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Genetic Engineering and Bio-technology Monitor

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Special article: Biotechnology in South Asia: Issues of Technological Capability and Development, by Rohini Acharya, Maastricht Economic Research Institute on Innovation and Technology (MERIT) and visiting PhD Fellow at the United Nations University Institute for New Technologies (UNU INTECH) at Maastricht, The Netherlands.

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UNITED NATIONS INDUSTRIAL DEVELOPMENT ORGANIZATION

LABNET

International Network for Lactic Acid Fermentation Technology

INFORMATION NOTE NO.: 1 | Date: November 1993

Development of an international network for lactic acid fermentation technology (LABNET)

Lactic acid bacteria (LAB), so named because of their ability to convert sugars to lactic acid, are an industrially important group of bacteria. They play essential roles in the manufacture, and, where relevant, ripening, of fermented foods and beverages such as cheeses, meats, bread, vegetables, fermented milks and wine. These are important products of the indigenous agri-food sector throughout the world. The fermented food sector is a growth area world-wide due to a consumer-expressed need for natural, safe foods. In addition, LAB have applications in the non-food industry, for example, in the area of the oral immunizations, because LAB are regarded as generally safe micro-organisms and as such are suitable hosts for oral vaccine production.

UNIDO has created a new programme in biotechnology for the benefit of developing countries in which new research advances for improvements to traditional lactic acid fermentation processes may be facilitated through linkages and networking arrangements of existing national and regional programmes of LAB. Several research groups in Asia and in Africa have taken steps to join the network. Professor K. Komagata of Japan, former Director of the World Data Center, is to prepare a proposal as a UNIDO consultant for a bioinformatics network in industrial lactic acid culture collections and is to help mobilize resources for its implementation. A computer software and database programme on lactic acid fermentation design that calculates on-line information about specific fermentations, including specific growth rates, substrate consumption and product formation will be one of the LABNET's resources. Once the UNIDO LAB network is in place and functioning, the European Laboratory Without Walls in the field of biotechnology of lactic acid bacteria will be requested to serve as the European node of the network.

A LABNET column about activities, including LAB cultures collections, research in progress, and commercial and industrial applications, that are taking place in the UNIDO LAB network will be regularly included in future issues of the UNIDO *Genetic Engineering and Biotechnology Monitor*. Groups interested in participating in the network are invited to write to UNIDO's Biotechnology and Genetic Engineering Unit in Vienna, Austria.

Further information is available from: The Biotechnology and Genetic Engineering Unit, United Nations Industrial Development Organization (UNIDO), Vienna International Centre, P.O.Box 300, ViennaA-1400, Austria Tel.(43-1)21131ext.4336, Fax:(43-1)2307355.

Lactic Acid Fermentation of Non-Dairy Food and Beverages - A UNIDO-Sponsored Programme

A UNIDO-sponsored joint research project to develop high protein content lactic beverages from vegetables is being carried out since January 1987 at Korea University in Seoul and MIT in Cambridge, MA, USA. The prime objectives of the Phase I research project were to establish optimum pretreatment conditions of cereal for lactic acid fermentation and to select and improve the microbial strains. In this study, the beneficial effects of

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prefermentation and extrusion cooking of rice prior to lactic fermentation were demonstrated. A strain of *Leuconstoc Mesenteroides* separated from a traditional Korean fermented fish product, Sikhae, could produce acceptable apple juice-like flavour from a rice-soy milk substrate.

Encouraged by the first phase results, a Second Phase UNIDO Project was launched in July 1990 with somewhat extended programme activities, entitled "Industrialization of lactic acid fermentation technology of cereals and its dissemination to the developing countries". It comprised three major activities: a continued joint research programme between Korea University, Korea Food Research Institute and the Technical University of Denmark, an international training course for food fermentation technology, and an international workshop on this subject.

Bacteria in fight against dysentry

The past few months have seen the appearance of several papers containing concrete evidence that innocuous organisms can combat major intestinal infections in humans and other animals. One group of reports has focused on the inoculation of a protective intestinal flora into livestock as a means of safeguarding them against colonization with *Salmonella* and other pathogens. Thus researchers at the Food Directorate, Health and Welfare Ottawa, Canada, have found that a cocktail of organisms isolated from the faeces of healthy adult hens, given by mouth to newly hatched chicks, protects them from invasion by an enteropathogenic strain of *Escherichia coli* that has been associated with numerous outbreaks of haemorrhagic colitis in humans (*Letters in Applied Microbiology*, 14:191, 1992). There are clearly the makings here of a routine method of controlling this and other serious human diseases.

Even more exciting is a paper published by a team including Sylvia M. Gonzales at the Centro de Referencia para Lactobacillos in Chacabuco, Argentina. Like the report from Ottawa, it originates in the belief that whereas the neonatal intestinal tract is free of germs, the complex flora subsequently acquired from the mother and other sources plays an important role in later defense against marauding pathogens. In this case, however, the aim is to evolve a strategy for prophylaxis against human diseases. Defined strains are thus being used.

Gonzales and colleagues worked with two strains, one of *Lactobacillus casei* and the other of *L. acidophilus*, which they obtained from human faeces. They isolated the organisms in pure culture, inoculated them separately into 10 per cent solutions of skimmed milk powder, and mixed the two fermented milks together after eight hours of incubation. The group chose as the target pathogen a strain of *Shigella sonnei*, because the dysentery caused by this organism is particularly common in their region of Argentina.

They found that milk fermented with *L. casei* and *L. acidophilus* was dramatically effective in inhibiting *S sonnei* infection. Every one of the mice dosed orally with the pathogen after feeding for eight days on the milk survived the infection. The corresponding survival rate in control mice was 60 per cent.

As described in the *Journal of Applied Bacteriology* (73:407,1992), pretreatment with milk also markedly inhibited colonization of the liver and spleen with *S. sonnei*. The organism disappeared from these organs by the tenth day, but remained at a high level in the untreated mice. There were also raised levels of antibodies against the pathogen in both the serum and intestinal fluid, suggesting that the fermented milk also increases the systemic immune response. The Argentine group also has preliminary evidence that the fermented milk can be used to treat and prevent infantile diarrhea. (Source: *Bio Technology*, Vol. 11, January 1993)

Lactic acid bacteria prevents tooth decay

Aizo Matsushiro, working in Osaka, has developed a preparation containing a particular strain of the lactic acid bacteria found in "live" yogurt, *Streptococcus salivaris*. Matsushiro found that this strain produces large amounts of an enzyme called dextranase. These bacteria can survive in the environment of the mouth, and are harmless to humans. According to Matsushiro, when in the mouth the bacteria suppress the formation of "firm" dental plaque, which is a major cause of tooth decay. Any plaque formed is "loose" and can be simply rinsed away. (European patent application 0524732) (Source: *Chemistry and Industry*, 15 February 1993)

From salad days to salad weeks

To keep salads with a heavy dressing fresh, extra bacteria should be added and the salad allowed to ferment, according to Martin Bonestroo, University of Wageningen, The Netherlands. The technique is said to extend the shelf-life of such salads to about five weeks if stored at temperatures below 7° C, and he says it makes them taste better — "a pleasant, mildly sour taste".

The use of the bacteria answers consumer pressures by making artificial preservatives unnecessary while saving a large amount of spoilage resulting from the micro-organisms that usually contaminate such salads. The technique uses *Lactobacillus* bacteria that have been isolated from the water in which soy curd has been soaked. These are the bacteria used to make yogurt and salami and grow well at 40-50° C.

The bacteria are mixed into the dressing, and after preparation and packaging, the salads are incubated for seven hours at 45° C and then refrigerated. The lactic acid produced during incubation is sufficient to prevent growth of other bacteria at lower temperatures. However, the technique can only be used on salads that have less than 70 per cent solid ingredients. (Source: *European Microbiology*, January/February 1993)

A. NEWS AND EVENTS

UNIDO News

UNIDO's programme in biotechnology

In the final year (1993) of operation as a UNIDO project, the capability of the International Centre for Genetic Engineering and Biotechnology (ICGEB), prior to its becoming an autonomous agency, has reached the product-development stage. The ICGEB has filed a European patent for its hepatitis vaccine, while commercialization possibility of an AIDS diagnostic kit is under active consideration. UNIDO, in collaboration with the ICGEB, has taken an initiative to develop a network of 17 affiliated centres of ICGEB to serve as biotechnological resources institutions and or reference centres for developing countries. Another new initiative is a proposal to extend the application of molecular techniques to conservation, i.e. molecular biodiversity. In the area of bioremediation Algeria, Indonesia, Kuwait, Mexico and Venezuela have offered to work closely with UNIDO.

The approach for new initiatives is based on interdependency between and within regions and collaboration with new partners - the financial and business communities and non-governmental organizations (NGOs). Actions have been taken to facilitate dialogues among biotechnology industry associations. Discussions with NGOs have begun.

A major initiative to facilitate the release and commercialization of transgenic products is the development of support resource databases relating to biosafety. This is part of the Biosafety Information Network and Advisory Service (BINAS) recommended to the UNIDO UNEP WHO FAO Informal Working Group on Biosafety as a follow-up to the Voluntary Code of Conduct on the Release of Organisms into the Environment being promoted by UNIDO since 1991. The implementation of BINAS includes a central server to be located at UNIDO and accessible over the Internet and X.25 public data networks. The BINAS activities will be supported by the ICGEB's on-going yearly training courses for officers of National and Institutional Biosafety Committees in risk assessment methodologies. Other data being included is a list of biosafety experts and procedures for field releases. This data and information will be made available to Member States through UNIDO's Biosafety Information Network and Advisory Service (BINAS) programme, to be promoted initially in Asia with cooperation from the ASEAN Subcommittee on Biotechnology.

To promote commercialization of biotechnological research and development, the Biotechnology and Genetic Engineering Unit has established a working relationship with financial institutions such as the Asian Development Bank and World Bank as well as with the biotechnology industrial associations, such as the Senior Advisory Group on biotechnology and American Biotechnology Company Association. A joint UNIDO - World Bank Conference on Marine Biotechnology in South-East Asia is planned to be held in Thailand and a meeting of biotechnology industry to be hosted by UNIDO in Vienna within 1993.

While major basic and applied multidisciplinary research work will continue to be carried out by joint research teams at the ICGEB's New Delhi and Trieste Laboratories and its affiliated centres in 17 countries, UNIDO promotes a number of international and regional research and development networks on themes of common interests. Major themes include lactic acid bacteria, bioconversions for the mushroom industry, cassava bioprocessing, marine biotechnology, bioremediation and a molecular inventory of biological diversity.

An innovative type of commercial venture on genetic resources prospecting recently practised, offers new opportunities for developing countries endowed with rich natural resources to benefit more equitably from the joint prospecting. In this connection, and in relation to biology trading in general, the issue of intellectual property rights is crucial to the growth of biotechnology development. As such, UNIDO is conducting an extensive and in-depth review on the current status and outstanding issues in relation to biotechnology with a view to promote closer international cooperation.

Special efforts have been made to strengthen the capacity of African countries to benefit from modern biotechnology. Zimbabwe has agreed to host a training workshop on genetic engineering techniques for scientists from African countries. An African consultant will also be engaged to promote biotechnology among small-scale entrepreneurs in Ghana.

To facilitate the exchange of information and knowledge on the application of modern biological techniques in developing countries, information will be disseminated to researchers in developing countries through the quarterly bulletin - the *UNIDO Genetic Engineering and Biotechnology Monitor*. Initially, areas to be promoted are biotechnology of lactic acid bacteria, bioconversions and mushroom biotechnology and cassava bioprocessing.

Finally, in collaboration with other units in the Division, a working group has been formed to conduct a review study on the issue of biotechnology commercialization and intellectual property rights, as recommended by the ACC (Administrative Committee for Coordination) Task Force.

Establishment of a biosafety information and advisory network (BINAS)

UNIDO is about to initiate a project aimed at strengthening its in-house capability in order to assist, on request, member countries to:

(a) Establish national and institutional biosafety committees;

(b) Access data related to field trials of GMOs;

(c) Access data needed for risk assessment of release of GMOs into the environment.

The objectives of the project are:

1. To strengthen capabilities of national and institutional biosafety committees by the provision of a decision support platform intended to minimize recourse to outside expertise.

2. To facilitate international technology transfer by providing the biotechnology industry with time saving access to information on national biosafety regulations and enforcement authorities.

The core services to be provided by BINAS will include:

1. National and institutional biosafety contact points

A database of national and institutional biosafety committees responsible for issuing and implementing regulations pertaining to containment standards and environmental releases of genetically modified organisms.

This will be accessible by industry and provide pointers to the appropriate authorities and sources of information.

2. Guidelines and regulations for contained and non-contained uses of genetically modified organisms.

A database of national biosafety regulations in industrial and developing countries will provide industry with the acceptable safety limits within which it would have to conduct its operations in a given country. It would also provide regulators with an overview of international biosafety standards.

3. Roster of experts

Databases of experts in the areas of contained applications, field testing, environmental impact assessment and regulatory standards. National and institutional biosafety committees will thus be given access to independent expertise, as needed.

4. Release data

A database of information on the release of genetically modified organisms to be compiled from ICGEB affiliated centres, public international and national institutions.

The core structure of this database will contain the following data fields:

(a) The national regulatory authority overviewing the release;

(b) The party conducting the release;

(c) A description of the release including data on the host organism, the genetic modification, environmental and field testing conditions (subject to confidentiality arrangements);

(d) A summary of data collected during the field trials;

(e) Mitigation and termination procedures for field releases.

Access to this information will facilitate both industry and national regulatory authorities with the planning and evaluation of applications for releases of genetically modified organisms. In addition, the familiarity gained from previous releases will reduce regulatory bottlenecks.

5. Molecular, organismal and ecological data

Access to molecular sequence data (vector and gene sequences) together with tools for their analysis and taxonomic and ecological data will be provided.

The purpose of these will be to provide national and institutional biosafety committees with the tools needed to evaluate the stability of genetic constructs.

6. Bibliographic data

A bibliography and, where possible, abstracts of scientific articles describing the release of genetically modified organisms.

7. Prior informed release data

Data related to compliance with Article 19.4 of the Biodiversity Convention. Article 19.4 includes the obligation to *"provide the Contracting Party into which the organisms are to be introduced any available information concerning the use and safety regulations required by the Contracting Party in handling such organisms, as*

well as any available information on the potential adverse impact of the organisms covered". BINAS can be used as the conduit through which such information could be made available in the public domain, thus facilitating industry to discharge its responsibility vis-à-vis the Convention.

8. Electronic bulletin board

To provide a forum for the discussion of topics related to biosafety issues.

The implementation of BINAS will include a central server to be located at UNIDO that will be accessible over the Internet and X.25 public data networks. Some of the data sources will be maintained on the BINAS server, whereas access to other data such as taxonomic and ecological databases will be provided via network links to other database hosts (MSDN, OECD, IRRO, etc.).

The BINAS activities will be supplemented by the on-going annual courses of ICGEB aimed at training officers of national and institutional biosafety committees in risk assessment methodologies.

The BINAS project further strengthens inter-agency collaboration amongst the members of the Informal Biosafety Working Group of UNIDO UNEP FAO WHO by linking their relevant databases. It will provide other international initiatives (e.g., SEI, IRRO, OECD, ISAAA) with a complementary biosafety information service.

Further information is available from: The Biotechnology and Genetic Engineering Unit, United Nations Industrial Development Organization (UNIDO), Vienna International Centre, P.O. Box 300, Vienna A-1400, Austria. Tel.: (43-1) 21131 ext. 4336, Fax: (43-1) 230 7355.

UN and other organizations' news

OECD group consider biotechnology

The Seventh Plenary Session of the Group of National Experts (GNE) on Safety in Biotechnology, formed by the Organization for Economic Cooperation and Development (OECD), was held in Paris on 14-18 December 1992. Working groups of the GNE are presently formulating general principles for the regulation of large-scale releases of crop plants and micro-organisms. Bio-fertilizers and live-genetically engineered vaccines are among the first micro organisms to be considered. Food safety issues, particularly those associated with aquatic food organisms, are also being reviewed.

Several draft documents are currently being proposed, but at this stage, are not publicly available. It is anticipated, following the release of these reports, that the role of the GNE may be expanded to enable it to undertake a wider range of tasks such as studies on public perceptions of biotechnology. (Source: *Australian Biotechnology*, Vol. 3, No. 1, February 1993)

After UNCED: Biotech, biodiversity and genetic resources

The United Nations Conference on Environment and Development (UNCED), or "Earth Summit", of June 1992, emphasized the essential role of biotechnology. The ambitious, 40-chapter "AGENDA 21", outlining the actions needed over the years 1993-2000, includes chapter 16, "Environmentally sound management of Biotechnology". The UN Secretary-General is currently reviewing the whole spectrum of UN involvement in Science and Technology, across all the many agencies concerned - food and agriculture (FAO), health (WHO), industrial development (UNIDO), development (UNDP), environment (UNEP), education, science and culture (UNESCO), and others.

Also signed at the Rio conference was the Convention on Biological Diversity, again underlining the role of biotechnology in the sustainable exploitation of genetic resources; but with controversy in the negotiations concerning intellectual property rights (I.P.R.) on technology, and rights of access to and utilization of germplasm. The new US administration has to consider whether they can reverse the previous refusal, without damage to US biotech interests.

