw, boiled or fried. The yield of leafstalk per plant is 1.5 times that of conventional cultivars of sweet potato plants. Further information from National Agriculture Research Centre of the Ministry of Agriculture, Forestry and Fisheries, 3-1-1, Kannondai, Tsukuba City, Ibaraki, Pref. 305, Tel.: +81-298-338-8481, Fax: +81-298-38-8484. (Source: *JETRO*, April 1997)

Mildew resistance in wheat

Weeds from the Middle East crossed with modern wheat have produced hybrids with stronger resistance to powdery mildew, according to USDA plant pathologist Steven Leath. Leath and Paul Murphy, a plant breeder from North Carolina State University, have already developed three new hybrids that are available to plant breeders seeking to boost the disease resistance of commercial wheat lines. In three years of field tests, the new hybrids demonstrated consistent resistance to all strains of powdery mildew.

To create the new hybrids, Leath and his colleagues pollinated domestic female plants with wild males. The plants were so genetically different that the resulting embryo could not survive within the female and had to be grown by tissue culture. The resulting offspring must be bred with another wild male. Using this method the researchers retain many of the traits growers want in their wheat. While traditional crosses involve a 50/50 gene exchange, the new method alters just one third of the genetic make-up. (Source: *The AgBiotech Bulletin*, April 1997)

Brazilian predator mite controls African cassava pest

Researchers at the International Institute of Tropical Agriculture (IITA) have found a predator mite that provides effective biological control against the cassava green mite, a major cassava pest in Africa. The predator, a tiny mite from Brazil, has improved yields by approximately one third in field trials over three years in West Africa. The project has been focusing on Benin, Cameroon, Ghana and Nigeria.

Cassava, also known as manioc, was introduced to Africa from Latin America in the fifteenth century. It is an important food crop because it can grow in poor soils or in drought conditions, and is a staple food for approximately 200 million Africans. For years, many of its major pests remained in Central and South America, but in the 1970s the cassava green mite was introduced to East Africa and crop yields were reduced by up to one half.

Since 1983, researchers have looked for a natural enemy that could control the cassava mite, but most predator species from Central and South America did not survive in Africa. The goal of the IITA research is to create a self-sustaining control programme that will not require ongoing intervention such as with pesticides. (Source: *Global Pesticide Campaigne*, June 1997)

Crops fight off aluminium

Mexican geneticists could have solved one of the most widespread agricultural problems in the world. They have genetically engineered plants that are resistant to aluminium poisoning, a problem that afflicts 40 per cent of the world's arable land.

Aluminium ions poison plants by stopping root growth, leading to nutrient deprivation. In most soils, the ions are anchored down and cannot be absorbed. But in acidic soils, aluminium ions float freely around and are taken up by the roots.

Aluminium poisoning severely limits the agricultural productivity of acidic soils, says research team leader Juan Manuel de la Fuente of the University of Irapuato in Guanajuato, Mexico. Modern agricultural practices and acid rain have acidified about 40 per cent of the world's farmland, he says. Adding lime to the soil temporarily removes acidification, but produces runoff pollution.

Fuente's solution is to mimic the way that some plants are naturally resistant to aluminium poisoning. The resistant plants appear to evade the toxic ion by exuding organic acids, especially citric acid, from their roots, he says. The acids grip onto the aluminium ions, stopping them from being absorbed.

The team engineered a bacterial gene called citrate synthase, which is involved in making citric acid, into the roots of tobacco plants. They found that the engineered plants produced ten times more citric acid than normal tobacco plants and grew healthily in acidic, aluminium-rich soils. The gene also worked in papaya plants.

"This finding opens the possibility of applying this technology to important crop plants such as maize, rice and sorghum, which are often grown in acidic soils and in which aluminium toxicity is a major problem", the researchers conclude. (Source: *Chemistry and Industry*, 16 June 1997)

Genetically modified sugar beet for field trials

Monsanto has applied to the US Environmental Protection Agency (EPA) for a licence to conduct field trials on genetically modified sugar beet in Ireland. This crop is very susceptible to weed competition and the tests will investigate sugar beet engineered for resistance to Monsanto's "Roundup" glyphosphate herbicide.

The proposed trials will take place in counties Carlow, Cork and Kilkenny and would be the first of their kind in Ireland. The EPA's Genetically Modified Organisms Committee had 90 days to consider the original application, but this deadline has been extended to request further information. The company, which has conducted similar sugar beet trials in seven EU countries, including the UK, Denmark and France, since 1990, described the queries as "routine". (Source: *Irish Biotech News*, April 1997)

ICRISAT's ecofriendly gift to check chickpea pod borer

Entomologists at ICRISAT have developed low-cost ecofriendly technologies to combat the chickpea pod borer, *Helicoverpa armigera*. This technology is rapidly becoming popular among farmers.

According to ICRISAT entomologist V.R. Bhagwat, "an integrated pest management (IPM) strategy using a botanical insecticide, a host-specific virus to protect chickpea from pod borers, and on-farm experiments have clearly shown the efficacy of this approach over local practices of farmers".

Ten on-farm trials were conducted in three Indian villages. In each experiment, a high-yielding variety of chickpea was subjected to four treatments: a neem-based (*Azadirachta indica*) botanical insecticide; nuclear polyhedrosis virus (NPV); a chemical insecticide; and a non-treated control. Pheromone traps were used to monitor pest incidence, and bird perches were provided to encourage predatory birds.

The NPV particles killed the larvae that were then crushed and mixed with water to be used as a cheap insecticide. The farmers were trained to monitor pheromone traps, count the larval population per plant, and determine the right stage to apply NPV. They also learned to prepare the viral spray. The experiment showed that the use of MPV was not only economical, but was also eco-friendly.