UNEP has follow-up responsibilities for the Bio-diversity Convention, and Expert Panels are advising the new Executive Director, Canadian Elizabeth Dowdeswell on science priorities; the financial mechanism for the new fund envisaged by the Convention; technology transfer, I.P.R. and germplasm; and whether a binding international protocol is needed on the safe transfer and use of modified organisms - perhaps a chance for the benefits of the European Community legislation to be extended world-wide. The Panels met in Nairobi (December 1992 and February 1993) and Montreal (March 1993). International conferences on the same topics included that at the African Centre for Technology Studies (ACTS) 26-29 January ("National Interests and Global Imperatives") and Trondheim, 24-28 May, when the Government of Norway hosted the "Norway UNEP Conference on Biodiversity". These meetings lead up to the first meeting of the Intergovernmental Committee on the Convention on Biological Diversity, the ICCBD, at UNEP in September 1993. Further details are available from: UNEP activities: Mr. Hamdallah Zedan, Coordinator for Biodiversity and Biotechnology, UNEP, P.O. Box 30552, Nairobi, Kenya. Fax. (254-2) 226886 or 219270. For

ACTS, contact Dr. Calestous Juma, P.O. Box 45917, Nairobi, Kenya. Tel.: 254(2) 741651/744047; Fax: 74399. For ACTS Biopolicy Institute, Witmakersstraat 10, 6211 JB Maastricht, The Netherlands. Tel.: (31)43258499; Fax: (31) 258433. (Source: *EBIS*, Vol. 3, No. 1, 1993)

UNESCO creates bioethics unit

The United Nations Educational, Scientific and Cultural Organization, under the Draft Programme and Budget for 1994-1995, "Social Change, Peace and Human Rights", will give increased attention to the exchange of information on bioethics, and study the possibility of formulating international instruments in this area.

Head of the new Bioethics Unit is George B. Kutukdjian, who will assist the International Consultative Committee of Bioethics to be established by UNESCO this year. Director-General, Federico Mayor, proposes focusing on issues concerning the human genome and protection of the genetic heritage. The committee will evolve from a Task Force headed by Noëlle Lenoir of France's Constitutional Council. (Source: *EBIS*, Vol. 3, No. 1, 1993)

Regulatory issues

Gene-therapy risks again under scrutiny

An attempt to devise safety standards for viruses used as gene-carrying vectors in human gene therapy sparked controversy at a recent meeting of the National Institutes of Health Recombinant DNA Advisory Committee (NIHRAC, Bethesda, MD). The Committee is at odds with officials from the Food and Drug Administration (FDA, Bethesda, MD), who share responsibility for evaluating, setting, and revising safety standards for vectors and other materials used in gene-therapy procedures.

The first line of gene-therapy vectors has consisted of RNA-containing retroviruses that, in their native form and under some circumstances, give rise to tumours in rodents and non-human primates. However, before such viruses are used in human subjects, their genes are extensively modified to render the viruses no longer "competent" to replicate by themselves or, presumably, to cause tumours of any kind.

Until recently, these retrovirus-based vectors were thought to be irreversibly disarmed. But last year researchers at Genetic Therapy Inc. (GTI, Gaithersburg, MD) identified a "break-through" replication-competent retrovirus in a vector batch that they were testing. This spontaneously produced, genetically reverted form of retrovirus was readily detected by using the quality-control assays run routinely just for such purposes. The breakthrough appears to have been a one-time occurrence among the 50 large-scale production runs conducted so far.

There are at least four safety barriers in place between GTI vector production - at which time a spontaneous breakthrough is most likely to occur - and the introduction of the carefully screened, vector-containing materials into patients. Moreover, based on the breakthrough incident at GTI and on tumour development in monkeys exposed to high doses of similar retroviruses, GTI estimates that the chances of gene-therapy patients developing malignancies following exposure to retroviral vectors are extremely remote.

FDA officials view the issue more cautiously and are proposing that a series of highly sensitive assays for detecting such viruses be put in place. (Extracted from *Bio Technology*, Vol. 11, January 1993)

Euroscientists grumble over gene laws

A survey questionnaire, mailed recently to 576 members of the European Molecular Biology Organization (EMBO) by, Isaac Rabino, an assistant professor for biological and health sciences at the State University of New York (Empire State College), compares the attitudes of scientists in various European countries about their governments' - and their fellow citizens' - views on genetic research.

The results, coming from 400 recombinant DNA researchers and published in the October issue of *Biotech Forum Europe*, are instructive: In Germany and Switzerland, more than 90 per cent of the respondents worry that their nation could lose its competitive edge in this field because of regulations and the negative climate of public opinion. France and the United Kingdom gave the most positive responses. And there is precious little respect among this group for current EC regulations, which must be incorporated into all national laws: of the scientists working in EC nations, only 20 per cent saw current EC directives as beneficial, while 27 per cent labelled them a "major constraint" to research.

The media got no more respect than EC legislators: 33 per cent of the respondents think media coverage has been harmful, leading to emotional and ill-informed public judgements. However, 67 per cent reported no negative impact on their own research, suggesting that perceptions of a negative public climate apply more to anticipated than current problems. (Source: *Science*, Vol. 258, 6 November 1992)

GMOs in the environment

The Second International Symposium on the Biosafety Results of Field Tests of Genetically Modified Plants and Microorganisms was held in Gosiar, Germany from 11-14 May 1992 with some 250 participants. A 296-page report of the proceedings has been compiled

The papers presented are collected under various headings:

- Field test results with traditionally modified plants and micro-organisms;
- New biosafety results of field tests with plants;
- New biosafety results of field tests with micro-organisms;
- Biomedication studies;
- Biosafety aspects of commercialization;
- New information on food safety and effects on non-target organisms.

The report represents an important statement by scientists from some 30 countries on the "State of the Art" of biosafety results. It is a major contribution to removing much of the "uncertainty" surrounding the conjectural risks of recombinant organisms in the environment. The Summary of Results prepared by the editors is available in English, French, Japanese and Spanish and concludes "hundreds of field experiments in many countries have been reported, and so far no harmful events to our environment were detected. No adverse consequences have resulted from work for more than 15 years in laboratories and in over 500 field releases".

The results presented at the Symposium were obtained in small and some large-scale field trials designed to obtain risk assessment data and to assess the performance of modified organisms in the environment. For plants, the biosafety issues considered included gene stability, gene transfer, dissemination of pollen and seed and direct and indirect effects of modified traits. For micro-organisms, the biosafety issues considered included persistence, dissemination, population dynamics, competition and community effects. With typical scientific caution the report notes that "in certain cases one is not 100 per cent sure that there is no risk at all. Thus, there is a need to assess the perceived levels of risk and to determine if they represent an increase over acceptable 'natural' levels".

Report available from Dr. Rudolf Casper, Biologische Bundesanstalt, Messeweg 11, D-3300, Braunschweig at DM 15. (Source: *EBIS*, Vol. 2, No. 4, 1992)

General

Hopes for treaty

Prospects for the international Biodiversity Convention agreed last year are looking brighter. The UN Environment Programme has announced that it will set up a "temporary" secretariat in Geneva to coordinate the treaty. The convention may come into force sooner than was expected at the June 1992 Earth Summit, because of changes of attitude in Europe and the USA.

Thirty countries need to ratify the treaty before it begins to operate, but disagreement within the European Community looked certain to deprive the convention of 12 votes until after 1993. The United Kingdom wants money for conservation in poorer member States to be channelled through the World Bank, not the Community.

In December 1992, however, Community countries pledged to ratify the treaty this year. Denmark, which took over the Community presidency in January 1993, wants the disagreement resolved quickly. In the USA, President-elect Bill Clinton was expected to reverse the United State's decision at Rio not to sign the treaty. (Source: *New Scientist*, 9 January 1993)

Cassava Biotechnology Network

The Cassava Biotechnology Network (CBN) was organized by CIAT in 1988. Since cassava is almost entirely grown and consumed by resource-poor people in tropical developing countries, the CBN attempts to provide an effective link between advanced researchers and the agricultural objectives and needs of small farmers and consumers. Thus, the main goal of the CBN is to exploit biotechnology and more basic research to overcome the negative features of the crop, enhance its advantages and open new opportunities for the crop; by doing this, the network will bring cassava science and technology to the level of other important crops.

As a first step, research constraints in cassava production, processing and utilization were identified and prioritized for biotechnological approach and more basic biochemical or genetic research. Constraints include viral diseases, photosynthesis under stress, root perishability after harvest, starch and protein quality and cyanide toxicity.

The CBN has received wide acceptance by the scientific community. In the first bi-annual scientific meeting of the CBN, held in Cartagena, Colombia, 75 communications were presented including socio-economic assessment of biotechnology research. Research concentrated on both developing an understanding of some critical cassava constraints such as cyanogenesis, and developing the tools for approaching such problems through biotechnology, e.g. molecular mapping and DNA fingerprinting, plant regeneration through somatic embryogenesis and genetic transformation mediated by *Agrobacterium tumefaciens* and biolistic techniques; *in vitro* conservation and cryopreservation. For more information on CBN contact: Dr. Claude M. Fauquet, Co-Director ILTAB, The Scripps Research Institute, 10666 N. Torrey Pines

Road, LaJolla, CA 92037, USA. (Source: *Bio Link*, Vol. 1, No. 1, 1992)

Rice biosafety workshop

In a programme sponsored by the US Department of Agriculture, the Rockefeller Foundation, and the World Bank, Stanford Law School and the Thai National Center of Genetic Engineering and Biotechnology organized a consultation on rice biosafety in Cholburi, Thailand, in early September 1992. The programme reviewed the existing state of knowledge with respect to gene flow from rice into its wild relatives and with respect to the possibility that such gene flow might present any environmental risk.

In addition, it reviewed the biotechnology regulatory situation in Asia; regulatory capabilities are being rapidly developed. A report of the consultation is now being prepared; to obtain a copy when it is finished, please contact: John Barton, Stanford Law School, Crown Quadrangle, Stanford, CA 94305-8610, USA. (Source: *Bio Link*, Vol. 1, No. 1, 1992)

PAN Asia and the Pacific

The Regional Centre for Pesticide Action Network Asia and the Pacific (PAN AP), previously hosted by the International Organization of Consumers Unions, has recently established an independent centre in Penang, Malaysia. In collaboration with other PAN Regional Centers, PAN AP responds to requests for information on pesticides.

PAN AP's successes include strengthening pesticide campaigns in Asia and the Pacific, involvement in the banning of pesticides and training farm workers on how to protect themselves from the dangers of pesticides and use alternatives. PAN AP was instrumental in the development of the Prior Informed Consent principles in the Food and Agriculture Organization (FAO) International Code of Conduct on the Distribution and Use of Pesticides. Other activities include work on the Dirty Dozen Campaign, conducting research and training workshops on pesticide-related topics, monitoring international and regional aid agencies, and providing input and oversight at events and meetings on issues relating to food, pesticides and agriculture.

PAN AP has recently launched a 10-country programme addressing the issues of women's exposure to pesticides. The Women and Pesticides Programme empowers women through providing information and training. The programme includes a seven-country case study on the impact of pesticides on women. It provides training workshops that include information on pesticide hazards and alternatives, utilizing the knowledge and experience of those acquainted with traditional agricultural practices.

PAN AP produces a regular newsletter, the *Pesticide Monitor*, which covers pesticide issues, PAN campaigns, available resources, and recent news on agriculture and pesticide legislation and policy. PAN AP also publishes books, flyers and other materials. Books published by PAN AP include *The Pesticide Handbook*, a profile of 50 pesticides; *Pesticides and You*, which answers basic questions about pesticides for the general public; and *Problem Pesticides, Pesticide Problems* and *The Pesticide Code Monitor*, both of which assist groups in monitoring the use and effects of pesticides. PAN AP's latest book, *Victims Without Voice*, includes in-depth interviews with 50 Malaysian women pesticide sprayers.

You can become involved by affiliating with PAN AP (open to groups in Asia and the Pacific), by subscribing to the *Pesticide Monitor*, by volunteering your expertise as a contact or referral person, or by contributing to PAN AP's collection by donating information related to agriculture, pesticides, and alternative pest management. For more information contact: PAN Asia and the Pacific, P.O. Box 1170, 10850 Penang, Malaysia. Tel: (60-4) 870271; Fax: (60-4) 877445. (Source: *Global Pesticide Campaigner*, Vol. 2, No. 4, November 1992)

Global biotech market set for fast growth

The global market for biotechnology products will reach $20 billion by 2002, says a new study by Consulting Resources Corp. (Lexington, MA) called "New Directions in Biotechnology". It puts the US market at $3.5 billion in 1992, reaching $15 billion by 2002. Antisense and gene therapies are leading second-generation technologies for the development of therapeutics. Among the most important know-how being developed in the diagnostics and agricultural segments are biosensors and transgenics. Demand for biotechnology production facilities is expected to accelerate in the mid-1990s, in line with the rate of product approvals. (Source: *Chemical Week*, 21 October 1992)

Biotechnology as an instrument to the solution of structural problems in developing countries

Biotechnology has the potential to contribute to the development of durable agricultural production systems, health care and environmental management in developing countries. However, up till now access to biotechnology for developing countries has remained very limited.

The Special Programme on Biotechnology and Development Cooperation, established by the Netherlands Minister of Development Cooperation in January 1992, aims to increase access for developing countries to biotechnological expertise and innovations and to contribute to the solution of developmental problems. In addition, it aims to support the establishment of a biotechnology policy and to contribute

to the prevention of negative effects resulting from the application of biotechnology.

To utilize the potential of biotechnology as an instrument for structural poverty alleviation, developing countries should be enabled to build a local research capacity and to carry out research programmes. Also, research in industrialized countries directed towards third world development should be stimulated. The programme will attempt to accomplish this by the integration of development aspects in the Dutch biotechnology policy, and by bilateral technical cooperation. International consultation and collaboration will form part of this approach.

The Special Programme will thematically focus on agriculture, health care and environmental management. Technical cooperation will be built up primarily with Kenya, Zimbabwe, Colombia and an Asian country yet to be selected.

A local needs and priorities assessment takes a central position in the programme. Thus, a problem-directed approach, rather than a technology push, will characterize the programme. Considerable parts of the projects under the technical cooperation will be carried out locally in the developing countries involved. (Source: *Australian Biotechnology*, Vol. 2, No. 5, October 1992)

AIDS vaccines trials set in high-risk populations

Experimental AIDS vaccines designed to prevent infection with HIV have moved one step closer to real-life human tests. The National Institute of Allergy and Infectious Diseases (NIAID) announced in early December that it is launching a trial of two candidate vaccines that will be given to people considered to have a high risk of infection with HIV as well as those at low risk. Previous small-scale tests of preventive vaccines conducted over the past six years have included only volunteers from low-risk groups. The new trial will evaluate safety and immune responses, not efficacy, but the high-risk cohort might give hints of whether experimental preparations will work.

The placebo-controlled, Phase II trial will recruit 330 uninfected volunteers at five different university medical centers. The volunteers will include drug users, people with sexually transmitted diseases, and minorities. All participants will be counselled and encouraged to avoid risky behaviours.

The focus of the tests is to assess whether people at high risk and minorities have different responses from the healthy whites who dominated the earlier trials. Since the new trial will enroll hundreds rather than dozens of people, safety problems with the vaccines are also more likely to surface.

The pair of vaccines selected for the trial are genetically engineered versions of the HIV surface protein called gp 120; both rely on viral strains common in the United States. One vaccine, made by Genentech of South San Francisco, is based on an HIV strain designated MN; the other, developed by Biocine of Emeryville, California (a Chiron and CIBA-GEIGY joint venture), relies on the SF-2 strain. (A vaccine made by Connecticut's MicroGeneSys has been tested by NIAID the longest, but was not included in the trial because it is based on the relatively rare 3B strain.)

No one knows when a Phase III trial with thousands of people at high-risk - the real test of AIDS vaccine efficacy - will take place. (Source: *Science*, Vol. 258, 11 December 1992)

TB - the shadow that follows the march of HIV

As HIV spreads across the developing countries of the world, a second epidemic is never far behind. HIV's unshakable shadow is tuberculosis - which in some regions has become the main cause of death among people with AIDS. At the World Congress on Tuberculosis in Bethesda, Maryland, November 1991, researchers and health officials warned that the spread of HIV is fuelling an explosion in the number of TB cases.

More than a quarter of the avoidable deaths in the developing world are already caused by TB, a disease that kills 3 million people a year - making it a bigger killer even than malaria. A third of the world's population is infected with *Mycobacterium tuberculosis*, but in most cases the disease remains dormant. The WHO is predicting that by the year 2000 infection with HIV will reactivate TB in a million people.

Almost two thirds of all people infected with TB live in Asia, and when HIV spreads across the region, the result will be "huge increases in HIV-associated TB and a rapid deterioration of the TB situation in the coming years", warned Hu Ching-Li, Assistant Director-General of WHO. Already in northern Thailand the number of TB patients who are infected with HIV has risen from 5 per cent in 1989 to 14 per cent in 1991.

But for now, the most devastating combination of the two infections is in sub-Saharan Africa, the home of 3.5 million of the 4.4 million people in the world infected with both TB and HIV. In Zambia, the number of TB cases has doubled in the past five years, largely because of HIV. In Uganda, researchers found that 65 per cent of new cases of active TB were people infected with HIV.

However, in a few developing countries, model TB-control programmes supported by the International Union against Tuberculosis and Lung Disease may be limiting the spread of TB. In urban areas of Tanzania, as many as half the people with TB are HIV-positive. But prompt diagnosis and successful treatment of 85 per cent of the cases seems to have kept the infectious phase of the illness to a minimum, so limiting the spread of

infection. The evidence for this comes from a study by the Tanzanian health ministry which shows that although the number of cases of active TB has doubled in the past decade, the number of new infections among children continues to fall.

Health officials from the rich industrialized countries admitted that they might be able to learn something from developing countries with such programmes. But while a large part of the international aid to combat TB has been directed at a few model programmes such as Tanzania's, in many areas most cases of TB go undetected and untreated. Most poor countries cannot afford the "short course" drug treatments that can be completed in six months. Instead, they use older, cheaper treatments that may have to continue for a year or more. Some countries have tried to ensure that patients complete their treatment. In China, some TB patients are paid to attend the clinic to take their drugs. For countries such as war-torn Mozambique, this approach is impossible. In a study in Zambia, almost half the patients who "defaulted" on their treatment blamed the cost of transport to the clinic.

The breakdown of health care systems burdened by both TB and AIDS is not confined to the developing world.

Following so soon after a ministerial-level plea for more international aid to combat malaria, the demand for massive infusions of money to fight TB may fail to move fatigued donors who are struggling to muster the resources to fight outbreaks in their own cities and hospitals. Josef Decosas of the Canadian International Development Agency believes that policy makers must focus on overall health in developing countries, rather than malaria, or AIDS, or TB, or any other single disease. (Source: *New Scientist*, 28 November 1992)

B. COUNTRY NEWS

Baltic States

Biobalt: Biotechnology in Estonia, Latvia and Lithuania

The International Network Biobalt is organized at Tallin Technical University (TTU), and aims by coordinated efforts of the three countries to promote integration of the Baltic States into the world biotechnological community. Scientific and commercial cooperation with the Scandinavian States and other European countries are emphasized.

BIOBALT aims to create a permanent international network, including organization of workshops, symposia and conferences. This process is supported by UNESCO (the UN Educational, Scientific and Cultural Organization), and the European Federation of Biotechnology; further support from the EC Commission, foundations and companies is sought.

In view of travel difficulties, the BIOBALT 1992 conference was conducted "extramurally" by publishing and distributing the submitted abstracts as a book. The book also contains comprehensive lists and descriptive keywords for the biotechnology centres and institutions in the three countries, indicating a highly developed range of products and services.

The Abstract Book is available on request to Professor Ado Köstner, TTU BIOBALT, Ehitajate tee 5, Tallin EE0108, Estonia. Tel.: (7)0142-532110; Fax: (7)0142-532446.

Bangladesh

Commercial bio-fertilizer production

The Bangladesh company BioLINK, in collaboration with the Department of Soil Science of the Bangladesh Agricultural University, has been producing *Rhizobium* bacterial inoculants from 1991 onwards. BioLINK was established in 1989 with a view to introducing appropriate technologies in the agriculture of Bangladesh. Recently, BioLINK's activities as sole producer of the biofertilizer were approved by the Government of Bangladesh.

BioLINK is using a number of highly effective *Rhizobium* strains as active ingredient. These are commonly termed as Baur 107, Baur 118, Baur 600, Baur 349, Baur 700, Baur 604 etc. Yeast-manitol liquid is used as a growth medium; processed Bangladesh peat soil is the inoculant's carrier.

BioLINK is producing about seven tons of different types of inoculants annually. The company has a production capacity of around 10 tons a year. The actual demand is, however, around 20 tons and is expected to grow. As inoculants are a new phenomenon in Bangladesh agriculture, most farmers are not familiar with it. Agricultural extension programmes may further enlarge the market. BioLINK has plans to produce *Azotobacter* inoculants, blue green algae and Azolla for rice and wheat. Another future plan is to produce plant-based biopesticides, such as the Azadirachtin compound from *Azadirachta indica* (Neem).

Bacterial inoculants have proved to be an appropriate alternative for the chemical nitrogen fertilizer Urea in the cultivation of food legume crops. In various field tests, the soya bean inoculants were found four times more effective than Urea; other inoculants were two to three times more effective. As it is relatively cheap, bacterial inoculants may significantly reduce the costs of soil fertilization. Moreover, inoculants have no adverse effects on soil or environment. Contact: BioLINK, Liaison Office, 23 Topkhana Road, Dhaka - 1000, Bangladesh. Fax: (+880) 2832978.

Belgium

Directory of biotechnology

A report has been published by the Ministry of Technology Development of Belgium's Walloon Region in cooperation with the Belgian Bioindustries Association (BBA), which lists and describes the companies, universities, institutes and research centres involved in biotechnology in Wallonia and Brussels. In a foreword to the report Mr. P. Crooy, Chairman of the BBA describes the growth of the association since it was created by four companies in 1986. It now has 52 members reflecting the thrusting and innovative development of biotechnology in Belgium. The Directory is available in French and English without charge from Belgian Bioindustries Association, rue de Crayer, 6, 1050 Brussels. Tel.: (32)26460564.

Canada

Life sciences park

Biotechnology will be the major industrial engine for the 1990s, just as computers software development were key developments in the 1970s and 1980s. Ottawa's new Life Sciences Technology Park will develop and market products and services resulting from basic research in biomedicine and biotechnology. The City of Ottawa has contributed $30 million to design the Park, and will start developing roads and service infrastructure for 21 acres that are being transferred from the Province of Ontario. Ontario Development will lease or sell Park properties to public or private research companies, with monies going to reimburse Ottawa for development costs. The Province will build a 54,000 ft^2 multitenant facility, expandable by another 54,000 ft^2. (Extracted from *Canadian Chemical News*, December 1992)

Denmark

Transgenics: Potential conflict with EC

Denmark is set to regulate, rather than ban, transgenic animals. While this is a softening of the Danish position on transgenics, it seems likely that the regulations will nevertheless be fairly restrictive: the scientific use of transgenics may be closely evaluated case by case, and there is pressure to consider social and economic factors in the regulation of transgenic farm animals. This is likely to put Denmark into conflict with measures on transgenics being drafted by the European Commission.

The change in attitude was apparent from a recent "consensus conference", a uniquely Danish instrument of democracy, organized by the Teknologinaevnet in cooperation of the Parliamentary Committee of Research. Consensus conferences, although they have no formal part in the legislative process, have profoundly influenced the content of Danish legislation.

On transgenics, the consensus document, drawn up by a panel of 14 lay persons after being presented with a range of opinions and evidence, made a number of recommendations:

- The experimental uses of transgenics should be decided on a case-by-case basis;

- Social, economic, and animal-health considerations should guide the regulation of transgenic animals for agricultural purposes.

The consensus document, in fact, addressed wider aspects of transgenic products. Although the panel was not against the use of foods containing or consisting of genetically modified organisms, it demanded obligatory labelling of all such products. It also explicitly expressed concern about the views from experts on the long-term safety of genetically engineered foodstuffs. On intellectual property, moreover, the panel endorsed the majority decision of the Parliament, taken in 1991, to oppose patenting of any life form.

Exactly how and when Denmark will proceed is unclear. But on transgenics, Denmark may follow the Dutch model of separate regulations for animal welfare on the one hand and animal experimentation on the other. Animal-welfare legislation, in fact, is currently passing through the Dutch Parliament's second chamber. (Extracted from *Bio/Technology*, Vol. 10, December 1992)

European Community

BRIDGE biosafety research results

Significant BRIDGE resources (10 million ECU) have been committed to the assessment of risks that may be associated with the release of GMOs into the environment. Sixty-two laboratories from the EC and EFTA countries are working on 14 transnational projects. The first meeting of these biosafety researchers took place from 6-9 December 1992 at Wageningen, The Netherlands.

The report of this meeting is now available. The topics covered include the following:

- Analysis of gene transfer between micro-organisms and plants;

- Fate of genetically engineered micro-organisms and genetically engineered DNA sequences in some environmental hot spots;

- The effects of selection on gene stability and transfer in populations of bacteria in soil;

- Safety assessment of the deliberate release of two model transgenic crop plants, oil-seed rape and sugar beet;
- Stability, genetic transfer and ecology of fungi used as biocontrol agents;
- Assessment of environmental impact from the use of live recombinant virus vaccines;
- Biosafety of genetically-modified baculoviruses for insect control.

It is hoped that the results of such research will play a positive role in the development and implementation of the Community's regulatory framework ensuring safety for man and the environment. (Source: *EBIS*, Vol. 3, No. 1, 1993)

EP passes directive on patenting of biotechnology inventions

The European Parliament in October 1992 passed, by a tiny majority, its first reading of the Directive on the legal protection of biotechnology inventions. It states that biological matter is patentable except for plant and animal species *per se*, including human beings. But it also passed, by a massive majority, a motion allowing farmers to use seeds obtained on their farm from seeds patented for replication, and the renewal of herds from patented livestock without the payment of further royalties.

The biotechnology industry remains strongly opposed to the concept of farmers' privilege because it fears that once one sector is granted this right other sectors may follow suit, depriving the patent holder of further revenue. Industry is also worried that farmers might sell second generation products, undercutting the market.

The farming lobby had opposed patenting of genetically modified animals and plants in the hope that it would not have to pay any royalties at all (ECN 3 February). According to the UK Bio-Industry Association, the National Farmers Union recently acknowledged the importance of ensuring adequate returns to breeders and patentees of biological inventions. The Directive, first proposed in October 1988, has now cleared a major hurdle in the legislative process. The next important step will be the establishment of a common position by the Council of Ministers. According to an EC spokesman, the Danish presidency will be keen to reach an agreement on the issue and bury it as it was a controversial part of the Maastricht Treaty debate. Once the Council reaches a common position a directive can only be delayed for a maximum of eight months. (Source: *European Chemical News*, 23 November 1992)

New bid for biotech forum

Europe is about to get another organization bidding to coordinate biotechnology efforts. SAGB and Cefic, in collaboration with nine other pan-European industry federations including EFPIA (pharmaceuticals) and ECPA (pesticides), are establishing the Forum for European BioIndustry Coordination (FEBC).

The trade groups believe FEBC will "strengthen existing coordination links between them and provide a more formal network for exchange of views and information". More important, the organization will promote the view that biotechnology should be regulated using a sector based approach and not a technology based one. Nevertheless, FEBC does not intend to usurp the work of the member federations. "While strengthening the European industry sector federation's communication network on biotech issues, the Forum will not replace the role or functions of the individual federations", explained SAGB's Brian Ager.

FEBC will develop positions on common issues, while leaving the federations free to state their own views on sector-specific issues affecting them. (Source: *European Chemical News*, 22 March 1993)

France

French oil sector warms to biofuel promotion

Oil companies in France appear to be stepping up plans to take advantage of the government's fiscal incentives to promote the use of biofuels alongside conventional diesels and gasoline. The government's eagerness is attributed to an urgent need to appease farmers facing cuts in EC agricultural subsidies.

The development of biofuels in France will rely on government subsidies in the shape of tax rebates on motor fuels. Such subsidies are estimated to amount to FF 1.8 bn/year if 5 per cent ester were introduced in diesel oil and to FF 3.5 bn if 5 per cent ethanol were introduced in gasoline. (Extracted from *European Chemical News*, 5 October 1992)

Germany

Hoechst goes ahead with insulin test unit

Hoechst has started up its controversial genetically engineered human insulin test plant at Frankfurt after agreeing to fulfil safety regulations it considers unnecessary.

In accepting a requirement to sterilize wastewater from its *E. coli* fermentation unit, Hoechst said it could not afford to lose any more time. Since its first

application to build the plant in 1985, the company has faced a number of setbacks because of opposition by environmentalists, and also changes in its production concept.

Only the first of the three production stages, the fermentation unit, is subject to the regulations of the German framework law on genetic engineering technologies. However, the original permit to build and operate was granted under the terms of the federal emissions control law. This requires that plasmids be inactivated at 120° C before disposal. Hoechst has argued that heat destruction of the bacteria is unnecessary because they are inactivated during the fermentation process. In December 1993 the state regional authority in Giessen ruled - for complex legal reasons - that the sterilization requirement must be upheld.

Operation of the insulin facility as a test plant is limited to two years. In May 1992 Hoechst applied for permission to operate the unit as a full-scale production plant, but this application has not yet been ruled on. (Extracted from *European Chemical News*, 4-11 January 1993)

German state unexpectedly approves first gene trials

A state ethics panel has given its approval for the first gene therapy trials in Germany - and the first gene therapy directed against cancer in Europe. The decision upsets the conventional wisdom that it is futile even to apply for permission because of the prevailing hostility in Germany towards any form of genetic engineering.

Gene laws in Germany are much more stringent than in any other country. Some state authorities have been accused of deliberately overinterpreting the letter of the law to delay licensing for as long as possible because of political opposition to genetic engineering. As a result, most German scientists working in the field look for collaborators in other countries. However, a proposal from Roland Mertelsmann of Freiburg University Medical Centre to treat cancer patients by stimulating their immune system was approved within three months without a hitch.

Data in Germany must be registered with the Public Health Office and the Paul Ehrlich Institute, which controls use of vaccines. Formal approval is given by an ethics committee within each state, in Mertelsmann's case, Baden-Wurtenberg.

Anticipating resistance, Mertelsmann chose a transfection method that does not use a retrovirus. His alternative - electroporation - is a standard method not often used because of its low efficiency. To compensate, Mertelsmann developed a method that uses an abundant tissue. The gene for the cytokine interleukin 2 (IL-2) will be inserted into autologous fibroblasts cultured from skin biopsy of patients with either renal cell carcinoma, colon cancer or malignant melanoma. Once stably transfected, a process that could take as long as nine months, the fibroblasts will be mixed with cancer cells from the patient, irradiated and injected subcutaneously as a vaccine.

Data on animal toxicity will be submitted shortly to the Paul Ehrlich Institute, which makes recommendations about safety for vaccines in Germany. Mertelsmann hopes to enrol his first patients by April. (Extracted from *Nature*, Vol. 360, 24-31 December 1992)

Requirements of gene technology laws to be eased

The Federal Government has agreed in principle to relax the way its gene technology laws are administered after a long campaign by scientists to reduce the number of forms and lengthy authorization procedures.

Molecular biology in Germany has been undermined by a powerful anti-genetic-enginering lobby that has stifled research and left the country trailing the rest of Europe. Laws introduced in July 1990 continued the trend by requiring elaborate safety procedures and time-consuming recordkeeping - irrespective of the level or risk involved in experiments. But a concerted campaign by academic and industrial scientists has now borne fruit.

The Government has agreed that procedures for monitoring experiments will be relaxed. The changes would not lower safety standards. Experiments that by definition pose no risk will no longer need to be reported to the authorities once a general authorization has been received. The Government is also expected to remove an automatic three-month delay in granting permission for experiments designated as "very low risk". The law is on the second of three readings in Parliament, and the Ministry of Public Health is confident that it will be in place by January 1994. (Extracted from *Nature*, Vol. 360, 26 November 1992)

Gene laws to be amended

Amid growing criticism from the chemical industry in particular, and with the realization that Germany is becoming a "no-man's land" for gene research and technology, the political parties in the Bundestage (except the Greens) have agreed to amend the 1990 genetic engineering framework act. The Social Democratic opposition has signalled its support for dismantling bureaucratic hurdles and harmonizing German legal standards with those in other countries.

The federal research minister, Heinz Riesenhuber, stressed that there would be "no concessions on the safety question" and that the protection of human health and the environment would continue to take precedence

over economic interest. He hopes the amendment can be passed during the current legislative session.

However, the governing Christian Democrat-Free Democrat coalition has made no secret of the fact that the rules are being changed to stem the "brain drain" of research-oriented companies and bioscientists from Germany.

The amendment would do away with declaration requirements and the three-month waiting period for new research projects in new research facilities at safety level 1 (simple fermentation processes, etc.). It would also simplify procedures for companies doing research or testing commercial processes at this stage. The requirement to have scaled-up projects at safety level 2 approved by federal authorities would be abolished, and this stage would be replaced with a simple registration procedure.

Furthermore, movement of genetically altered organisms within the European Community would be allowed without prior government approval, and the physical examination requirements and procedures for workers in genetic projects would be simplified or abolished.

The chemical industry will be closely monitoring the progress of the amendment. At its recent general assembly in Frankfurt, the industry association VCI called for deregulation of gene-splicing technology both in Germany and the EC. (Source: *Chemistry & Industry*, 2 November 1992)

Instructions for shipping non-infectious and infectious biological substances

The European Commission under its BRIDGE biotechnology research programme, has supported the Information Centre for European Culture Collections based at Braunschweig, Germany to produce a report "Instructions for shipping non-infectious and infectious biological substances". The report gives an overview of the different regulations governing the shipment of biological materials and provides a code of good practice. It should be of interest to any laboratory or culture collection sending biological specimens in the post. It is available without cost from: Information Centre for European Culture Collections, Mascheroder Weg 1b, 2 D-3300 Braunschweig. Tel.: (49)531618715; Fax: (49)531618718.

India

Forum to protect genetic resources

A joint forum of farmers' associations here have demanded a central legislation declaring India's resources as "national property" to safeguard indigenous genes and plant resources from patenting.

The forum, being convened by the "Gene Campaign" group, has threatened mass action by farmers from all over the country to retain control of the genetic resources belonging to India.