The farmers who participated in the trial harvested an, average of 887 kg ha^{-1} from NPV-treated plots compared to 631 kg ha^{-1} from the nontreated plots, and 534 kg ha^{-1} from farmers' plots grown according to traditional practices. Dr. Bhagwat said that research should next focus on integrating the botanical insecticide and NPV into a user-friendly package to help fight the pod-borer. (Source: *SAT News*, No. 20, July 1996/April 1997)

Food production and processing

Bittersweet biotech

Grapefruit juice has always been less popular than sweeter varieties. A California company, however, may soon be using a novel purification method to change that. Broadening the scope of their patented radial-flow-chromatography method (Superflo), originally designed to purify drugs cheaply and with higher yields, Sepragen Corp. (Hayward, CA) has filed for a patent to use the technology for debittering fruit juices. By modifying Superflo, a single-step debittering process (SepraDebitt) extracts proteins responsible for giving juice its bitter taste. The filtration technology uses high-volume liquid raw materials and has many applications, including ridding fresh water of toxic pollutants, as well as purifying beer and wine, Sepragen says. Not only will the debittering process make such juices as grapefruit and cranberry more palatable to more people, it will also free the citrus industry from the vagaries of the weather. Icy winters produce sour fruit, resulting in huge losses for the fruit juice industry; because the taste is so overpowering, bitterness prevents a juice from being blended, says Sepragen president Vinit Saxena. (Source: *Nature Biotechnology*, Vol. 15, March 1997)

Extraction industry applications

Plutonium eater eyed for nuke fuel

Researchers at Towa University, Japan, have discovered a micro-organism that can selectively extract plutonium ions from an aqueous solution. It is probable that the micro-organism can be used in the nuclear fuel cycle, such as in reprocessing, where only plutonium is extracted from used nuclear fuel.

The researcher collected six varieties of bacteria with affinity to uranium taken from uranium mines in northern Australia, and verified that the best one collected 0.615 grams of uranium per gram of bacterium.

The professor also found that in an extremely acidic environment, the bacterium absorbed nearly no uranium, but did efficiently absorb plutonium. For this reason, the micro-organism can be used in the process of separating plutonium from uranium where the two coexist. The experiments suggest that 1 gram of bacterium will be able to absorb up to 0.3 grams of plutonium. (Source: *McGraw Hill's Biotechnology Newswatch*, 2 June 1997)

Industrial microbiology

Corn plastic

A biodegradable plastic made from a by-product of corn refining could help meet the growing demand for environmentally friendly containers, according to scientists at the University of Illinois. They say that the plastic decays naturally in the soil and enriches it with nitrogen.

The plastic is made from zein, a protein in corn gluten. The Illinois team found that pure zein is too brittle and water-absorbent to use as a plastic, but its properties improve when added to certain fatty acids. The team then coated it with hot flax oil to make strong, waterproof sheets ready to be moulded into sandwich boxes, plates and food trays.

Zein is normally extracted from corn during ethanol manufacture and used in sweet and pill coatings. The team says that only a small proportion of available zein is currently extracted. Graciela Wild Padua says that cheaper ways to extract zein are needed before the plastic becomes commercially viable. Her team is now working on zein-based clingfilm. (Source: *Chemistry and Industry*, 21 April 1997)

Enzymes have softer touch

Textile companies may soon be treating cotton with enzymes rather than inorganic chemicals, according to a team from the University of Georgia. The new process could save energy and be easier on the environment.

Textile manufacturers currently use sodium hydroxide to remove the waxy outer layer from cotton fibres, which is known as scouring. Scouring is needed to make the cotton fibre absorb dyes.

The Georgia team led by Ian Hardin have replaced the sodium hydroxide process with a mixture of enzymes, including pectinases and cellulases. Although enzymes have not been used for scouring before, some textile processes employ amylase to break down the starch that strengthens yarns during weaving, and cellulase to produce a stone-washed effect in denim.

Using enzymes should lead to energy savings, since the treated cotton would not require washing with hot water after scouring. The environment should also benefit since enzymes break down easily and the waste water would not contain any inorganic salts.

Hardin is also using enzymes to remove colour from textiles. Textile plants use ozone and activated peroxides to break down the aromatic dye compounds before they are released. The Georgia researchers have degraded the dyes using lactases and dehydrogenases from white rot fungi. The only problem is that a different enzyme is needed for each type of dye.

Enzymes from white rot fungi could also be used to treat solid textile wastes. Hardin has been using the enzymes to treat protein waste left over after shearing sheep. In the next few months he also plans to begin work on using enzymes to depolymerise waste nylon. (Source: *Chemistry and Industry*, 5 May 1997)

Energy and environmental applications

Collaboration on bioreactor

Elf Atochem and Membrane Extraction Technology, based at Imperial College, London, are developing novel membrane bioreactor technology. A six-month pilot-scale trial has begun at Elf Atochem's chlorotoluene derivatives plant at Widnes, UK.

Elf Atochem expects to treat 5,000 tons/year of the waste stream. The bioreactor is said to overcome the drawbacks of current purification options which are either energy intensive or impact heavily on the environment.

The production stream at Elf Atochem's Widnes site results in a by-product of aluminium chloride solution contaminated with aromatic solvent. (Source: *European Chemical News*, 7-13 April 1997)

Wastewater purification system

The Orient Green Company in Japan has discovered a microbe that rapidly decomposes putrefied organic and inorganic substances, and through its usage, has established an environment-friendly and economical system for purifying living and industrial wastewater.

The microbe, called *OM Nakamura Bacillus*, is found in soil, lives under natural conditions, and forms bacterial clusters containing more than several hundred different strains of yeast and bacteria. It is capable of decomposing even cellulose, a substance which normally resists

decomposition. The company's new water purification even cellulose, a substance which normally system is based on this bacillus' ability to decompose putrefied matter.

In this process, living and industrial wastewater is at first treated by a precipitate removal filter, then fed into an agitating tank containing the *OM Nakamura Bacillus*. The wastewater is agitated, then fed into a mixing tank for mixing with circulating water. The mixed wastewater is simply passed through primary and secondary filters, by which it is regenerated into clean, fresh water. The wastewater is cleaned by a simplified two-stage process to a quality level that enables use as industrial water. By treating the water with a tertiary process for bacteria removal, the water is purified to a standard enabling use as potable water.

The wastewater purification plant is available in diverse sizes in conformance with the volume of wastewater to be treated. A plant with the capacity to treat 1 ton of wastewater requires 50-153 cubic centimetres of *OM Nakamura Bacillus* and 64-100 tons of circulating water for mixing with the wastewater in the mixing tank.

This biotechnology-based wastewater treatment system regenerates clean water simply by passing the wastewater through a series of filters and, in contrast to conventional types of forced wastewater treatment systems, there is no need for coagulant or precipitation agents. Only a small amount of electricity is required, so utility costs are minimized, and there is no generation of secondary pollution. In addition, the plant consists of simple devices, so construction costs are small and operation and maintenance costs are also minimal.