In a statement, the forum demanded removal of the restriction on processing, movement and trade of farm products; spending of 75 per cent of the Plan expenditure exclusively on the rural sector; ban on entry of multinational companies in the agriculture sector and protection of genetic resources by rejecting patents and monopolistic forms of intellectual property protection demanded in international negotiations.

The members of the forum declared they rejected "outright the proposal to impose controls on our plants and seeds through patents or similar forms of international negotiations like GATT and the Biodiversity Convention. We will fight for the rights of our peoples to use these resources without hindrance whether in research, industry or agriculture".

The forum launched a "seed satyagraha" to resist efforts by foreign corporations to seek control of Indian plants and genes. "Patents will allow foreign companies to debar Indian scientists from using our own genetic material for our own needs making a mockery of the self-reliance achieved by Indian agriculturists and scientists in feeding the country", they said. (Source: *The Hindu*, 18 January 1993)

Indian biopesticides launch

Sandoz India Ltd., a subsidiary of the Swiss company Sandoz, launched a *Bacillus thuringiensis Berliner* based biopesticide in September 1992. The product is delivered in water dissoluble microgranule form under the brandname *Delfin*. It is active against caterpillars preying on cabbage and cauliflower. Being the first product of its kind to be introduced in India, it has been granted a special registration by the Central Pesticides Board to enable Sandoz India to import it from its associates in the USA, where it has been in use for the last four years. However, the company has been asked to conduct additional toxicity trials before marketing.

Similarly, Hindustan Lever Ltd. (HLL), the Indian subsidiary of Unilever, has successfully produced a bio-insecticide based on *Bacillus thuringiensis israelensis*, using molasses as culture medium. It has been tested successfully against insects attacking plants like cabbage, pigeonpea, cotton, safflower and maize. The insecticide has also been found effective against black flies and mosquitoes and can be used in malaria control. HLL has applied for a licence to the Central Pesticides Board to use the bio-insecticide. (Source: *Biotechnology and Development Monitor*, No. 13, December 1992)

New technology mission

The Ministry of Science and Technology plans to launch a technology mission in biotechnology and genetic engineering.

Faced with declining budgetary support, the Ministry plans to channel the funds to these areas on a priority basis, the Ministry said.

Biotechnology and genetic engineering are likely to play a key role in several sectors. Ministry sources said in view of the priority given to this area, the decision to merge the Department of Biotechnology (DBT) with the Department of Science and Technology (DST) has been shelved. The DBT, along with the Department of Ocean Development (DOD), both currently headed by the DST secretary, since the retirement of the secretaries, were slated for merger with the DST as part of the Government's austerity measures.

Preservation and commercial exploitation of medicinal and aromatic plants will also be given priority by the Ministry. An extimated 1,500 out of 2,000 drugs used in the country have come from plant origin. A large number of them are known to be facing extinction due to indiscriminate exploitation. (Extracted from *Times of India*, 26 November 1992)

Indo-American hybrid seeds

Indo-American Hybrid Seeds (IAHS), was established in 1965 in Bangalore, by Mr. Mammohan Attavar with a US$ 14,000 loan from the Ball Seed Company of Chicago, where he had received training in plant breeding. Starting out with the production of hybrid flower seeds for export to the American market, it has by now firmly established itself in the Indian horticulture industry. Through tissue culture, IAHS has been strengthening its presence in the market of flowers, vegetables and fruits in India and abroad.

The bulk of IAHS's business is hybrid seeds of flowers and vegetables, e.g. hybrid tomato, cabbage, cauliflower, capsicum, ladyfinger, watermelon and muskmelon. The company has a turnover of more than Rs. 150 million, half of which is from exports.

The company is producing cut flowers, for instance blue tinted lilies and chrysanthemums, for nurseries in the Netherlands, Denmark and the UK. For 1992, it had orders worth Rs. 13 million in revenues for about 2.3 million tissue cultured ornamentals. Around 10 ton of hybrid tomato seeds are produced in 15 to 20 varieties, exclusively for Petoseed Company (USA). Banana and cardamon plants are produced for the Indian market. Micropropagation facilities are also extended to mango, guava, coconut, oil palm, rubber, sunflower and castor oil seeds.

IAHS's tissue culture laboratory comprises five growth rooms with a capacity to accommodate 400,000 cultures. It offers facilities for media preparations of 10,000 culture bottles per day. It has climate-controlled greenhouses with a shade blocking and fogging systems for hardening plants for the domestic market. The laboratory also deals with disease screening, and cleaning plants for viruses and bacteria. Research laboratories for micropropagation, somatic embryogenesis, biochemistry, immunology, virology, plant health, cellular and molecular biology are also being set up. Address: Indo-American Hybrid Seeds, P.O. Box 7089, 17th Cross, 2nd A Main K R Road, Banashankari 2nd Stage, Bangalore - 560070, India. (Source: *Biotechnology and Development Monitor*, No. 14, March 1993)

Indonesia

The CRIFC ICI seeds collaboration

The Central Research Institute for Food Crops (CRIFC) in Indonesia, and ICI Seeds Americas of Slater, Iowa, are working together to develop insect-resistant corn through genetic engineering. The target pest in this work is the Asian stem borer, which can cause yield losses of up to 40 per cent. Recent advances in genetic engineering have made possible the conferring of resistance to this serious insect pest by transforming commercial lines with insect control protein genes isolated from *Bacillus thuringiensis* (Bt).

Currently, corn breeders in Indonesia (at the Malang Research for Food Crops) are reviewing germplasm in order to select lines most appropriate for inclusion in this biotechnology programme. In addition, ICI Seeds has proprietary germplasm that also may be suitable and it is hoped that, in the long-term, commercialization of the insect-resistant plants can be achieved through partnership with a private company in Indonesia.

Dr. Ibrahim Manwan, Director of CRIFC, is bringing together a team of Indonesian scientists who will participate in this collaborative research.

As the project progresses, there will be field trials of transgenic plants both in Indonesia and the United States. ICI Seeds has considerable experience in working with federal regulators on the development of viable strategies for field testing transgenic corn, and has conducted field trials in Iowa and Hawaii. As part of the ABSP programme, regulatory issues in Indonesia are being considered. The material generated by the CRIFC ICI Seeds collaboration will allow programme participants the opportunity to gain direct experience in the regulatory area. (Source: *BioLink*, Vol. 1, No. 2, 1993)

Israel

Israel tests for HIV

People visiting Israel for more than three months will have to be tested for HIV. Starting in January 1993, visas for anyone infected with the virus will be limited to stays of less than three months, says the interior ministry.

Tests will be required first for foreigners living and working in Israel, then for travellers staying more than three months. The largest group likely to be affected will be Palestinians from Israeli-occupied territories who work in Israel but are officially considered to be foreigners.

But the measure will also affect the large numbers of foreign scientists and technicians in Israel's high-technology industries, as well as visiting researchers.

Israel has admitted that for the past six months prospective immigrants have had to take an HIV test. People found to be infected have been refused entry. (Source: *New Scientist*, 14 November 1992)

Italy

New biology institute in Milan

A new biology research institute in Milan was opened in October 1992.

The Dibit Institute was financed by the private foundation, H. San Raffaele, which runs a large hospital and research centre in Milan. It has attracted some of the best biologists in Italy to do research in cell biology and related disciplines, taking advantage of the Institute's close links with clinical departments.

Jacopo Meldolesi, the Director of Research, would like to create a facility with a reputation to match those of the Institute Pasteur or the Max Planck institutes.

Meldolesi, whose own interest in signal transduction and second messenger systems forms one of the major research projects at the new institute, hopes in the next two years to double the current number of scientific staff to around 200. More than a third of the institute's research budget comes from outside sources, including the national research council and the European Communities. Further financial independence is provided by the drug companies Roche and Bayer, both of which intend to rent space in the institute for fundamental research on drug discovery. (Source: *Nature*, Vol. 360, 5 November 1992)

Advanced biotechnology centre

The National Cancer Research Institute (IST) has promoted an "Advanced Biotechnology Centre" of 16,000 m^2, situated in the University Hospital IST complex in Genoa.

The Centre will form the first nucleus in the "Genoese Science Park for Biotechnology", involving the laboratories of the University, the National Research Council and other scientific institutes in the creation of a critical mass of researchers, including also the presence of companies having related interests.

Facilities are included for: training, conferences, and technology transfer; large-scale facilities are available by specific agreements; the facilities conform to latest national and international regulations for biological and biotechnological research.

Basic research activities at the centre will include molecular biology; developmental biology; biochemistry; bioengineering; genetics; immunology. The centre intends, through its proximity to the hospital, to become involved in drug development, from research projects to clinical trials. For details, write to: IST-ABC, Viale Benedetto XV, 10, 1-16231 Genoa. Tel.: (30)10-352823 - 3534521 - 3534515; Fax: (39) 10-355573. (Source: *EBIS*, Vol. 3, No. 1, 1993)

Japan

National Institute of Bioscience and Human-Technology (NIBH) reorganized

On 1 January 1993, the Agency of Industrial Science and Technology of MITI reorganized the existing four chemical laboratories into the National Institute of Bioscience and Human-Technology (NIBH) and two other institutes.

The NIBH is expected to play an important role in achieving basic and original researches on a wide range of fields covering bioscience and human-technology. It has eight research departments with patent micro-organism depository. These departments are: Biomolecules Department, Biomolecular Engineering Department, Molecular Biology Department, Applied Microbiology Department, Bioengineering Department, Biosignalling Department, Human Informatics Department and Human Environment System Department. (Source: *News Release*, January 1993)

Lithuania

Lithuanian institute spearheads Baltic biotechnology

The Institute of Applied Enzymology, Vilnius, Lithuania, is rapidly emerging as the most dynamic biotechnology concern in the Baltic States. It was built in 1975 by the USSR-controlled Ministry of the Medical Industry, which provided assured budget support. Lithuania's declaration of independence in 1991 meant

that the Institute and its staff of more than 700 became increasingly dependent upon the revenue generated by sales of its products.

Thanks to the foresight of its Director, Arvydas Janulaitis, the Institute has been at least partially successful in bridging the funding gap created after suspension of Soviet support by earning hard currency from Western countries. It was Janulaitis who took the decision to develop an unrivalled collection of restriction enzymes. The manufacturing costs for these enzymes are low, the technology relatively simple, and they can be sold in small quantities and easily shipped abroad - all important considerations for an organization competing with Western companies that have access to the latest equipment and a well-developed transport infrastructure. Through his contacts abroad Janulaitis has been successful in selling his enzymes to 15 foreign companies (including US-based New England Biolabs) and the Institute now earns around $340,000 a year from this source.

Contact the Institute of Applied Enzymology at Fermentu 8, Vilnius, 232028 Lithuania. Tel.: +7 0122 641 279; Fax: +7 0122 642 624; Telex: 261 133 FER SU. (Source: *European Microbiology*, January February 1993)

Malaysia

Ecogen Malaysian institute agreement

Ecogen (Langhorne, PA) has signed an R&D agreement with the Malaysian Agricultural Research and Development Institute (MARDI; Kuala Lumpur) to survey and isolate entomoparasitic nematodes to control agricultural pests. MARDI, the governmental pesticide research and evaluation agency, will isolate the nematodes and perform field tests on local pests. Ecogen will identify and work to commercialize the nematode isolates. Ecogen has similar agreements in Australia and Italy. (Source: *Chemical Week*, 31 March 1993)

C. RESEARCH

Research on human genes

Gene abnormality in melanoma

Researchers have located a genetic abnormality connected to melanoma. Investigators at the University of Utah said they had strong evidence that one copy of a gene that controls cell growth is missing among members of certain families. Those who inherit the abnormality could be as much as 50 times more susceptible to developing skin cancer. The group has not identified the gene itself yet, but they believe it is deleted from a small region on chromosome 9.

Two other findings indicate that the Utah researchers are homing in on the right area - and that it may be important in all cases of melanoma. They also suggest that the discovery may have implications for other forms of cancer, including leukaemia, lung cancers and certain brain tumours. Another study pointed to chromosome 9 as one of the earliest problem areas in melanoma, even if other genes were involved. Other research has pointed to a genetic abnormality on chromosome 1, but that work has been difficult to confirm. (Extracted from *Biotechnology Newswatch*, 7 December 1992)

Gene therapy plan targets melanoma

Clinical trials of a vaccine to treat skin cancer could start in Britain by the end of 1993. The vaccine, which is a simple form of gene therapy, joins a number of experimental strategies that aim to stimulate the immune system to attack cancer cells.

Angus Dalgleish, from St. George's Hospital in London, says that although the Holy Grail of research is to find a gene to turn off cancer cells, a simpler approach might be better in the short term. Dalgleish and his team have focused on a protein called MHC Class I, which is normally vital for triggering an immune response to foreign proteins. T-cells of the immune system "recognize" proteins as foreign only if they are bound to MHC proteins. Cancer proteins are not foreign, but they are abnormal and the immune system sometimes attacks them. However, melanoma cells usually lack MHC class I proteins. As a result, the abnormal cancer proteins go unrecognized and the cells proliferate unchecked.

Dalgleish and his colleagues want to use MHC Class I as a "vaccine" to alert the immune system to melanoma cells. They have cultured melanoma cells in the laboratory from patients, and inserted into these cells the gene responsible for producing the MHC Class I protein.

In mice, the vaccine has produced encouraging results. It increased the amount of MHC Class I protein produced by the mice and their tumours shrank. But scientists stress that this type of vaccine is unlikely to work on its own against an established tumour. It is intended to be given after surgery to remove a primary melanoma, reducing the chances of cancer cells spreading. Dalgleish hopes to seek ethical approval to start safety trials. The vaccine would be given to people with severe melanomas. (Source: *New Scientist*, 26 September 1992)

Sampling foetal cells from mother's blood could make gene testing safer

Several groups are working intensely to develop an alternative to amniocentesis or chorionic villus sampling that would sample maternal blood instead when

looking for Down's syndrome and a variety of genetic disorders - a method that would be safer and could be done months earlier.

Professor Maria Pallavicini described work at the University of California in San Francisco using fluorescent markers to tag the rare foetal cells in a mother's blood. By searching the adult blood for certain cell types made only by the foetus, researchers were able to single out foetal cells from 11 of 18 samples.

Researchers at the University of Tennessee, in collaboration with Integrated Genetics of Massachusetts, used cells from maternal blood to analyse abnormal foetuses among 69 pregnancies. The group led by Dr. Sherman Elias, purified foetal cells from blood samples taken from mothers known to be carrying foetuses with chromosomal abnormalities. Using fluorescence in situ hybridization, they were able to visualize problem chromosomes. They said the data pointed to the method's eventual usefulness in the clinic, but that more work was needed. (Extracted from *McGraw Hill's Biotechnology Newswatch*, 7 December 1992)

Chance discovery of cholesterol immunity gene

Rosa Giovanelli and Cristoforo Pomaroli were married in the village church on 14 November 1644, and they passed on a unique inheritance which went undiscovered for nearly three and a half centuries.

Medical researchers have discovered that 40 of the tiny, northern Italian resort of Limone-sul-Garda's 1,000 residents, all related to each other, possess a miraculous genetic mutation which makes them immune to cholesterol - an important cause of coronary heart disease, one of the biggest killers of the twentieth century.

Until now Limone's only claim to fame has been its lemon orchards - the oldest and most northerly in Europe.

Researchers from the University of Milan, led by Professor Cesare Sirtori, have already reproduced the protein, made by the Limone gene, which clears the arteries of cholesterol.

A Swedish pharmaceutical company is believed to be on the brink of announcing a deal to mass-produce the protein in tablet form. Eventually, genetic engineering may be used to ensure that the benefits of the mutant gene are passed on. (Extracted from *The European*, 19-22 November 1992)

Single mutation leads to two distinct diseases

Two distinct, inherited diseases - fatal familial insomnia (FFI) and a subtype of familial Creutzfeldt-Jakob disease (CJD) - are both associated with a single mutation at codon 178 in what is known as the prion protein (PrP) gene. A large team of researchers, headed by Pierluigi Gambetti of Case Western Reserve University, Cleveland, has carried out research that suggests that a common polymorphism at codon 129 of the PrP gene interacts with the mutation at position 178 to determine which disease is manifested. Gambetti's team sequenced the PrP gene from two groups of 15 subjects with established FFI or CJD and found that all carried a mutation at codon 178 that resulted in the substitution of asparagine for aspartic acid in PrP. They also found that codon 129 in the gene encodes methionine in all FFI subjects and valine in all CJD subjects. The researchers suggest that an interaction between methionine or valine at position 129 in PrP with asparagine at position 178 might result in two abnormal isoforms of the protein that differ in conformation and cause distinct diseases by forming insoluble protein aggregates. (Reprinted with permission from *Chemical & Engineering News*, 2 November 1992. Copyright (1992) American Chemical Society)

Liver detoxification enzyme structure solved

A new high-resolution, three-dimensional structure of glutathione S-transferase (GST), a liver detoxification enzyme, could help researchers understand how the liver metabolizes carcinogenic substances. The X-ray crystal structure was obtained by Richard N. Armstrong of the University of Maryland, College Park; Gary L. Gilliland of the Center for Advanced Research in Biotechnology, Rockville, Maryland, and the National Institute of Standards & Technology; and two colleagues. The researchers mapped, at 2.2-Å resolution, more than 4000 atoms and 434 amino acids that make up the enzyme. The structure shows that GST has two domains, one that binds glutathione and another that takes on different shapes in different isoenzymes to bind a variety of toxic molecules. A tyrosine residue in the active site is involved in activation of glutathione, which reacts with the toxic substance to render it harmless. (Reprinted with permission from *Chemical & Engineering News*, 2 November 1992. Copyright (1992) American Chemical Society)

Gene responsible for metastatic tumours

Cancer researchers from the German Cancer Research Centre in Heidelberg and from the Nuclear Research Centre in Karlsruhe have made a significant discovery. They have identified the gene responsible for metastatic tumours. In a tumour of the pancreas in rats, this gene, code-named CD-44, has been proved to be capable of enabling the degenerate cancer cells to spread throughout the body. These itinerant cells are especially feared as metastatic tumours. In most cases it is not the initiating tumour that leads to death but rather the metastic tumours which destroy organs and tissue. CD-44 is not an unknown quantity for the scientists. Previously, however, the gene was known only as an adhesive molecule which assists the cells of the immune

system on their journey through the blood vessels and the lymphatic system. It appears that the tumour cells exploit this characteristic. This discovery opens up new perspectives for the scientists in their fight against metastasis: one day, monoclonal antibodies directed against CD-44 could perhaps block the lethal command chain in the tumour. (Source: *Scala*, October 1992)

Protein warns of colon cancer relapse

A simple and safe way of analysing the activity of colon cancer cells could help doctors to predict whether the disease is likely to recur after surgery. People at risk could then be given preventive anticancer drugs.

A research team led by Ibrahim Al-Sheneber, a surgeon at McGill University and the Royal Victoria Hospital in Montreal has found a protein that was significantly higher in specimens of colon tissue from people who later died from colon cancer than in people who survived for five or more years. The protein, known as proliferating cell nuclear antigen, or PCNA, is associated with cell division. To identify the protein, the researchers used a monoclonal antibody which "recognized" only PCNA.

Al-Sheneber and his colleagues examined the tissue samples and medical records of 40 patients who had part of their colon removed because of cancer. They looked at both cancer cells and normal tissue from the colon, and used a "proliferation index" to describe the amount of PCNA in the cells. They found that in people who died of colon cancer both cancerous and normal cells had a higher proliferation index.

Al-Sheneber believes that PCNA analysis could provide a better prediction of the outcome of the disease. Surgeons removing cancerous tissue could ask the pathologist to tell them the proliferation index in addition to the Dukes stage. Al-Sheneber cautions that it is still too early to decide on treatment solely on the proliferation index. (Source: *New Scientist*, 12 December 1992)

US tests genetic approach to liver disease

Children with acute liver failure are about to receive transplants of genetically engineered liver cells in a trial by American researchers that may one day lead to a gene therapy for liver disorders. This follows experiments with mice in which genetically modified liver cells survived and continued to function for more than a year after being transplanted.

For the animal experiments, Savio Woo of the Center for Gene Therapy at Baylor College of Medicine in Houston and his colleagues first isolated liver cells from transgenic mice that produce the human protein α1-antitrypsin in their livers, from where it is secreted into the blood. The liver cells were then transplanted into mice, which do not express the human protein, but otherwise are genetically identical to the donors. This was done by injecting the cells into the portal vein, which carries blood to the liver, or into the spleen, from where they migrate to the liver.

A few days later the human protein appeared in the mouse blood, showing that the transplant had been successful. The protein's level remained stable in the animal for the rest of its natural life - 400 days. Similar experiments with dogs and baboons were also successful.

Woo's technique may one day be used to treat the metabolic disorder phenylketonuria (PKU), in which the gene for the hepatic enzyme known as phenylalanine hydroxylase (PAH) is defective. PAH normally converts the amino acid phenylalanine into tyrosine, but in children where the enzyme is missing phenylalanine accumulates in the body and causes severe mental brain damage. Such children are normal at birth and can be treated with a special diet that is low in phenylalanine but treatment has to start when they are a few days old.

Another of Woo's experiments involved a PAH-deficient mouse strain developed by William Dove and colleagues at the University of Wisconsin in Madison. Woo inserted the gene for mouse PAH into liver cells isolated from these mice and found that this fully restored enzymic activity to the cells. Woo intends to transplant these cells into the PAH-deficient mice to see whether they can treat PKU in the animals. (Source: *New Scientist*, 10 October 1992)

New contraceptive method

An entirely new type of contraceptive may be possible using a monoclonal antibody that prevents fertilized eggs from implanting in the uterus. Researchers at the University of Oxford have isolated and multiplied an antibody that targets early embryonic cells.

Phyllis Starkey and colleagues at the university's Nuffield Department of Obstetrics and Gynaecology isolated antibodies which bind to early embryonic cells called trophoblasts.

Starkey's team isolated an antibody to a particular trophoblast which anchors the fertilized egg to the uterine wall. Starkey believes that the antibody could provide the basis for a new form of contraception. In women "immunized" with the antibody, it would either coat a fertilized egg preventing it from implanting in the uterus, or trigger the woman's immune system to destroy the egg.

Unlike the contraceptive pill, single doses of the antibody treatment could last a considerable time, perhaps months. The antibody treatment would not disrupt the normal menstrual cycle.

The job of commercializing the antibody has passed to Isis Innovation, which has filed for patents on both the antibody and the cell-line from which it can be mass-produced. They have also patented the use of the antibody in birth control applications. Some form of subsidy so that the contraceptive could be supplied cheaply to developing nations might be worked out. (Extracted from *New Scientist*, 17 October 1992)

Leukaemia translocation

It has been more than a decade since scientists figured out that many leukaemias arise when a cancer-causing gene is activated by an abnormal DNA-swap between two different chromosomes - but just which genes were involved? Now two teams of biologists, at Jefferson Medical College in Philadelphia and at Stanford University, have linked several forms of leukaemia to a swap - called a translocation - involving a newly discovered oncogene on chromosome 11.

The researchers scoured the DNA of patients with acute lymphocytic leukaemia (ALL), a common childhood leukaemia, for evidence of a translocation. Although the process leading to a translocation is little understood even today, the researchers found what they were looking for when they discovered that a gene (dubbed "ALL-1") located on chromosome 11 can fuse to another gene (called "AF-4") located on chromosome 4. Looking at patients with other forms of leukaemia, the researchers also found translocations between ALL-1 and genes on eight other chromosomes. Furthermore, they found that ALL-1 is related to the trithorax gene in fruit flies, which helps regulate development. The normal ALL-1 gene might play a similar role in humans, with a translocation causing it to malfunction. (Source: *Science*, Vol. 258, 27 November 1992)

Research on animal genes

Mutant mice offer hope for childhood disease

The search for better treatments for cystic fibrosis has accelerated sharply with the development of a realistic animal model for the disease. In a race with other scientists, Scottish researchers have bred mice with an altered gene which displays all the key features of cystic fibrosis, such as lung disease and digestive problems. The mice will help scientists to understand how the disease develops and enable them to test new drugs and gene therapies.

Research into CF changed gear three years ago when scientists in Canada and the US pinpointed the gene responsible for the disease. They found that the gene codes for a protein known as CFTR which normally transports salt across cell membranes in the lungs, gut and sweat glands. If the gene is defective, this process is disrupted. But scientists have been unable to show exactly how. This is in part because the disease has no natural parallel in animals. This has made it impossible to study tissues at each step of the disease.

David Porteous and his colleagues at the Medical Research Council's Human Genetics Unit in Edinburgh have "made" a mouse that transports salt abnormally, and has early signs of lung defects and digestive problems.

The team began by inserting a circular piece of DNA into the mouse gene that codes for CFTR. This disrupts the gene, stopping it from functioning. The altered gene was inserted into mouse embryo cells which grew into male mice that carried the mutation in their sperm cells, enabling them to pass it on to the next generation. The resulting animals had one copy of the normal gene and one of the defective gene, like human carriers of CF.

The team is not the first to develop mice with an altered CF gene. A team from North Carolina announced it had developed a mouse model for CF. However, these mice die soon after birth, which could make them impractical for study. Meanwhile, at the University of Cambridge a third team has developed another mouse model very similar to the North Carolina mouse. Both animals die from a severe gut disease that affects some CF patients.

Jim Wilson and Francis Collins at the University of Michigan, say that time will tell how reliable a model the Edinburgh mice will be. Different animals in the colony had different manifestations of the disease, which could shed light on the differences between humans with CF, but could also complicate studies of the therapies, they say. (Source: *New Scientist*, 19 September 1992)

Knockout mice

Geneticists can now create mice in which any gene they choose has been "knocked out" so that it no longer functions. The ability to breed mice which consistently develop genetic disorders such as cystic fibrosis, sickle-cell anaemia and atherosclerosis provides medical researchers with a powerful new tool for untangling causes and testing treatments. The mutant mice are also shining new light on long-standing questions in immunology and developmental biology.

The technique, developed independently by Mario Capecchi of the University of Utah and Oliver Smithies of the University of North Carolina, Chapel Hill, has become routine. A copy of the gene of interest is first disabled by inserting a special marker gene into its middle; this renders the original gene meaningless, although the marker can still be read. The defunct gene is then cloned in a test tube, and the multiple copies are injected into the nuclei of stem cells taken from mouse embryos. When the cloned genes are added, most will end up missing their targets, but a few

will displace their functional rivals, thus knocking out the function.

When the survivors are inserted into mouse embryos and the embryos brought to term, their cellular offspring get into everything, including the animals' coats. So if the stem cells came from black mice, and the recipient embryo is light-coated, the result is a chimera - light with dark patches, each patch a sign of cells that contain the altered DNA. Breeding the chimeras together eventually yields entirely black progeny which contain only the disabled gene.

Knock-out mice are already producing results, though not always the ones researchers had hoped for. A knock-out model for cystic fibrosis (CF) - the commonest inherited disease among white people - was announced last month by Dr. Smithies's laboratory. Though he remains optimistic, his initial studies indicate that murine CF differs significantly from its human counterpart, so in this case mice may not be a perfect model. But knock-out mice carrying intractable diseases caused by multiple genetic defects, such as atherosclerosis and Alzheimer's, are showing more promise.

With so many potential uses, the demand for knock-out mice is large. Many researchers hope that the government-funded Jackson Laboratory in Bar Harbor, Maine, will become an international repository for knock-out mice. Jackson has committed itself to this role and is willing to accept, breed, and distribute at cost new strains of knock-outs. (Source: *The Economist*, 5 September 1992)

Research on plant genes

In first field trial, Envirogen bacteria clear the air of common contaminant

A genetically-engineered version of trichloroethylene (TCE) degrading bacteria is currently awaiting its first field trial, said Ronald Unterman, vice-president of R&D for the Lawrenceville, New Jersey, hazardous waste bioremediation company. This "domesticated" cousin of the natural microbe will eventually "be the superior organism" for TCE degradation, he said.

In the trial using the natural organism, conducted at an undisclosed site in New York State, the company's biocatalyst-reactor system containing the microbes was installed on an existing plant that clears TCE from contaminated groundwater. The plant is based on a two-step process, first taking the chemical from the water into the air and running that through carbon filters.

Envirogen diverted a slipstream through its bioreactor and then compared the microbe-treated to conventionally-treated air. The bacteria destroyed 90 per cent of the airborne TCE, said Unterman. Following the microbial treatment, the air was pumped through carbon filters, which cleared most of the remaining TCE.

Unterman estimates that bioremediation could reduce the cost of TCE degradation by about 50 per cent in plants where carbon filters are used.

Envirogen has started the second phase of the experiment, in which the company will try to increase the rate at which the microbes break down the chemical. Discussions about using the technology are under way with several corporations as well as the US Department of Energy.

The company is examining the genetically engineered version. Unterman's group isolated the gene that destroys TCE and inserted it into *E. coli*. These microbes can be fed glucose, which Unterman calls a non-competitive substrate. Their TCE-busting can also be optimized and massive amounts of these bacteria can be grown at low cost.

The company has talked to the EPA to determine which permits, if any, will be needed for a trial with a gene altered bacterium. Unterman said that the EPA will probably not require a permit if the engineered microbes are confined to a closed system, such as the one used in the current field trial, but he added that Envirogen plans to conduct public reviews as well. It could take between six months and a year to start a trial of genetically-engineered TCE-busting microbes. (Extracted from *Biotechnology Newswatch*, 16 November 1992)

Wheat strains resistant to leaf-rust

Following two decades of intensive research, the International Maize and Wheat Improvement Center in Mexico City has announced a "lasting cure" for leaf rust.

The researchers found their answer in a Brazilian-grown wheat plant with natural defences against leaf rust - defences that work even against a disease that can attack repeatedly and can change form over time. The Brazilian strain was crossed with higher-yielding wheat varieties. Crops grown with the hybrid seeds have proved to be largely rust-resistant over a 12-year experimental period. Past efforts at developing resistant strains have foundered when the rust mutated to a new form, but scientists have identified a gene involved in what they call "slow-rusting", which means that the disease is kept at such a low level in plants that the fungus does not have the incentive to mutate.

The Centre is now distributing these strains to a network of more than 100 countries. (Source: *Science*, Vol. 258, 23 October 1992)

Research on viral genes

A new approach pays off

"A fairy tale come true". This is how David Lewis of South Dakota State University describes his group's discovery that ordinary light and a dye like the brighteners used in washing powder may help to prevent the HIV virus which causes AIDS, from spreading in infected patients.

Lewis and his collaborators at two Texas bio-medical laboratories focused their work on disrupting the viral envelope. In test tube experiments, they have found that a hydrophobic fluorescent dye - one of a newly-designed class of 1,8-naphthalimide photo-chemicals containing bromine - dissolves in the fatty portion of the envelope and locks the envelope proteins together when exposed to blue light, in a "photodynamic" reaction.

The envelope becomes rigid, trapping the viral genome inside, and prevents a key protein on the surface of the virus, gp 120, from binding to receptors on healthy cells. The method thus disrupts reproduction and further infection.

"We have found that only very low concentrations of this dye are actually needed to neutralise HIV-1", Lewis says. It is better than 99.99 per cent effective at less than 70 per cent of the concentration at which AZT is only 90 per cent effective under comparable conditions". What is more, unlike other photodynamic reactions, this one needs no oxygen. So it does not generate potentially harmful free radicals.

One drawback: blue light does not readily penetrate human tissues. Lewis hopes to modify the dye so that it is activated by red light, which could allow treatment by incandescent light or even sunlight. Lewis is also investigating the possibility of using azulene, a compound that absorbs red light.

Lewis is still testing for toxicity in mice and cautions that clinical trials are still five years away. (Source: *Chemistry & Industry*, 19 April 1993)

HIV destroys cells long before onset of AIDS

One of the greatest puzzles in AIDS research is what happens during the years between infection and obvious disease. Scientists have often called this the latent phase, because little or no virus can be detected in the blood and the infected person appears well. But evidence is mounting that the virus is anything but latent at this time: instead, it is busily invading and destroying key components of the immune system.

The latest clues come from a mouse with a human thymus - the gland in which the T-cells of the immune system mature and "learn" the tasks they have to perform in the body. Anthony Fauci, head of the US Government's AIDS research effort at the National Institute of Health, told scientists at a meeting in Paris that HIV infects and destroys the epthelial cells that make up much of the thymus. Studies of such mice show that holes appear in the thymus as little as two weeks after infection then the gland gradually disintegrates. This destruction of the T-cells' "training centre" may play "an important role" in the disease.

Fauci's team learnt how to make the "reconstituted" mouse from Mike McCune, of SyStemix, a company in California. Stem cells from a human foetal liver are injected into the capsule, or outer covering, of the mouse's kidney. In these conditions, the stem cells develop into a complete human thymus. When HIV is injected directly into the thymus, it infects the epithelial cells. This surprises researchers, because the cells lack the main receptor molecule for HIV, CD4.

A different type of dentritic cell involved in making T-cells respond to infections also seems to suffer early damage from HIV. Taken together, these findings suggest that HIV is destroying other parts of the immune system long before the number of T-cells starts to tumble. (Extracted from *New Scientist*, 7 November 1992)

Mystery syndrome

A search by the WHO in developing countries has so far revealed fewer than 20 cases of the unexplained HIV-negative immune deficiency syndrome that caused uproar at the international AIDS conference in Amsterdam in July 1992.

A meeting organized by the WHO in Geneva heard of scattered reports of the syndrome from Rwanda, Ivory Coast and Thailand - countries with strong AIDS research programmes. Ten developing countries were asked to send details of any cases. However, many lack the facilities for accurate testing.

Representatives of the US Centers for Disease Control told the Geneva meeting that the number of confirmed cases of the syndrome seen in the US since 1985 has now risen to 47, up from 30 in August 1992. World-wide, there are fewer than 100 cases.