For further details, contact: Orient Green Company Limited, 4-18-1-701, Sakae-machi, Tachikawa City, Tokyo 190, Japan. Tel.: +81-425-22-297, Fax: +81-425-25-8083. (Source: *Tech Monitor*, May-June 1997)

Bacterial strain could help pollution fight

Microbiologists at Cornell University have isolated a bacterial species able to decompose certain chlorinated pollutants into ethylene.

The team suggest the strain, *Dehalococcoides ethenogenes* 195, could be used *in situ* to detoxify sites contaminated with the industrial solvent perchloroethylene (PCE). The organisms are irregular cocci that do not seem to belong to any recognized line, but are related to the cyanobacteria.

PCE is a common groundwater pollutant suspected of carcinogenicity. The Cornell group, led by Stephen Zinder, discovered the strain can metabolize it anaerobically in the presence of hydrogen gas—first into vinyl chloride, then ethylene. Previous research isolated only partially dechlorinating strains that convert PCE to dichloroethylene. (Source: *European Chemical News*, 16-22 June 1997)

F. PATENTS AND INTELLECTUAL PROPERTY RIGHTS

Europe to update bio-patent laws

The European Parliament has voted in favour of a directive on patents for biotechnology inventions, opening the way for European Union legislation on the issue to be brought in line with that in the USA and Japan.

After 10 years of debate, the directive is now likely to be incorporated into the national laws of the 15 EU member States. The Parliament rejected a similar directive in 1995.

Biotechnology and chemical companies have claimed that the absence of proper patent legislation has held back EU investment in some areas of pharmaceuticals and crop protection.

In a recent study, EuropaBio found that strong patent protection was considered to be one of the most important factors influencing biotechnology investment decisions in Europe. (Source: *Chemical Marketing Reporter*, 21 July 1997)

MEPs agree protection for biotech inventions

The European Parliament has voted with a majority in favour of the European Commission's proposed directive on the legal protection of biotechnological inventions. The directive is now on course to come into force in 1999.

The vote followed a debate in Strasbourg which revealed a rift among parliamentary members.

The chief aim of the directive is to provide legal security for biotechnological inventions rather than attempt to solve related ethical problems. Nonetheless, the members of Parliament endorsed many amendments proposed by the legal committee in June, designed to strengthen ethical provisions regarding the exclusion of patenting.

Parliament voted to set up an ethics committee and adopted amendments designed to ensure patenting will exclude procedures leading to the cloning of humans, plant and animal varieties, or essential biological procedures for plant and animal breeding. (Source: *European Chemical News*, 21-27 July 1997)

Haemophiliacs win court case over blood products

Four drug manufacturers are to pay out a total of $670 million to more than 6,000 HIV-infected haemophiliacs in the US over blood products supplied during the early 1980s.

A Chicago federal judge has given tentative approval for the companies to pay in line with their market share of the products at the time.

From 1978 to 1985 the companies provided blood products which, according to the ruling, "ran a high risk" of patients acquiring the HIV virus. The four agreed the compensation settlement in April this year but the final decision was delayed as several states looked for compensation for the haemophiliacs' medical bills.

The companies offered to pay each claimant $100,000 for medical care, but agreed to reimburse federal programmes a total of $12 million for the funds already spent on healthcare.

The sum will be paid to each claimant provided it is approved by the federal judge in Chicago. Each member of the class action lawsuit who signs a separate agreement with the companies entitling them to a $100,000 payment must agree not to pursue any claims against the government. (Source: *European Chemical News*, 12-18 May 1997)

Gene chip patent

A patent dispute has arisen over gene chip technology which forms the basis of powerful high throughput screening systems. The US biotechnology company Affymetrix is challenging a nine-year old patent held by the newly formed company Oxford Gene Technology.

The patent in question is owned by Oxford University which has assigned it to Oxford Gene Technology. It relates to a method of immobilizing oligonucleotides (short strands of DNA) so that specific gene sequences can be identified. The technology allows thousands of sequences to be analysed simultaneously.

Affymetrix has no patents relating to the actual gene chip itself but it does have patents on the method of fabrication. Affymetrix' challenge to the patent centres on its claim that the method of producing the gene chip is obvious and insufficiently inventive. (Source: *European Chemical News*, 12-18 May 1997)

Bill mandates patent extension if PTO dallies

US biotechnology companies made uncomfortable by the revamped patent legislation that accompanied the GATT (General Agreements on Tariffs and Trade) treaty in 1994 can breathe a sigh of relief if new legislation originating in the House of Representatives is passed by the US Congress. The bill (HR400) was introduced at the beginning of January 1997 and would protect companies from delays in processing at the US Patent and Trademark Office (PTO), Washington, DC) by granting extensions to patents as compensation for delays.

The GATT treaty granted patent rights to the inventor 20 years from the filing date, which suited most patent seekers, since the average delay is just 1.5 years. But biotechnology patents—contentious and complex as they often are—can exact long delays from the PTO, up to 10 years or more in certain instances.

The new bill would include some measures to address problems arising from GATT legislation, such as interference delays (when two or more parties claim the same invention—an isolated gene, for example) and delays resulting from appeals to applications initially denied by the PTO. But the bill would take it a step further, requiring the PTO to respond to the initial application within 14 months, and within four months for every communication after that. Slower responses would result in an extension to the patent, once issued.

The bill boosts the upper limit on extensions for administrative delays from five years under GATT to 10 years, with no upper limit for the time spent in appeals and interference.

New legislation aims to extend protection beyond the current two to five year extensions allowed by Hatch/Waxman. The time devoured by long-term clinical trials often leaves little protection period left, especially if

the approval is for a secondary indication or a new indication for a previously patented therapeutic compound. (Extracted from *Nature Biotechnology*, Volume 15, April 1997)

Official fees in the European Patent Office reduced

From 1 July 1997 the filing, search and designation fees levied by the European Patent Office are being very substantially reduced. In addition the deadline by which the designation fee must be paid is to be deferred to six months after the publication of the European Search Report, i.e. the same deadline as the examination fee. The filing fee is reduced from DM 600 to DM 250; the search fee from DM 1,900 to DM 1,700, and the designation fee from DM 350 to DM 150 per state and from DMK 5,950 to DM 2,550 for all available states.

These reductions in fees will be extremely welcome, as official fees in the European Patent Office have been strikingly higher than those in other countries. Unfortunately it appears that it will not be possible to defer the designation fee on entering a PCT application designating Europe into the Regional Phase. (Source: *Australasian Biotechnology*, Volume 7, Number 2, April 1997)

One stop shopping for intellectual property

IP OneStop offers a complete package of services to guide clients through the entire intellectual property (IP) process, from the preliminary idea stage to the final product. Clients may choose what service they need, whether it is simple information or a complete package of protection and maintenance. The service covers patent processes in various countries.

Services include:

- Information, consultation, resources;
- Preliminary and patentability searches (worldwide);
- Trademark searches (worldwide);
- Patent intermediary services;
- Legal advice;
- Patent drafting, filing, maintenance;
- Trademark filing;
- Copyright opinion;
- Seminars (Patent/Trademark/Copyright, etc.); and
- Technology and business expertise.

IP OneStop combines the professional search services of patent intermediary Betty Vankoughnett with the legal services provided by Furman & Kallows.

Contact Betty Vankoughnett, IP OneStop, Intellectual Property Services, c/o POS Pilot Plant Corp, 118 Veterinary Road, Saskatoon, Saskatchewan, Canada S7N 2R4. Tel.: 800/230-2751 or 306/978-2804; Fax: 306/975-3766; e-mail bettyv@pos.ca (Source: *The AgBiotech Bulletin*, April 1997)

G. BOOKS, JOURNALS, REVIEWS AND BIOINFORMATICS

Books, journals and reviews

Information systems for biotechnology

Information Systems for Biotechnology (ISB) is a USDA-funded programme providing information on agricultural and environmental biotechnology research, product development, regulatory issues and biosafety. ISB projects develop tools to provide scientists, regulators, teachers, administrators and the interested public with value-added information in a readily accessible form. These tools include web sites carrying searchable databases, documents and resource lists and the *NBIAP News Report*, a monthly newsletter distributed electronically and in print at no cost to subscribers.

Contact: Information Systems for Biotechnology, 120 Engel Hall, Virginia Tech, Blacksburg, VA 24061-0308, USA. Tel.: 540/213-3747; E-mail: nbiap@vt.edu; website at http://www.nbiap.vt.edu/

Crop protection compendium

Crop Protection Compendium—Module 1 provides fast, friendly access to the latest scientific information on crop protection. Available in CD-ROM format, it covers: 1,000 major pests and their natural enemies; pathogens, weeds, nematodes and vertebrates, including quarantine pests; 150 crops in 150 countries. Specific emphasis is placed on South-East Asia and the Pacific region.

Contact: Pam Sherman, Marketing Manager, CAB International, 198 Madison Avenue, New York, NY 10016, USA. Fax: 212/686-7993; E-mail: cabi-nao@cabi.org

Microbial pathogens handbook

The Handbook of Foodborne Microbial Pathogens, originally published in French, is now available in English translation. The author, Dr. Pierre Gelinas, is a researcher at Agriculture and Agri-Food Canada's Food Research and Development Centre in St. Hyacinthe. His book describes the main microbial pathogens according to their incidence and the threat they pose to public health. Bacteria, viruses, protozoans, worms, algae and moulds are all clearly and understandably catalogued in the handbook, as well as the illnesses they generally cause and the specific prevention and control measures that can be taken against them.

The book has been described as an "indispensable tool" for scientists, students, administrators, inspectors and food handlers in every sector of the industry. Cost of the book is CAN$ 49.95 plus $5 shipping and handling.

Contact: Pierre Gelinas at 514/773-1105 or on his website at http://fond-gouv.gc.ca/gelinas.htm. To order the book, contact Polyscience Publications Inc., P.O. Box 148, Morin Heights, Quebec J0R 1H0. Tel.: 514/226-5870 or 800/840-5870; Fax: 514/226-5866; E-mail: polysci@ietc.com

Biodiversity, Science and Development: Towards a new partnership

Biodiversity, Science and Development, by F. Di Castri, and T. Younès (1996), attempts to close the gap between the disciplines of agriculture, biology, genetics and anthropology. The book is the outcome of a conference held at UNESCO in Paris in 1994, carrying the same title. it contains over 60 chapters, most of which can be characterized as a contribution to a recent trend in biological sciences: "conservation biology", a discipline studying the human impact on the survival of species and conservation questions.

CAB International. Wallingford, Paris. 646 pp. ISBN: 0 85198 973 X (hardback). Price: US$ 107.

Community Management and Common Property of Coastal Fisheries in Asia and the Pacific: Concepts, Methods and Experiences

Community Management and Common Property of Coastal Fisheries in Asia and the Pacific: Concepts, Methods and Experiences, R.S. Pomeroy, Ed., are the proceedings of a workshop hosted by the International Centre for Living Aquatic Resources Management (ICLARM) in Silang, Cavite, Philippines, in June 1993. As overfishing spreads and conventional fishery management systems fail to avoid it, the world is now looking at local fishing communities and their customary management systems. These are no more perceived as "backward" and "rudimentary", but as the truly complex systems that they are, capable of ensuring long-term resource conservation. But, to what point and under what conditions may communities today continue their long-time held resource management strategies? These are the main issues discussed in the papers collected in this book, which is a very valuable contribution to the debate on the rights of fishing communities to their resources.

ICLARM Conf. Proc. 45, Manila, 1994, 189 pp., ISBN 971-8709-56-8. Order copies from: The Editor, ICLARM, MCPO Box 2631, 0718 Makati, Metro Manila, Philippines. Priced at US$ 6.

Biosafety: Scientific Findings and Elements of a Protocol

Published by the Third World Network (TWN), *Biosafety: Scientific Findings and Elements of a Protocol* is a report prepared by an Independent Group of Scientific and Legal Experts on Biosafety as a contribution to the formulation of a legally binding international biosafety protocol by Governments in the frame of the Convention on Biological Diversity. The book contains a comprehensive overview of the risks posed by genetically engineered organisms (GMOs), and also a set of criteria which should be used to evaluate the effects of GMO introduction into the environment. The elements that a meaningful Protocol should include are summarized in the final section of the book. A very useful tool for information and campaigning.