Virologists still have no conclusive evidence that the syndrome is caused by a transmissible agent. Michael Merson, director of the WHO's Global Progamme on AIDS, said that the syndrome was worthy of research, but stressed that the top priority must continue to be research into HIV-positive AIDS, which already overwhelms health services in many developing countries. (Source: *New Scientist*, 3 October 1992)

Research instrumentation

Automated infrared DNA sequencer

The Model 4000 Automated DNA Sequencer from LI-COR is an infrared (IR) fluorescence-based sequencer that automates the electrophoretic separation and base calling of DNA fragments. DNA primers are labelled with a novel, IR-fluorescent dye which provides excellent sensitivity for detection. A solid-state laser diode is used to excite the labelled fragments and the IR emission is detected with a silicon avalanche photodiode. The use of solid-state detection components greatly increases reliability, while reducing the initial purchase price, operating costs, and bench space requirements. Up to 11 samples can be sequenced within 4 to 7 hours of sample loading. The Model 4000's Base ImagIR™ software presents data in real time during electrophoresis using an image format like an autoradiogram. Base ImagIR's sequencing software then uses the image to sequence 500 bases per sample with 99 per cent accuracy. Multitasking software also allows two additional sequencers to be operated by the same computer, which reduces the cost of future expansion. For application flexibility, the Model 4000 can use gels of various heights, thicknesses, and composition, as well as a variety of combs and lane loading formats. Further information available from LI-COR, Inc., 4421 Superior Street, Lincoln, Nebraska 68504, USA. (Source: *News Release*, 20 January 1993)

DNA shuttle for drug delivery

Researchers at the University of Leicester are investigating a molecular system to limit radiation damage to DNA. It could ultimately have wider pharmacological uses, giving therapeutic agents a more precise aim. While test-tube experiments have demonstrated that the essential concept is sound, further work is needed to verify that the system can operate in a living cell.

Professor Martyn Symons and Professor Paul Culls are using electron spin resonance spectroscopy to identify the nature of ionising damage to DNA. Essentially electrons get knocked out of guanine to create radical cations, and become entrapped at cytosine and thymine, forming the corresponding radical anions. The effect of radical centres along the DNA chain varies, but can result in the strand breaking, risking the possibility of misrepair.

The team at Leicester is trying to locate the radical anions, remove the offending electrons and replace them at the radical cations. This requires a redox reagent that can move easily along the DNA strand.

Symons reasoned that because DNA is itself a polyanion, then a polycation could home in specifically on the DNA. The naturally occurring polyamine spermine was found to work ideally. At physiological pH values it exists as a polyammonium cation, with four charge centres well separated along the molecule.

Spermine not only electronically binds to the DNA with high affinity, but, according to nuclear magnetic resonance data, moves freely and rapidly along the molecule, or as Symons puts it, "shuttles up and down the DNA like mad".

The next step was to fix the redox reagent to the spermine shuttle. Some work was done with transition metals, but because these need to be packed up in a bulky chelator this would impede their progress into the cell nucleus. Instead the Leicester work has concentrated on adducts such as ascorbate and nitroxide radicals.

Using double-stranded "naked" DNA at low temperatures, it seems that the spermine-adduct system is capable of attaching itself to the DNA, rapidly screening it and picking up and depositing electrons at the appropriate points. Symons is well aware, however, that complexities of the cell will present further challenges when the work reaches that stage.

However, he does believe that a drug delivery system based on polyammonium cations could result in highly specific targeting of DNA, reducing side effects and allowing a reduction in dose levels. (Source: *Chemistry & Industry*, 4 January 1993)

New affinity absorbent

PROSEP®-G is a protein G affinity adsorbent developed by Bioprocessing Ltd. The protein G is immobilized on porous glass, which is more rigid and durable than conventional polymeric matrices. The company says that PROSEP®-G will not only bind antibodies which bind to protein A affinity matrices, but also binds antibodies which may be difficult to bind to protein A, for example, Rat IgG_{2b} and Human IgG_3. PROSEP®-G can also be used for the purification of Fab fragments. In addition, the physical properties of PROSEP® make the matrix very simple to handle and facilitate high flow rates.

Further information available from **Bioprocessing Corporation**, Medomsley Road, Consett, County Durham, DH8 6TJ, UK. (Source: News release, November 1992)

Framing streak camera

A researcher at Hamamatsu Photonics, Dr. Hiroyasu Itoh, has been studying an effect known as electroporation. When a cell is deformed by an electric field, some of the pores in its outer membrane open for a moment. This might allow the introduction into the cell of drugs or foreign genes which cannot go through the normal channels in the membrane. The catch is that the pores open and close within a millionth of a second of the electric field being turned on.

When he started his research a few years ago, Dr. Itoh used a special Hamamatsu camera with an exposure short enough to capture an unblurred snapshot of the cell as a pore formed. But because electroporation does not always occur in the same way each time the electric field is turned on, he could not get a coherent series of pictures of the process from single snapshots of different attempts. What he needed was a camera that had both a short exposure time and a rapid shutter speed, so that he could record the whole process as it happened to one cell.

The result, which was commercialized recently, is known as a framing streak camera. It can take pictures at intervals of less than a millionth of a second, with a shutter speed of only 50 billionths of a second. At this impressive speed, Dr. Itoh is able to catch the full sequence of events as the pore opens and closes. He hopes to use the new camera to sort out the optimal conditions for electroporation of different types of cell, and so improve the success rate for introducing foreign substances into the cells. (Extracted from *The Economist*, 21 November 1992)

D. APPLICATIONS

Pharmaceutical and medical applications

Oily leaf extract protects against mosquito bites

Oil extracted from leaves of an aromatic shrub could be used to keep mosquitoes at bay, according to Indian researchers.

Extracts from *Vitex negundo* have been known to treat rheumatic swellings, while smoke from its leaves has relieved headaches. But a chance investigation by researchers at the National Chemical Laboratory, near Bombay, points to the shrub as a possible source of mosquito repellant.

Their curiosity was aroused when they observed Khandala tribe members burning *Vitex* at night for mosquito protection.

Alumina chromatography pinpointed the repellant activity to the fraction extracted with a mixture of benzene and chloroform and another extracted from chloroform.

Experiments showed that the oily liquid obtained after steam distillation protected the user from mosquito bites for up to an hour. (Source: *Manufacturing Chemist*, December 1992)

UK companies in world biotechnology first

Amersham International and Celltech Biologics, two British companies, have played a major role in achieving a world first in the development of a radio-labelled monoclonal antibody (Mab) for the detection of colorectal and ovarian cancer.

OncoScint® CR/OV, developed by CYTOGEN Corporation of Princeton, New Jersey, is the first monoclonal antibody-based *in-vivo* imaging technique. It is to be used with INDICLOR™, highly purified indium-111 chloride, a radio imaging agent manufactured by Amersham International plc.

The OncoScint® CR/OV contains a monoclonal antibody manufactured in Slough, UK, by Celltech Biologics, part of the Celltech Group. This is the first time that the US Federal Drug Agency has granted a licence for the production of an injectable grade antibody in a multi-product facility. It is also the first such approval for a monoclonal antibody manufactured using large scale mammalian cell culture. The two products, a monoclonal antibody and an innovative imaging agent, will be used, linked together, in hospitals. The OncoScint® CR/OV antibody binds to colorectal and ovarian cancers cells, while the radioactive INDICLOR™, provides an image of the location and spread of the cancers, detected by gamma cameras. The product is injected into patients. It may provide earlier diagnosis of small tumour deposits in the abdominal cavity in patients with recurrent ovarian or colorectal cancer, which are often missed by conventional tests. Diagnostic testing with the new imaging product does not replace CT scans and other standard tests, but can be used with them.

Colorectal cancer is the second most common malignancy in the world, while ovarian cancer is the leading cause of gynaecological cancer death. The prognosis for both depends first on the timing and accuracy of detection and staging, and secondly, on the accuracy and thoroughness of medical or surgical treatment. The new technique offers an easy to use, whole body non-invasive yet sensitive imaging technique that, in combination with other appropriate tests, can greatly improve the amount and quality of information available for the diagnosis and treatment of these cancers. The joint introduction of OncoScint® CR/OV and INDICLOR™, represents not only a new type of product but also a new concept, calling for several pharmaceutical companies and medical specialties to work in concert. (Source: *News Release*, 4 January 1993)

Vegetable extract enhances immune function

Professor Masatoshi Yamazaki of the Faculty of Pharmaceutical Sciences at Teikyo University says his studies have shown that a specially prepared vegetable extract enhances the body's immunomonitoring capacity and is effective against cancer.

Yamazaki prepared the extract from cabbages, spinach and onions by placing the vegetables in a blender, subjecting the juice to centrifugation, then

adjusting the pH of the supernatant. In animal experiments, Yamazaki intravenously injected the extract into mice and found that it induced a substantial elevation in blood tumour necrosis factor (TNF), similar to the action of interferon. Yamazaki says that by increasing blood levels of TNF, the extract is effective against cancer. (Source: *McGraw Hill's Biotechnology Newswatch*, 5 October 1992)

B-cell lymphoma vaccine progress

Research is progressing on a vaccine to fight a common blood-cell tumour that has proven resistant to other forms of treatment. In the future, the vaccines might be potent enough to eliminate tumours completely. A Stanford University team of scientists has promulgated an optimistic progress report on their work in developing a vaccine designed to battle B-cell lymphoma. The researchers obtained proteins from the cancer cells of individual patients with B-cell lymphomas and attached a chemical booster to the proteins to stimulate a stronger than normal response from the immune system. Nine patients were injected with the modified proteins over a six-month period. Tumours up to one inch wide were completely eradicated from two patients. The immune system of seven of the nine patients were ready to attack any remaining tumour cells. The researchers are trying to increase the potency of the vaccine by altering the way it is made and administered. (Extracted from *Wall Street Journal*, 22 October 1992)

Enzyme blockers aim at cancer spread

By targeting an enzyme that allows tumour cells to break free from their cellular matrix, British Bio-technology Ltd. (BBL), in Oxford, UK, hopes to give oncologists a way to contain cancer metastases. The company has a lead compound, BB-94, in early phase clinical trials in patients with metastatic breast cancer. Results are expected in the first quarter of 1993, said John L. Gordon, the firm's director of research. Another trial, giving BB-94 intraperitoneally to patients with malignant ascites resulting from abdominal tumours, is slated to start around the same time. BBL is collaborating with Cancer Research Campaign and the Imperial Cancer Research Fund in testing these compounds, said Gordon. Preclinical trials have been encouraging with survival significantly increased in mice. The group treated with BB-94 lived up to 150 days, while the controls died around day 25.

The drug inhibits a family of enzymes called the matrix metalloproteinases (MMP). Under normal circumstances, these enzymes are secreted in small amounts and are needed in tissue growth and repair. But tumour cells secrete high levels of the enzymes, using them to burrow through the body's cellular matrix and move freely from the primary tumour to remote parts of the body.

BBL is developing a number of synthetic MMP inhibitors. By aiming each at a specific enzyme, BBL plans to develop treatments for several ailments, including inflammatory diseases and eye injury. The company is also working on vascular metalloproteinases for treatment of hypertension and heart failure. (Source: *McGraw Hill's Biotechnology Newswatch*, 16 November 1992)

Test helps choose cancer treatment

Tamoxifen, the most prescribed drug for breast cancer, may actually enhance tumour growth in some patients. Although the drug fights the female hormones feeding the tumour, in some women, Tamoxifen is metabolized to more closely resemble oestrogen, which can promote tumour growth. Researchers at The University of Texas Health Science Center at San Antonio may have found a way to see whether this is occurring - and whether a different therapy should be prescribed. They received a US patent after developing a technique to measure the metabolized Tamoxifen in the blood. Armed with a $966,000, three-year grant from the National Cancer Institute, the researchers have started analyzing blood samples from breast cancer patients. In a separate but related project, the Health Science Center is participating in the first study to test Tamoxifen in healthy women who are at risk for breast cancer to see if it can prevent the disease before it ever starts. (Source: *BioBytes*, November 1992)

Increasing taxol yields

Alternative production methods for the anti-cancer drug taxol are closer to feasibility due to a proliferation of research breakthroughs on new sources of the drug.

Over the past year, Bristol-Myers Squibb Company and its major partners Hauser Chemical Research Inc. of Boulder, Colorado, Phyton Catalytic Inc. based in Ithaca, N.Y., and Weyerhauser Company of Tacoma, Washington, have made strides towards increasing the amount of taxol that can be recovered from the Pacific yew tree by means other than clear-cutting.

The race for new sources of taxol has several other entrants, which have no ties to Bristol and could be potential rivals in the nascent taxol supply market. Researchers from University of Florida at Gainesville have discovered different methods of increasing the yield of taxol than the processes developed by Bristol and its partners.

The original method for extracting taxol is from the bark of the Pacific yew tree, but it takes four to six trees to yield two grams of taxol, the amount required to treat one patient. The cost of this process and the scarcity of these trees is the reason other sources are

being investigated. Bristol says it intends to phase out bark-derived taxol by 1997.

At present, there are four alternate routes of taxol production. These include extracting taxol from renewable sources; semi-synthesis of chemically similar materials into taxol; plant cell culture technology, which involves producing taxol from cells of yew tissues; and total synthesis of taxol in the laboratory.

Producing taxol from renewable sources, such as the twigs and needles of the trees of various taxol species, can potentially yield more taxol than the bark-based method. However, it is necessary to establish tree nurseries for this to be a viable alternative. Since the yew tree grows slowly, sources say, it will be close to seven years before this route will be economically feasible.

Partially synthesizing taxol from chemically similar materials such as deacetylbaccatin III is a fairly promising method, but the most promising and quickest method of taxol production is cell culture technology.

The alternative that seems the most remote at this point is total synthesis of taxol in the laboratory. Barring unexpected breakthroughs, complete synthesis of taxol, sources say, does not seem likely to occur in the near future. (Extracted from *Chemical Marketing Reporter*, 28 December 1992)

Yew tree yields anticancer culture

Taxol, a natural anticancer drug derived from the bark of Pacific yew trees, may soon be available in greater amounts by growing cells in culture. Frank DiCosmo of the Center for Plant Biotechnology at the University of Toronto in Canada claims that his cultures yield up to four times as much taxol as bark from *Taxus brevifolia*, the only existing commercial source of the drug. Besides yielding more of the drug, the culture route does not require whole trees to be killed.

DiCosmo and his colleagues snip the tissues they need from the ornamental yew (*Taxus cuspidata*) or another relative called *Taxus canadensis*. When placed in nutrient agar and incubated, the plant cells proliferate and grow randomly into a mass of cells called a callus. After 30 days or so, the researchers grind up and process the cultures to yield around 0.02 per cent by weight of taxol, almost twice as much as from the bark of the Pacific yew.

The researchers also grow the tissue as cells suspended in a broth. With this method they have succeeded in raising the yield to around four times that from bark. DiCosmo expects taxol produced in this way to be available commercially within five years.

Escagenetics, a company in California, is also culturing yew cells to make taxol, while several groups of chemists are trying to synthesize it from raw materials. (Source: *New Scientist*, 9 January 1993)

Cancer test kits

Cancers can be detected and treated at an earlier stage than ever before thanks to kits just launched by a Northern Irish company. The company, Biosyn, was set up to market the technology developed by Queen's University, Belfast.

Tests with the kit are quick and cost half the price of the current method of detecting tumours which relies on highlighting already advanced cancer cells with radioactivity. The cheap test opens the way for regular screening for lung and gastric cancers. These types of cancer account for 70 per cent of cancers treated in the western world.

Each kit consists simply of 100 plastic strips. Little wells along the strips have been coated with synthetic peptides, which have been treated with biotin, a fluorescent marker

The peptides react with a protein on the cancer cells to form a distinctive residue which can be easily identified in a local doctor's surgery.

The kit, which can also be used to test tumours that have been removed, eliminates the wait for hospital test results. A similar kit, using different peptides, can assess the progress of rheumatoid arthritis by analysing synovial fluid from joints. (Source: *New Scientist*, 14 November 1992)

Genetic test for inherited thyroid cancer

A single blood test on a newborn child can tell with more than 99 per cent accuracy whether it has inherited a gene that will cause it to develop a form of thyroid cancer. Children with one affected parent have a 50 per cent risk of developing medullary thyroid cancer say the American researchers who developed the test. The cancer affects 1 in 50,000 people in the West.

Medullary thyroid cancer attacks large secretory cells within the thyroid gland. The cancer can be treated successfully if it is caught early.

Until now, the only way of detecting medullary thyroid cancer has been by screening the blood for the hormone calcitonin. The test shows the presence of the cancer.

The new blood test can identify, immediately after birth, individuals with a greater than 99 per cent chance of having inherited the cancer gene. Only

susceptible individuals need then be screened for calcitonin.

Terry Lairmore, a surgeon at Washington University School of Medicine in St. Louis, pointed out that the research team has not yet identified the specific gene that causes medullary thyroid cancer. Instead they looked for genetic markers located close to the gene. These markers are situated on either side of the area of the chromosome containing the cancer gene, and their inheritance in the population can be followed from generation to generation. A child who has inherited these markers can be predicted to have inherited the disease. According to the researchers the probability that predictions could be wrong is less than one per cent. (Extracted from *New Scientist*, 14 November 1992)

US alters cold virus to treat cystic fibrosis

The National Institutes of Health's Recombinant DNA Advisory Committee has approved three proposals to use genetically engineered cold viruses to ferry healthy genes into the airways of 25 people suffering from cystic fibrosis.

At this stage, the CF experiments are designed mainly to test the safety, rather than the effectiveness, of the treatments. Patients will receive one dose of healthy CF genes - either in the lungs or nose - and then be evaluated, before further treatment. The treatments target the cells that line the airways. Because these slough off every few months, researchers say patients would probably have to undergo repeated treatments to derive any long-lasting benefit.

Besides representing the first efforts to use gene therapy to combat CF, the experiments proposed by the National Heart, Lung and Blood Institute, the University of Michigan and the University of Iowa in conjunction with Genzyme Corporation, will mark the first time that adenoviruses have been harnessed for human gene therapy. Normally, these viruses cause cold-like respiratory infections. Trials of gene therapies now under way for other conditions employ either retroviruses or tiny bubbles of fat, called liposomes, to deliver potentially therapeutic genes.

The cold viruses used to carry healthy CF genes will be stripped of their ability to replicate and so cause illness. Despite this, there are still safety concerns. Patients will be isolated from other people for between three days and one month after treatment. This precaution is to ensure the patients have stopped "shedding" any of the artificial viruses that fail to invade airway cells, before being allowed to mix with other people. Other worries are that the genetically altered virus will recombine with wild adenovirus to create new infectious strains, or that repeated treatments will trigger immune responses that make the therapy worthless.

After their proposals cleared the crucial hurdle of receiving approval, leaders of the three teams said they hoped to begin their experiments early in 1993. However, they must receive final authorization from NIH director Bernadine Healy and the Food and Drug Administration. (Extracted from *New Scientist*, 12 December 1992)

Cystic fibrosis gene therapy protocol approval

Genzyme Corporation and the Departments of Internal Medicine and Physiology and Biophysics at Howard Hughes Medical Institute at University of Iowa Medical School have announced that the Recombinant DNA Advisory Committee (RAC) of the US National Institutes of Health (NIH) approved their human gene therapy protocol involving cystic fibrosis patients.

The protocol is designed to test the feasibility of using a replication deficient adenovirus vector to deliver the Cystic Fibrosis Transmembrane Conductance Regulator (CFTR) gene in a small number of CF patients. (Source: *News Release*, 4 December 1992)

Animal and livestock applications

Transgenic bull permitted to breed

The Dutch Parliament has decided that the world's first transgenic bull, should be allowed to procreate because his owners now suggest that his extra gene might be of benefit to patients with cancer or AIDS.

The bull carries a modified version of the human gene for lactoferrin, a protein that is produced in milk and forms part of a mammal's natural defence against infection. The idea of introducing this gene into cattle was that it might help to prevent mastitis.

Gene Pharming Europe, a company based in Leiden, and the veterinary research institute IVO-DLO, wanted to breed from the bull to find out if his female descendants would benefit from the lactoferrin gene. Gene Pharming and the ethical committee which advises the Government later agreed to change the aims of the experiment. They suggested that milk from the bull's daughters could be a source of human lactoferrin to fight human infections, such as sepsis and the gut infections common in patients with AIDS. This change of direction brought heavy criticism of both the company and the committee.

According to the Dutch Society for the Protection of Animals (SPA), there are already several research groups close to producing human lactoferrin from genetically manipulated yeasts and moulds, making such animal experiments redundant.

Researchers at the University Hospital in Bern, Switzerland, say human lactoferrin can reduce the severity of gut infections in cancer patients. The head of Gene Pharming, Herman de Boer, says that given intravenously, rather than as a food, lactoferrin might help in the treatment of sepsis. Preliminary results from his company show that lactoferrin binds to certain toxins produced by the bacteria that cause sepsis, he says. (Source: *New Scientist*, 9 January 1993)

Agriculture applications

Double trouble

A two-pronged attack on pests has been developed by researchers at Kansas State University and the US Grain Marketing Research Laboratory. They have combined a disruptive insect gene with an insect virus to make a biopesticide which they claim kills pests quickly and safely, while also devising a possible way to immunize plants against pests.

Chitinase enzyme genes, taken from the tobacco hornworm, are introduced into baculovirus, a biopesticide already in common use.

The chitinase, normally produced in moulting, degrades the chitin in the insects' shells, while the virus acts on the gut lining. The dual attack of enzyme and virus thus prevents proper feeding and moulting.

In a related project, researchers at Kansas State University are trying to use the chitinase gene to give plants internal protection from insects and fungal pathogens.

Subbaratnam Muthukrishnan explains that plants produce chitinase to defend themselves under insect attack. By introducing a recombinant chitinase gene into the plant, Muthukrishnan hopes that the plant will be able to produce lots of the enzyme all the time.

By attacking the insects on two fronts - using the biopesticide and plant immunization - the researchers hope it will take the pests longer to develop resistance.

Preliminary tests are underway but it is likely to be another five years before the biopesticide and plant immunization techniques can be launched commercially. The researchers hope that in the future their work will protect crops like tobacco, wheat, corn and rice. (Source: *Chemistry & Industry*, 19 April 1993)

Sunflower to guard tomato

Scientists at the Bangalore based Indian Institute of Horticultural Research (IIHR), have found the sunflower to be an effective "trap crop" in tomato fields. It can be dovetailed with existing integrated pest management strategies.

Heliothis armigera, which can cause up to 80 per cent damage to the crop in severe cases, could be managed efficiently by the new technique. The sunflower crop attracts and traps the young larvae, which can then be easily collected and destroyed or used for multiplying Nuclear Polyhedrosis Virus (NPV), to cripple other larvae invading the tomato crop.

The entomologists have already tried out *Trichogramma brasiliensis*, NPV and early sunflower as a trap crop as a part of the strategies for an integrated pest management programme. So far, the application of NPV at 500 larval equivalent per hectare has effectively controlled the fruit borer. However, in spite of NPV being very effective, the research institutions cannot supply the viral culture to the farmers. To redeem this situation, use of early sunflower as a trap crop is being studied at the institute. Initial trials showed that the sunflower was an effective trap and the third instar larvae could be easily collected from its head. Once this is done, it is possible to inoculate the virus and multiply the viral culture for spraying in the fields.

Scientists at IIHR are concentrating on this aspect and striving to arrive at the optimum number of sunflower rows that could be raised with tomato crop. Efforts are now being directed towards standardizing other agronomic practices such as the time of planting, planting density and collection schedules etc. (Source: *Biotechnology and Development Review*, No. 2, November 1992)

Vermiculture biotechnology for sustainable agriculture

World-wide there has been an increasing awareness about alternative agricultural systems, alternatively known as biological or low input agriculture because of their greater ecological and environmental friendliness. These systems integrate traditional practices with modern understandings of life sciences. A transition from chemical to sustainable agriculture, however, would normally take three to six years. This is the time required to trigger the soil biology to get the same yields without excessive reliance on chemical fertilizers and pesticides. This time, however, can be reduced to as short as three months by harnessing vermiculture biotechnology into the soil.

Vermiculture biotechnology uses earthworms for processing various solid and liquid wastes into valuable resources and cleaning up the environment with cost effective waste management technology.

Bhawalkar Earthworm Research Institute (BERI), Pune, after 12 years of extensive field research, has been

able to develop a package for farmers to affect a swift changeover to sustainable agriculture without a loss of yield.

There have been encouraging results in such diverse crops as grapes, banana, coconut, vegetables, flowers, etc. The energy input in the process is very small compared to other conventional waste treatment processes and hence the operating cost becomes almost nil. Other benefits accruing to the farmers include complete savings on annual expenditure on chemical fertilizers, cultivation and weeding, reduced soil salinity and reduced pesticides spray as plants develop. According to the recent estimates, the net profit of the farms have almost doubled since they switched over to this method of farming.

Vermiculture biotechnology could play a key role in reclaiming wasteland development and in promoting sustainable agriculture. Various organic wastes are utilized as valuable raw materials for soil biotechnological processes which also reduces the environmental pollution. Work is under way to extend the area of operations to treat non-toxic waste water for converting industrial effluents from distillery, tannery, slaughterhouse and sewage etc., into resources in the form of vermicastings.

BCIL has signed an MoU with BERI for assisting in transfer of the vermiculture biotechnology. (Source: *Biotechnology and Development Review*, No. 2, November 1992)

Industrial microbiology

Biodegradable plastic disposable razors

Kai Corp. will market two types of disposable razors, both made of a biodegradable plastic Biopol.

The completely biodegradable plastic Biopol was developed by Imperial Chemical Industries PLC (UK), and is functionally the same as conventional plastics, but is produced by the fermentation process using glucose from corn, sugarcane or sugar beet as the raw material. When buried in the ground or cast into the sea after use, it starts decomposing after about three months by micro organism action, and is completely decomposed into water and carbon dioxide within two to three years.

The biodegradable plastic is used on all parts other than the metal blade. The metal blade is oxidized and corroded in the natural environment, so the entire razor assembly will be completely returned to natural substances in the ground. Even when incinerated, it will be decomposed into carbon dioxide and water, so no toxic substance is left. Further information available from Kai Corporation, 1-17-6, Higashi-Kanada, Chiyoda-ku, Tokyo 101, Japan. (Source: *JETRO*, August 1992)

Genetic engineering to produce enzymes for organic chemistry synthesis

Genetic engineering could be used to produce enzymes for use in organic chemistry synthesis, according to Dr. A. Ian Scott of Texas A&M University (College Station). So far Scott has produced enzymes to make compounds such as vitamin B12, penicillin, and periwinkle alkaloids. The ability to produce complex enzymes could allow the production of compounds too complex to make by conventional means. The enzymes needed for a particular production pathway can be detected in cells by nuclear magnetic resonance spectroscopy. Simply putting all the needed enzymes together in a brew can allow the reactions to proceed smoothly to the desired product. Adding mutant enzymes to alter the final product can let researchers tinker with the final product to try to improve say, penicillin. (Extracted from *Science News*, 5 September 1992)

New biodegradable plastic

Showa Chemicals (Japan) has jointly developed a 50-micron thick plastic which could help lower medical waste. The company developed the material with the Ministry of International Trade and Industry. The material is made up of polycaprolactone (up to 80 per cent) and polyethylene and can be used in the manufacture of a variety of products. Polycaprolactone is a structurally weak, biodegradable plastic, which is broken down by the enzyme lipase. Lipase is secreted by micro-organisms in the soil, causing plastic to be degraded into small fragments. Polycaprolactone can be strengthened using a specially designed structure for the polyethylene. The company plans to market products manufactured from this new plastic late in 1992. (Extracted from *Asian Wall Street Journal*, 1 June 1992)

Energy and environmental applications

Treatment of natural rubber waste by micro-organisms

The National Institute of Bioscience and Human-Technology and Fuji Latex Co., Ltd. have jointly succeeded in degrading waste natural rubber products using micro-organisms at a high efficiency.

In experiments conducted on natural rubber gloves 0.2 mm thick, the gloves were degraded almost entirely in about two weeks. Waste rubber products used to be incinerated or buried in the ground, but combustion at high temperatures damages the furnaces and burial has an adverse influence on the environment. The establishment of this highly efficient natural rubber waste degradation technology is expected to lead to the development of a clean, low-cost system for automatically treating waste rubber products.

The micro-organism was *Nocardia sp.* strain 835 A, a rubber degrading micro-organism

isolated from farm soil in Tsukuba City, Ibaraki Prefecture, Japan.

The testpieces were degraded when the fine fragments passed through a double-layer gauze. The degradability was the highest in the case of 2.5 and 5 g, and virtually complete degradation occurred in 15 days at the shortest.

The research team plans to search for a better rubber degrading micro-organism and to improve the culture conditions. Further information is available from: National Institute of Bioscience and Human-Technology, AIST, Research Planning Div., 1-1-3, Higashi, Tsukuba City, Ibaraki Prefecture 305, Japan. (Source: *JETRO*, January 1993)

Reactor for methane-eating bugs

Field trials of a bioreactor designed to break down chlorinated hydrocarbons are scheduled to start in early 1993, according to Asea Brown Boveri Environmental Services, Inc. (ABB-ES), which design the system.

The company also said that the US Patent and Trademark Office has notified ABB-ES that it will soon receive the patent for the "Methanotropic Air-tight Rotating Bioreactor" (MARB). The patent covers modifications ABB-ES scientists have made to the rotating disk system that is commonly used in microbial waste water cleanup, said Sam Fogel, the company's director of bioremediation systems.

ABB-ES's bioreactor consists of a series of rotating polyethylene disks coated with methane-eating microbes, in a tank made airtight to contain volatile chemicals. Water runs through the bottom of the tank, while the methane oxygen food source is pumped through the top. As the disks rotate, the bacteria are alternately fed, then submerged into the contaminated water. For treating non-chlorinated compounds, the reactor can function without methane.

In nature, the aerobic bugs that ABB-ES is using are found just above the anaerobic zone in swamps and marshes, areas that are rich in methane.

The Portland, Maine-based firm has tested MARB in pilot-scale treatment of groundwater from three Super-fund sites. The water was contaminated with coal tar, toluene, trichloroethylene, chloroform, vinyl chloride and methyl methacrylate (MMA). In all cases, said Fogel, the bioreactor brought pollutant concentrations to below detectable levels.

Fogel added that his research team was surprised at the speed with which the microbes processed the compounds, which was about six hours to reduce 500 parts per million of MMA to less than one ppm.

Rather than using a pure strain, ABB-ES has chosen a consortium of methane-eating bugs that have the ability to degrade several different kinds of compounds.

However, the reactor could be adapted to accommodate several pure strains of bacteria, as well as bioengineered ones, down the line.

In the upcoming trial, ABB-ES plans to treat groundwater contaminated with vinyl chloride, mixtures of chlorinated chemicals and petroleum constituents. Concentrations of contaminants will range from less than one ppm to more than 500 ppm.

ABB-ES will most likely license the technology, or hire a firm to fabricate it, if the trials show that the technology works and is cost-effective. (Source: *McGraw Hill's Biotechnology Newswatch*, 7 December 1992)

E. PATENTS AND INTELLECTUAL PROPERTY RIGHTS

Extension of term of pharmaceutical patents in Europe

The European Patent Convention has been amended to provide for extension of term of European patents beyond the present maximum of 20 years. If regulatory requirements have caused marketing of a patented pharmaceutical to be delayed for more than five years beyond the filing date of the patent, a supplementary protection certificate may now be obtained. The Certificate must be sought on a country-by-country basis, and its maximum term is five years beyond the date at which the original patent would have expired. From 7 January 1993, applications for supplementary protection certificates can be filed in Britain, France, Germany, Italy, the Netherlands, Belgium, Luxembourg, Denmark and Ireland. Similar provisions will not be available until 1 January 1998 in Greece, Portugal and Spain. The requirements vary from country to country, and specific advice should be sought. (Source: *Australasian Biotechnology*, Vol. 3, No. 1, February 1993.

Biotech patents: EC debate moves to Council

The European Parliament in October 1992 completed the contentious first reading of the Commission's proposal for a Council Directive on the legal protection of biotechnological inventions after four years. The Parliament accepted in principle the main aims of the proposal, to clarify and harmonize throughout the community the patent law as applied to biotechnology, and consistency with the European Patent Convention. In its amendments, it has demanded more explicit clarification of the exclusions from patentability

(allowed under the EPC if contrary to public order and morality).

Exclusion would apply to "the human body or parts of the human body *per se*; processes for modifying the genetic identity of the human body for a non-therapeutic purpose which is contrary to the dignity of man; and processes for modifying the genetic identity of animals which are likely to inflict suffering or physical handicaps upon them without any benefit to man or animal". The Commission in its amended proposal to Council has incorporated the above-quoted elements. Regarding the "farmer's privilege" (for sowing farm-saved seeds from his harvest), the Commission, "though initially opposed to the amendment, has finally accepted it to allow the Council to discuss it as part of a continuing cooperation procedure" (under the provisions of Article 100A).

The 37-page amended proposal, COM(92)589 final-SYN 159, of 16 December, is available on request from DGXII E-1, Commission of the European Communities, rue de la Loi, 200, B-1049 Brussels, Belgium. Tel.: (32) 2 2965619. Fax: (32) 2 2955365, or (32) 2 2964322. (Source: *EBIS*, Vol. 3, No. 1, 1993)

Release of sample of deposited micro-organism authorized by Australian Patent Office

The first Certificate of the Commissioner of Patents authorizing release of a sample of a micro-organism from a deposit made under the Budapest Treaty was issued by the Australian Patent Office in May 1992. Under the Australian Patents Act an applicant may rely on a deposit of a micro-organism in an approved International Depositary Authority under the Budapest Treaty to satisfy the requirements of sufficiency of disclosure. Once the application is open to public inspection, an interested person may request the Patent Office to issue a Certificate authorizing release. However, before the specification is laid open to public inspection, the applicant may specify that such sample is only to be released to an independent third party expert. This is analogous to the so-called "expert solution" available under the European Patent Convention. (Source: *Australasian Biotechnology*, Vol. 3, No. 1, February 1993)

1992 Biotech patent race

Pharmaceutical makers Merck (Rahway, NJ), Abbott Laboratories (Abbott Park, IL), and Boehringer Mannheim (Mannheim, Germany) head the list of firms receiving US biotechnology patents in 1992, according to Micro-Patent (New Haven, CT), a publisher of patent information. Merck received 61 US patents, while Abbot Labs gained 48. Boehringer and Hoechst (Frankfurt) received 45 and 41 US patents, respectively. Eastman Kodak (Rochester, NY) obtained 39. (Source: *Chemical Week*, 10 February 1993)

Biotech patent bills

Biotechnology companies would have an easier time obtaining process patents under legislation introduced in both houses of Congress in early February. Several complex court cases have created uncertainty over patent protection for processes, and the bills introduced would clarify the procedures. (Extracted from *Chemical Week*, 10 February 1993)

Patenting of genetic material

The international journal *Science* recently published three interesting papers in this area. (Ref. *Science*, Vol. 257, 14 August 1992, pp. 903-918.)

In the first paper by Rebecca Eisenberg who is a Professor of Law at the University of Michigan, it was noted that the National Institute of Health has filed patent applications on more than 2,750 partial complementary DNA sequences of unknown function. The rationale for patenting is discussed in this paper.