Third World Network, Penang, 1996, 94 pp. Available from: TWN, 228 Macalister Road, 10400 Penang, Malaysia. Fax: (604) 226-4505. E-mail: twnpen@twn.po.my

Researchable Constraints in the Seed Sector in Developing Countries

Prepared by Mark Wright for the British Overseas Development Agency supported Crop Post-harvest

Programme, *Researchable Constraints in the Seed Sector in Developing Countries* assesses seed sector areas that warrant support. The actors interviewed were mainly public research centres and breeders organizations, although NGOs working on *in situ* conservation and farmer-led breeding programmes were also contacted. Although the book keeps close to the mainstream approach to genetic resources development in its focus on major crops, it fully stresses the importance of subsistence farmers for biodiversity conservation and the need to set up research and legal frameworks that support low-input, sustainable agriculture. The report does not intend to be comprehensive, yet one misses a discussion on the whole issue of intellectual property rights (IPRs), especially now that developing countries are under World Trade Organization pressure to put into place laws that would dramatically influence—and constrain—the seed sector.

Natural Resources Institute, 1996, 75 pp. This report is available from: Natural Resources Institute, The University of Greenwich, Central Avenue, Chatham Maritime, Kent ME4 4TB, United Kingdom. Fax: (44-16434) 88 00 66. Internet: http://www.nri.org

Biopolitics: A Feminist and Ecological Reader on Biotechnology

Biopolitics: A Feminist and Ecological Reader on Biotechnology is an anthology that aims to "bring together, expose and offer a multitude of approaches, perspectives, tools and concepts with which to problematize the conditions, consequences, possibilities and limitations of biotechnology". The 16 articles—most from well-known writers—are organized into an introduction and four thematic sections: Biotechnology as Culture, Biohazards, Bioethics, Biopolitics. This is a good reader on the basic critiques against genetic engineering and the science and political premises that nurture it. Contains a short but very helpful resources section with: glossary, further reading list, and name and thematic index.

Zed Books and Third World Network, London and Penang, 1995, ISBN 1-85649-336-9, 294 pp. Available from Zed Books, Ltd., 7 Cynthia Street, London N1 9JF, UK; and from Third World Network, 228 Macalister Road, 104000, Penang, Malaysia.

Dynamic diversity

Three useful booklets in the series "Dynamic Diversity" have been published by the Intermediate Technology Development Group of the UK, one each on domestic animal diversity, aquatic diversity and agricultural diversity. They include introductions to the wider issues of livelihood resources, such as food security, erosion of biodiversity and the complex international context. The basic elements for understanding how traditional local communities sustainably manage their biological resources are presented in easy to understand language with good examples and illustrations. Recommended as primers and educational tools.

Patrick Mulvaney, editor, Janet Bell, researcher, *Livestock Keepers Safeguarding Domestic Animal Diversity through their Animal Husbandry* (1996, 17 pp.); *Farmers Safeguarding Agricultural Biodiversity through their Crop Husbandry* (1996, 22 pp.); *Fisherfolk Safeguarding Aquatic Diversity through their Fishing Techniques* (1996, 21 pp.).

Order copies from: Intermediate Technology Development Group, Myson House, Railway Terrace, Rugby, CV21 3HT, UK. E-mail: enquiries@itdg.org.uk; Internet: http://www.oneworld.org/itdg

Especies útiles de un bosque tropical húmedo

Especies útiles de un bosque tropical húmedo, Daniel Querol and others (eds.), is a very interesting book describing livelihood biodiversity in a tropical forest area in southern Nicaragua. Edited by Daniel Querol, author of *Genetic Resources, our Forgotten Treasure* (Third World Network, Penang, ISBN 983-9747-01-0). The bulk of the book contains descriptions (with fine original drawings) of over 100 forest tree and plant species—both native and introduced—together with the main uses given to them by the people living in the area. The identification and description were done by teams including both local and academic experts. The book also contains short reports on wild animals, fish and birds observed in the area, plus common and scientific name indexes. Interestingly, the editors state the collective and ancestral nature of the knowledge published, and threaten to sue anyone patenting local resources.

Güises, Montaña Experimental, Río San Juan, Nicaragua, 1996, 246 pp. Request copies from: Güises Montaña Experimental, Apartado 2715, Managua, Nicaragua. E-mail: gme@uni.rain.ni

Bioprospecting in South Africa, Towards the Development of Equitable Partnerships

Biodiversity Prospecting in South Africa, by Sarah A. Laird and Rachel P. Wynberg, is—according to the authors—the first study of this kind undertaken in the country. The booklet gives an overview to the issue, explains the international and national legal framework of bioprospecting and has some boxes on current or past industry involvement in bioprospecting (Essential Sterolin Products, Hoechst, South African Druggists, SmithKline Beecham). In the last chapter, the authors propose guidelines and recommendations for Biodiversity Prospecting in South Africa. They address the principle of prior informed consent and the need to accord with local communities traditional resource rights.

Land and Agriculture Policy Centre (LAPC), 1996, 104 pp. Order from: The LAPC Publications Officer, Box 243, Wits, 2050 South Africa.

Seed Supply Systems in Developing Countries

Seed Supply Systems in Developing Countries, P. Louwaars and G.A.M. Marrewijk, is a really impressive work by two researchers of the Dutch Technical Centre for Agricultural and Rural Cooperation and the Wageningen Agricultural University. The book is an essay on how current seed supply systems in those countries could lead to the rise of farmers' standard of living. Apparently free of "radical" positions neither for nor against the two main existing paradigms, the authors comprehensively describe and analyse both the informal and formal seed supply systems and point sharply to the advantages and limitations of both systems. After such an evaluation, the book proposes a third way, "integrated seed supply systems", that builds on the positive aspects of each actor (farmers and breeders). It ends with some case studies of seed supply systems and seed industries. Large amount of data and quotations, beautiful presentation and the rigorous but easy—and sometimes even entertaining—language are other positive aspects of this book.

CTA and Wageningen Agricultural University, 135 pp., ISBN 92 9081 1471. Order copies form: CTA, Postbus 380, 6700 AJ Wageningen, The Netherlands.

Seed production and marketing in Asia and the Pacific

For anyone following the evolution of the seed sector in Asia, the Asian Productivity Organization (APO) in Tokyo is a useful information source. An intergovernmental body, the APO organizes round tables, conferences and study tours on issues affecting productivity of various sectors in Asia, including agriculture and the seed market. They publish a range of reports on Asia's seed industry. One recent volume (1995) is *Seed Production and Marketing in Asia and the Pacific.* It contains 13 country reports plus sectoral studies on plant breeding, the use of biotechnology, intellectual property rights and other seed legislations, the growing role of the private sector, etc. A very handy and detailed overview of Asia's seed sector. Readers in Asia and the Pacific can acquire any two books for free, while further requests or other readers are charged a very small fee (US$ 1).

Asian Productivity Organization, Tokyo, 1995, 331 pp. For orders or a full publications list (very broad and interesting) contact: APO, Aoyama Dai-ichi Mansions, 4-14, Akasaka 8-chome, Minato-ku, Tokyo, Japan. Fax: (81-3) 34087220. E-mail: <apo@gol.com> or visit their homepage on the Internet at http://www.ftf-tokyo.com/apo-tokyo/

Biotechnology textbook

A classroom-tested biotechnology textbook written by education staff of the North Carolina Biotechnology Center is designed to help science teachers, students and business professionals throughout the world better understand biotechnology. *Recombinant DNA and Biotechnology*, written by Dr. Adrianne Massey and Dr. Helen Kreuzer and published by the American Society for Microbiology Press, is a how-to book that focuses on teaching and learning basic biotechnology and molecular biology. It comes in two versions: *A Guide for Students*, which sells for US$ 35.95, and *A Guide for Teachers*, which costs US$ 39.95.

Contact: Both versions can be ordered in paperback from ASM Press by calling 1-800/546-2416.

Book on biodiversity

Published by The Johns Hopkins University Press, *The Idea of Biodiversity: Philosophies of Paradise*, by California State University, Monterey, Professor David Takacs describes how, in response to the environmental crisis, scientists have become advocates for the natural world. In the process, scientists are redefining both what it means to be a biologist and the boundaries of science, politics, ethics and nature itself.

Contact: For copies contact Vicki Aversa at (410) 296-0346 or by e-mail at vaversa@erols.com. Professor Takacs can be reached at david_takacs@internet.monterey.edu

Public controversy in biotech

A new book, *Public Controversy in Biotechnology: An Insider's View*, has recently been published by Academic Press/R.G. Landes Co. The book by Stanford University professor Henry I. Miller, MD provides an analysis of how American and other countries' public policies on biotechnology are formulated.

Contact: Jasna Marcovac, Academic Press, 525 B Street, Suite 1900, San Diego, CA 92101. Tel.: 619/699-6382; Fax: 619/699-6715; e-mail: jmarkovac@acad.com. Miller may be contacted at miller@hoover.standford.edu

Lost Crops of Africa Vol. I: Grains

Lost Crops of Africa Vol. I: Grains by the National Research Council, 1996. 408 pp; index, ISBN 0-309-04990-3, paperback. Available from: African Grains Report, FO 2060; National Academy of Sciences, 2101 Constitution Avenue, NW, Washington, DC 20418, USA.

The National Research Council of the United States has recently released the first in a series of books under this title. It focuses on the native foods of the sub-Saharan African and the promise they hold.

Seeds of about 60 species of wild grasses are still gathered for food, of which 10 have been domesticated by African farmers. Some of these are African rice, finger millet, fonio, pearl millet, sorghum and TEFL. All in all, Africa is reported to have more than 2,000 native grains and fruits.

The "loss" noted in the publication is not affecting African farmers since they are still using it as food. Rather, the loss affects the mainstream of international science and people outside rural regions, the authors explain. The earlier low esteems regarding the nutritional value, flavour and the yield of African grains had evidently constrained its use in the West. This volume focuses on native cereals and dispels the myth. The authors describe where and how each grain is grown, harvested and processed and list the benefits and limitations of each as a food source. They argue that African cereals are a storehouse of resources whose qualities offer promise to Africa and to the rest of the world.

Volumes 2 and 3 will be focusing on cultivated and wild fruits, respectively. Future volumes on other food crops are in the offing.

Contact: African Grains Report, FO 2060, National Academy of Sciences, 2101 Constitution Avenue, NW, Washington, DC 20418, USA.

Social change and conservation

Edited by Krishna B. Ghimire and Michel P. Pimbert

Protected areas and conservation policies are usually established with only local nature and wildlife in mind. Yet they can have far-reaching consequences for local populations, often undermining their access to resources and their livelihoods. Published in association with the United Nations Research Institute for Social Development, *Social Change and Conservation* is the first comprehensive discussion of the social consequences of protected area schemes and conservation policies. Drawing on case-studies from North America, Europe, Asia, Central America and Africa, it critically reviews current trends in protected area management, and shows how local people have been affected in terms of their customary rights, livelihoods, well-being and social cohesion. Loss of secure local livelihoods ultimately threatens conservation as poverty and environmental degradation intensify in and around the protected areas. The leading authorities who have contributed to this ground-breaking volume argue for a thorough overhaul of conservation thinking and practice.

Contents:

(1) *Social Change and Conservation: An Overview of Issues and Concepts*, Krishna B. Ghimire and Michel P. Pimbert

(2) *Biodiversity and Human Welfare*, Piers Blaikie and Sally Jeanrenaud

(3) *National Parks and Protected Area Management in Costa Rica and Germany: A Comparative Analysis*, Jens Bruggermann

(4) *Salvaging Nature: Indigenous Peoples and Protected Areas*, Marcus Colchester
(5) *Women, Forest Products and Protected Areas: A Case Study of Jaldapara Wildlife Sanctuary, West Bengal, India*, Chandana Dey
(6) *Local Development and Parks in France*, Andréa Finger-Stich and Krishna B. Ghimire
(7) *Conservation and Social Development: an Assessment of Wolong and other Panda Reserves in China*, Krishna B. Ghimire
(8) *Ecotourism and Rural Reconstruction in South Africa: Reality or Rhetoric?* Eddie Koch
(9) *Management of Wildlife, Tourism and Local Communities in Zimbabwe*, Chris McIvor
(10) *Protected Areas, Conservationists and Aboriginal Interests in Canada*, James Morrison
(11) *Parks, People and Professionals: Putting "Participation" into Protected Area Management*, Michel P. Pimbert and Jules Pretty

Krishna B. Ghimire is a project leader at the United Nations Research Institute for Social Development (UNRISD). Michel P. Pimbert is a Director of The World Wide Fund for Nature (WWF Switzerland).

£18.95 paperback ISBN 1 85383 410 6. February 1997, 340 pages. Further details from: Earthscan, Freepost 1, 120 Pentonville Road, London N1 9BR; Tel.: 44 (0) 171 278 0433. Fax: 44 (0) 171 278 1142.

Biotechnology

This handbook of biotechnology organizations and contacts also lists firms involved in non-medical applications of biotechnology (for example, bioremediation) and provides review articles on topical subjects like the patenting of biotech inventions, financing options, EU funding and the Department of Trade and Industry's Biotechnology Means Business initiative.

Copies can be obtained from BioCommerce Data, Prudential Buildings, 95 High Street, Slough, Berkshire SL1 1DH, UK.

Gene technology

M.T. Dawson, R. Powell and F. Gannon, eds.

Gene technology sets out to describe the components of molecular genetics to the newcomer, and does so in a very successful and logical manner. Much of this success is based on expanding the genetic engineering theme, whereby DNA and RNA are considered as materials and/or templates, and the wide range of enzymes available to the molecular biologist are viewed as tools to cut and paste or copy from a template.

Scientists who interact with molecular biologists but who find the jargon somewhat intimidating will, if they find time to read *Gene technology*, be relieved to learn that, in general, the concepts are quite logical and straightforward. This alone will be good reason to own a copy. Oxford: BIOS Scientific 1996, pp. ix + 118, £17.95, ISBN 1 872748 76 7.

Bioinformatics

DNA vaccines

In 1993, researchers at Merck Research Laboratories in Pennsylvania discovered that injecting mice with a gene for the influenza A virus immunized the animals against the disease. Since this amazing discovery, scientists around the world have been working hard on what has been heralded as the "third generation of vaccines". If you would like to know more, with pointers to all sorts of research and review articles on the topic, browse your way towards the DNA Vaccine Web site run by Robert Whalen at the CNRS, Paris. http://www.genweb.com/Dnavax/dnavax.html

Online agriculture atlas

Want to know the average rainfall in Chengdu, China, in July? Get the minimum winter temperature in the Indus River valley? Scope out the Tasmanian rail system? Plug into the new World Water and Climate Atlas for Agriculture, now on the Web (atlas.usu.edu) and on CD-ROM. The atlas is a joint production of the International Irrigation Management Institute, based in Sri Lanka, and scientists at Utah State University in Logan. It includes three decades of temperature and rainfall data from 56,000 weather stations worldwide. And it has developed a new measure, "evapotranspiration", which helps irrigators gauge total water expenditure in an area by combining what is used to grow crops with that lost by evaporation.

Utah State engineer George Hargreaves says he is already using the atlas to help the Inter-American Development Bank decide on appropriate crops to finance in Honduras. World Bank environmental official Ismail Serageldin calls the atlas "a user-friendly program that agronomists can use to assist even the poorest farmers". (Source: *Science*, Vol. 276, 4 April 1997)

IDRC Website

The International Development Research Centre in Ottawa has established a Website offering access to a rich source of information and knowledge about development and the research carried out by developing world scientists, many of whom work in close collaboration with Canadian researchers.

IDRC Publications Online allows you to search IDRC's collection of more than 3,000 multimedia documents, including an electronic weekly that features articles and interviews with many of the principal actors in international development today. The IDRC Library maintains a comprehensive list of Internet sites relating to international development called To the World; on-line books; a/v materials; and databases.

Contact: The Website is located at http://www.idrc.ca (Source: *The AgBiotech Bulletin*, June 1997)

BIOSAFE

A brochure entitled "Community Documentation Centre on Biotechnology Safety and Regulation—Guideline for Users" has been issued by the Institute for Systems, Informatics and Safety (ISIS) of the Joint Research Centre at Ispra, Italy.

The Documentation Centre (BIOSAFE) has been created to collect and analyse information which is relevant to the Commission for the harmonization of the existing member States' legislation on the production and exploitation of genetically modified organisms. BIOSAFE produces an annual bulletin containing information on various aspects of the harmonization of the legislation and a list of publications with abstracts and an index. The bulletin is circulated to all competent authorities responsible for the implementation of the Biotechnology Directives, and to any other interested parties free of charge.

The Documentation Centre has announced that the documents listed in the bulletins will soon be accessible on the WWW site "Biotechnology & Environment". The site will also contain updated information on SNIF (Summary Notification Information Format) and on the EC Decisions

and Directives concerning the contained use and the deliberate release of genetically modified organisms.

Contact: European Commission, Joint Research Centre, Public Relations and Publications Unit, I-21020 Ispra (VA), Italy. Tel.: 39/332-789889; Fax 39/332-785409; E-mail: prp @jrc.it; Website:http://www.jrc.org/jrc/index.asp (Source: *The AgBiotech Bulletin*, June 1997)

Plant breeding news

The Food and Agriculture Organization (FAO) of the United Nations is hosting an electronic newsletter called *Plant Breeding News* designed to promote the exchange of information among all interested persons including plant breeders, researchers, policy makers, crop extension experts, NGOs, students, etc. The newsletter is meant to be an informal forum on plant breeding technologies and related issues including announcements, inquiries, technical discussions, unreferred articles, etc. Participation is free and is based on voluntary contributions of information from members. By subscribing you will receive one monthly PBN edition.

Contact:
E-mail to: MAILSERV@MAILSERV.FAO.ORG

Leave the subject blank and write in the first line of the e-mail message: SUBSCRIBE PBN-L

You will soon receive a welcome message confirming your subscription.

If you have any problems with your subscription, please contact: PBNL@MAILSERV.FAO.ORG (Source: *The AgBiotech Bulletin*, June 1997)

Plant genome data and information center

The Plant Genome Data and Information Center has recently been actively updating its Website. New additions include: the 1996 USDA National Research Initiative Competitive Grants Awards for Plant Genome; the Plant Genome Grant Information Directory; a Directory of Sponsored CRIS Projects and Bibliography Series; the recent Probe Newsletter; and other information.

Contact: The Website is at http://www.nal.usda.gov/pgdic (Source: *The AgBiotech Bulletin*, June 1997)

IMGT database

The international ImMunoGeneTics database (IMGT) specializes in immunoglobulins (Ig), T-cell receptors (TCR), and the major histo-compatibility complex (MHC) of all vertebrate species. Comprising annotated sequences and alignment tables, IMGT includes two databases: LIGM-DB contains more than 19,000 Ig and TCR sequences from 78 species, and MHC/HLA-DB contains alignment tables for Class I and Class II human leucocyte antigens. [IMGT contact: Marie-Paule Lefranc (lefranc@ligm.crbm.cnrs-mop.fr)]

IMGT database access

- WWW at CNUSC (Montepellier, France): http://imgt.cnusc.fr:8104; informatics, denys.chaume@cnusc.fr; bioinformatics, giudi@ligm.crbm.cnrs-mop.fr
- WWW at European Molecular Biology Laboratory—European Bioinformatics Institute (Hinxton, UK): http://www.ebi.ac.uk/imgt; contact malik@ebi.ac.uk.
- Sequence Retrieval System: http://www.ebi.ac.uk/srs/srsc (Select "Search sequence libraries"; on the next screen, click off the "Swissprot" box and click on "IMGT").
- Ftp: ftp//ftp.ebi.ac.uk/pub/databases/imgt
- CD-ROM: Database accompanying the Nucleotide Sequence Database of EMBL.

(Source: *Human Genome News*, October-December 1996)

Genes on the Internet

As the European Parliament discusses the European Commission's Proposal of Directive on the Legal Protection of Biotechnological Inventions, and pressure on the countries in the South increases to force them to implement intellectual property rights, NGOs may be interested in having direct access to what is actually being patented. Although comprehensive information on patents is very highly added-valued, some sites in the Internet allow to have a first glimpse at what is out there for free. Here are some of these Internet Patent Sites:

The Biotechnology Information Center (BIC) maintains a service with all the US-granted patents in the area of agricultural biotechnology. The service includes a comprehensive list of such patents from 1994 on, and the complete patent text for those of 1994 and 1995 in a WISE server which does not allow for sophisticated cross searches. Still, the possibility of having the complete text of patents is highly interesting. Website: http://www.nal.usda.gov/bicBiotech_Patents/

More concerned in maintaining its very expensive set-up than in making its information easily accessible for the public, the EPO does not provide free information on its patents. So do not look for such information in its home page. Website: http://www.Austria.EU.net/epo/

IBM has set the IBM Patent Database, which gives access to US patents. It allows searches by terms and by US patent numbers, including crossed searches in different fields. Both an abstract of the invention and the patent claims are easily accessible for every patent, which makes this database very interesting. It is a pity that it only covers US patents, which are published only after they have been granted. Website: http://patent.womplex.ibm.com/

The United States Patent and Trademark Office (USPTO) and the Center for Networked Information Discovery and Retrieval (CNIDR) have put on the Internet the US Patent Bibliographic Database. The database provides the same basic information as the IBM database, but for the patent claims, which are not included. The only advantage with respect to the IBM site are confidentiality and the possibility of utilizing the US patent classes. Website: http://www.uspto.gov

The Canadian Intellectual Property Office (CIPO) offers access to a test version of the Canadian Patent Bibliographic Database, covering the period from 1 October 1989 to the present. The information is not very interesting, but for the fact that it includes FILED patents, which means that the info is more recent than that given in the USPTO. But it does not contain any abstract or claim, just to check if a given patent has been awarded in Canada. Website: http://strategis.ic.gc.ca/sc_innov/patent/engdoc/cover.html

MicroPatent® is a commercial provider of patent information with a free subscription service that includes the free retrieval of the full text of the new patents at the USPTO. Website: http://www.micropat.com/

The Internet also hosts web pages dealing with Rights beyond patents. The Working Group on Traditional Resource Rights (WGTRR) has set home page. The WGTRR staff has taken the question of links very seriously: they have a good collection of links with organizations active in areas related to Traditional Resources Rights. Website: http://users.ox.ac.uk/~wgtrr

Some interesting Internet Websites are not about genes or biotechnology but about trade and intellectual property laws. Persons interested in WTO questions may find it useful to have on-line access to the official texts of the different Treaties. The Final Act and Agreement Establishing the World Trade Organization, the General Agreement on Tariffs and Trade, the results of the Uruguay Round (including GATT 1994) can be accessed through the Web page of the "International Trade Law Monitor" of the Law Faculty of the University of Tromsø, Norway.

The Page provides links to the GATT treaties, to the WTO homepage and to a free program called "Guide to WTO". This interactive guide can be downloaded and it gives reasonably objective information on the structure and history of WTO. Website: http://itl.irv.uit.no/trade_law/nav/freetrade.html

The WTO homepage offers press releases, derestricted documents, including the ones for the recent Singapore Ministerial Conference, as well as the latest editions of WTO's own newsletter called "WTO FOCUS". Website: http://www.wto.org

More critical information on trade and the processes in WTO can be found on the Website and the gopher of the Institute of Agriculture and Trade Policy (IATP). Website: http://www.igc.apc.org/iatp/trade.html

The International Institute for Sustainable Development (IISD) also offers interesting information on trade laws and the WTO. Of special interest might be a moderately critical analysis on WTO's performance in its first two years. Website: http://iisd1.iisd.ca/trade/wto/

A Call to Action (CD-ROM)

A Call to Action is a CD-ROM co-published by the FAO's Initiative for Domestic Animal Diversity, probably one of the few concrete results of the World Food Summit. Addressed to Governments, NGOs, international agencies and training and research groups, this nicely presented CD contains information on the importance of animal genetic diversity, a sample of customized project management software, guidelines for domestic animal genetic resources management plans, and a presentation to the Domestic Animal Diversity Information System, DAD-IS, a database which is available through the Internet (http://www.fao.org/dadis). The CD—and the on-line database—contains data on 3,800 domestic animal breeds of 180 countries, and a preliminary list of contact persons and institutions working on animal genetic resources in every country. The DAD-IS includes a security system that requires passwords in order to access more precise and detailed data, thus giving countries control as a measure to comply with the provisions of the Convention on Biological Diversity. The CD is worth having if you are interested in domestic animal biodiversity.

Available from: FAO, Viale delle Terme di Caracalla, 00100 Rome.

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