The second paper by Reid Adler who is the Director of the Office of Technology Transfer, NIH, gives a historical perspective for the patenting of gene sequences and describes the evolution of patent law in relation to this.

The third paper by Thomas Kiley who is an Attorney and Director of some biotechnology companies, states that the proposal by the National Institute of Health to patent products resulting merely from sequencing the human genome is a mistake. He feels at worst that it is wrong in patent law and at best that it relies on deficiency in law concerning what is defined as useful.

These three papers certainly provide food for thought for those interested in the commercialization of molecular biology and should provide definitive texts for patent attorneys having to come to terms with the implications behind patenting of genetic sequences. (Source: *Australasian Biotechnology*, Vol. 2, No. 6, December 1992)

F. BIOINFORMATICS

Biological Reaction Engineering

Principles, Applications and Modelling with PC Simulation

This book, by I. J. Dunn, E. Heinzle, J. Ingham, J. E. Prenosil, is the result of 10 years' experience in organizing and teaching courses in biological reaction engineering. It gives engineers and scientists all the information they need to analyse the behaviour of

complex biological reactors using mathematical equations and a dynamic simulation computer language.

Part I treats the fundamentals of modelling (mass balance equations involving reaction kinetics and mass-transfer rates), making them readily understandable to those new in the field. Part II gives 45 example problems, complete with models and programmes.

The text book is the first of its kind to include a diskette with a commercial simulation language. The diskette can be run on any DOS personal computer.

Users will appreciate how the simulation runs can be interrupted for interactive parameter changes and instructive plotting.

1992. Ca 460 pages. Hardcover, Fr. 215. ISBN 3-527-28511-3. Further information is available from VCH, P.O. Box 4020 Basel, Switzerland.

Biotechnology and Development Monitor to continue

Biotechnology and Development Monitor (BDM) has since September 1989 produced 12 excellent issues covering key issues and news items relating to biotechnology in developing countries. Distributed free, it has seen demand grow from a few hundred to 4,000; and has gained a reputation for excellence.

BDM is not a specialized scientific publication, but a resource for science policy-makers and advisers in developing countries, international agencies, and in all other circles having related interests.

It is therefore welcome news that the Directorate-General for International Cooperation (DGIS) of the Netherlands Ministry of Foreign Affairs has agreed to fund a follow-up project over the next two years. In its future development, publication will be based on a network of institutes in different regions of the world; and publication will be trilingual, in English, French and Spanish.

For further details, contact Editor, Professor Gerd Junne, Biotechnology & Development Monitor, University of Amsterdam, Department of International Relations and Public International Law, Oudezijds Achterburgwal 237, 1012 DL Amsterdam. Tel.: (31) 205252177; Fax: (31) 205252086.

IITA

The International Institute of Tropical Agriculture (IITA) in Ibadan, Nigeria has replaced its TRIPP Newsletter with the *Tropical Root and Tuber Crops Bulletin*.

The Bulletin is printed in English and also French.

For more information, contact: Alfred Dixon, Bulletin, TRIP, IITA, PMB 5320, Ibadan, Nigeria.

BIOTECH-Africa Consultancy

The *Tropical Agbiotech Monitor* is a quarterly newsletter published by the Biotech-Africa Consultancy group of Guelph, Ontario, Canada. It will summarize current research findings in tropical agricultural and forestry biotechnology for developing countries. Information will be gathered from major scientific journals, books, conferences, and interviews.

The newsletter will include:

- Complete citations of relevant publications;
- Contact addresses for articles, new protocols, etc.;
- Major coming events relevant to biotechnology of tropical agriculture and forestry;
- Feature articles on important topics, when necessary.

For more information regarding the newsletter, contact: Dr. John C. Afele, Biotech-Africa Consultancy, 240 College Ave. W, Guelph, Ontario, Canada N1G1S7. Tel.: (1-519) 763-4246. Fax: (1-519) 767-0755.

Biosafety: The safe application of biotechnology in agriculture and the environment

The mandate of the International Service for National Agricultural Research (ISNAR) is to assist developing research systems. In this 39-page booklet, they provide a practical guide for policy makers and research managers, on the safe use of biotechnology products within their countries. It is a masterpiece of clear communication, treating the issues with balance and perspective; the result will be appreciated in developed and developing countries.

The document suggests a series of steps to establish a national biosafety system, starting with a national committee to establish policies and procedures.

The authors advocate maximum use of existing institutions, personnel and legislation. They summarize five key principles:

1. Regulatory review should focus on the characteristics and identified risks of the biotechnology product, not the process by which it is created.
2. For those biotechnology products that require review the review process should be designed for efficiency and effectiveness while assuring the

protection of public health and environmental safety.

3. Regulatory requirements for modern biotechnology should be integrated into the overall regulatory system, which governs the release of new products in the agricultural sector.

4. The degree of familiarity with the behaviour of similar organisms when released into the environment should determine the level of regulatory oversight required. This may range from minimal to extensive, depending on the degree of hazard identified.

5. Regulatory programmes should be flexible and capable of adapting quickly to the new knowledge and understanding produced by the rapid advances in biotechnology.

The booklet reviews the evolution of the biosafety and regulatory debate, underlining the significance of other work such as that of OECD, the UNIDO/UNEP/WHO/FAO Working Group on Biosafety, and the US National Research Council.

The authors are from three continents: Gabrielle Persley, biotechnology manager at the World Bank, previously project manager of the WB/ISNAR/Australian study on biotechnology in the service of world agriculture; Val Giddings, senior geneticist with the biotechnology programme of the US Department of Agriculture, Animal and Plant Health Inspection Service, and previously project manager for the US Congress Office of Technology Assessment Report on "Field Testing of Engineered Organisms: Genetic and Ecological Issues"; and Calestous Juma, Founding Executive Director of the African Centre for Technology Studies in Nairobi, author of several books including "The Gene Hunters".

Single copies of *Biosafety* are available free from ISNAR to professionals in developing countries working in the area of agricultural research policy, organization or management.

For others, copies may be purchased from:

Winrock International Agribookstore,
1611 North Kent Street,
Arlington VA 22209-2134 USA.
Price: US$ 8.95 plus shipping.

ISNAR
P.O. Box 93375
2509 AJ The Hague
The Netherlands
Tel.: (31) 703496100;
Fax: (31) 703819677

Issues in the Commercialization of Biotechnology

The Expert Group Meeting on the Commercialization of Biotechnology was held by the United Nations Industrial Development Organization (UNIDO) from 28 October to 1 November 1991 at Vienna. The overall objectives of the meeting were (a) to review both general and product-oriented policies and programmes in developed and developing countries related to the commercialization of biotechnology in selected areas, focusing on health care and food processing; (b) to identify the elements for success and constraints for bringing products to markets; and (c) to propose modalities for promoting the application of biotechnology, in particular through international cooperation.

The proceedings of the meeting have now been issued as one of UNIDO's General Studies Series - Issues in the Commercialization of Biotechnology (ISBN 92-1-106279-9). Apart from giving the report of the meeting, with its conclusions and recommendations, the book reproduces the technical papers presented under four broad headings covering commercialization issues in health care; commercialization issues in food processing and agro products; case studies of country specific experiences; and safety issues, education and training.

The publication, which runs to 240 pages and costs $45, may be obtained from UNIDO Documents Unit (F-355), Vienna International Centre, P.O. Box 300, A-1400 Vienna, Austria.

Directory of the Latin American Biotechnology Industry

The Inter-American Institute for Cooperation on Agriculture has started the preparation of the Directory of the Latin American Biotechnology Industry. The first volume covers Mexico and was published in 1992. It includes basic information on 34 companies with biotechnology activities in the country. The volumes on Argentina and Uruguay are ready for publishing. The other Latin American countries will be covered during 1993 with financial support provided by the Canadian International Development Agency.

ATCC: new gene mapping kit for *Saccharomyces cerevisiae*

The American Type Culture Collection (ATCC), in collaboration with the Maryland Olson Laboratory at the University of Washington, Seattle, is distributing a kit for mapping *S. cerevisiae* by using the prime set of overlapping mapped genomic clones from *S. cerevisiae* AB972.

The kit includes two hybridization membranes containing DNA from over 1,170 clones covering over 95 per cent of the Saccharomyces genome, two transparent templates for localizing clone positions on the membrane, and one tube of positive control DNA.

ASCII files containing data on the clone set and the clone/member position are provided on a floppy disk for use on either PC-DOS or Macintosh computers. Details from: ATCC Marketing, 12301 Parklawn Drive, Rockville, Maryland 20852-1778, USA. (Source: *Biotechnology Bulletin*, February 1993).

OECD report on biotechnology, agriculture and food

The report, edited by Sir Barry, former director of the AFRC Institute of Animal Research and Genetics Research, is the result of a two-year study by an international panel of experts and gives a global perspective on the scientific potential of - and industrial opportunities in - agrofood biotechnology. It includes up-to-date surveys of biotechnology advances in plants, animals, food and non-food products, together with sections on industrial strategies, patent protection, economic impacts and public acceptability (ISBN 92-64-13725-4). Details from: OECD Publications, 2 rue Andre-Pascal, 75775 Paris Cedex 16, France or from HMSO.

"Technology and Transition: A survey of biotechnology in Russia, Ukraine and the Baltic States", by Anthony Rimmington with Rod Greenshields. Pinter Publishers, London. 227 pages. UK £47.50

The book is balanced in describing the successes (microbial protein, lysine production), and the relative failure to keep up with genetic engineering and recombinant products. It particularly highlights the appalling pollution inflicted on the environment and local population by the badly-run single-cell protein plants. The alternative structures emerging in the transition to a market economy are described, in the countries indicated by the title.

Of particular interest is the success of Lithuania in enzyme production, thanks to the energies of Professor Janulaitis.

Of special value is the Directory of biotechnology R&D and production centres, with contact details.

Special emphasis is given to the opportunities for foreign contact and investment; a list is given of contracts, joint ventures and collaborations with Western companies.

Sustainability through Biodiversity: Designing Crucible of Culture, Creativity and Consciousness

Dr. Anil Gupta of the Indian Institute of Management has produced a thoughtful working paper on managing biodiversity from a well-researched perspective. "Sustainability through Biodiversity: Designing Crucible of Culture, Creativity and Consciousness" looks into the various aspects of local people's relationship to biodiversity, particularly in India. He draws out the ethical and cultural traditions associated with biological resource management and discusses the institutional framework for supporting the role of indigenous people in working with biodiversity. This paper No. 1005, January 1992, is one of a series of working documents put out by the IIM on local knowledge, conservation of genetic resources and related issues. Available from Indian Institute of Management, Ahmedabad 380 015, India.

Proceedings of a Workshop: Biotechnology Policy and the CGIAR

The International Service for National Agricultural Research, a research centre operating under the auspices of the Consultative Group on International Agricultural Research, has published the proceedings of a workshop on "Biotechnology Policy and the CGIAR". It contains the summaries of a seminar held in The Hague last September where two main policy issues of relevance to the CG's International Agricultural Research Centres (IARC's) were discussed: biosafety and intellectual property rights. Seventy participants attended from the public and private sectors, national research programmes, IARC's and development agencies. Single copies of the report are available free of charge. Available from ISNAR Publications Service, P.O. Box 93375, NL-2509 AJ The Hague, Netherlands. Tel.: (31-70) 349.61.00, Fax: (31-70) 381.96.77.

Theta Market Report No. 301: therapeutic proteins markets

This report examines the biotechnology protein therapeutics market. The market for the major US-approved biotechnology protein-based therapeutic products is analysed by market size, growth, potential and competition. The manufacturers of these products are analysed from a marketing perspective.

There are currently 15 major new protein-based therapeutic drugs with sales of over $2 billion that have been approved by the FDA for use in the US. In addition, there are approximately 25 new indications awaiting FDA approval for these same drugs.

The report estimates the current size of the market; determines current and projected five-year growth; assesses market shares of the market leaders and profiles seven competitors, and provides insights into trends.

Theta conservatively estimates the growth of this market including new indications and new protein-based drugs to be $3.5 billion by 1997 and believes the market share mix will be quite different in the next few years as new protein drugs and new indications for current protein drugs are approved.

Findings from the report reveal that over 140 biotechnology drugs are in development by over

60 companies; a growing number of alliances, joint ventures and licensing agreements are being drawn up between "bio to bio" companies; the outlook of management has changed with more interest in retaining long-term value and remaining independent; raising capital is still paramount as the cost of technology, clinical trials and scale-up facilities, keeps rising; and that in the current market, there is an abundance of potential corporate partners.

The information used to prepare the report was obtained from a number of sources including US Government data, industry surveys, interviews with marketing managers/product lines, annual reports and 10K's, trade publications and journals, trade shows, product and sales literature and Theta's databases. Price: $795. (Source: *News Release*, January 1993)

Japan Biotech Industry Directory

The JBA (Japan Biotechnology Association) has recently published the 1992 edition of the directory of member companies which are actively involved in bioindustry development in Japan. The one-page description of each of the 189 promoting member companies includes the Research Projects, expenditure, number of researchers and location of the main research facilities for biotechnology and non-biotechnology fields. Coordinates are provided of a contact person in each company. The JBA also has 113 supporting member companies, 55 public sector members and 1,611 private members. This directory (in English) is issued by the JBA International Cooperation Committee in order to promote exchange of information and opinion with overseas organizations. It is available from Japan Bioindustry Association, 10-5, Shimbashi 5-chome, Minato-ku, Tokyo 105. Tel.: (81) 334333545; Fax: (81) 3345911440. (Source: *EBIS*, Vol. 2, No. 4, 1992)

Seed Industry Leaflets

The International Seeds Trade Organization ASSINSEL (International Association of Plant Breeders) and GIBiP (Green Industrial Biotechnology Platform) have worked together to publish a series of opinion papers on the role of the Seed Industry for Consumer and Society. In the first of the series plant breeders address some of the natural concerns people have about seeds and biotechnology. It poses the questions - what is plant breeding; is it necessary and safe; how can plant biotechnology be developed in a responsible way? It concludes that plant breeders and biotechnologists have a major role to play in creating a sustainable future and that a sound legal and regulatory framework is required to encourage the industry to continue long-term significant investment.

In another leaflet the benefits of preserving world crop genetic resources are highlighted. These are described as mankind's living inheritance which cannot be replaced if lost. The approach of industry to preserve world crop genetic resources is outlined. Details: Zaadunie BV External Concern Relations, 1600 AA Enkhuizen, the Netherlands. Tel.: (31) 2280666403; Fax: (31) 2280666400. (Source: *EBIS*, Vol. 2, No. 4, 1992)

BioCommerce Data Ltd.
New UK Biotechnology Directory for 1993

The BioIndustry Association and BioCommerce Data Ltd. have scheduled publication of the fourth edition of their popular directory of British biotechnology for January 1993. The UK Biotechnology Handbook '93 provides full page profiles of over 700 organizations involved in biotechnology including universities, venture capital providers and government agencies as well as over 530 companies. The book also includes in-depth review articles by eminent authors dealing with such topics as environmental regulations, the UK diagnostics industry, biodiversity, reaching the US market, European coordination and recent British public offerings. The articles will be topical and informative and provide a source of information complementary to the directory listings.

For further details contact: BioCommerce Data Ltd., Prudential Buildings, 95 High Street, Slough, SL1 1DH, England, UK. Tel.: +44 (0) 753 511 777; Fax: +44 (0) 753 512 239.

G. SPECIAL ARTICLE

Biotechnology in South Asia: Issues of Technological Capability and Development

Rohini Acharya

1. Introduction

After many decades of relative anonymity, technology and especially technological change and its links to economic growth have become centre stage in the debate on development. Much of the recent analysis has concentrated on technological innovation and technology gaps between industrialized countries. The effect has been that a considerable amount of research on these issues has also found its way to developing and industrializing countries. The phenomenal success first of Japan and more recently of South Korea and the other Asian NIC's has been largely attributed to technology and the ability of the economy to adapt to technological change. In turn other industrializing countries, especially those with a certain degree of technical skills and financial resources are looking more closely at this model of development in order to reduce the widening technological and economic gaps between the industrialized world and themselves. Of all the reasons that are attributed to the success of the Japanese

and South Korean models of development, the one that appears to be receiving the closest scrutiny in most developing countries is that of strategic targeting. The debate however raises a number of other questions relating to technological capability and the ability of the economy to adapt itself to accepting and adopting a new technology in an efficient manner.

The paper presented here looks at some of the recent discussions in the context of biotechnology research and development in industrializing countries. Industrializing countries in this context are developing countries which are characterized by a certain level of technological capability, skills and a knowledge base which is able to adapt new science based technologies to the local environment. Biotechnology is an interesting case to look at because it can be adopted by countries having a wide range of technological skills ranging from relatively simple activities such as plant breeding to the highly sophisticated genetic engineering research which is only within the reach of the more scientifically advanced nations. Based on a survey carried out recently of six south Asian countries, the paper attempts to examine issues of technological capability and the likelihood of these countries developing a successful biotechnology industry based on their technological capabilities. What is meant exactly by technological capability and strategic targeting is outlined during the course of the paper.

2. Technology and Economic Development

Through the years economists have debated the many possible causes for why different countries experience different rates of economic growth with respect to each other and why economic gaps develop between countries. A number of different frameworks have been used to explain production structures and economic growth rates in different countries, including differences in initial labour and capital endowments, changing skills among the population, and the theory of technology gaps between nations. This final analysis, that of technology gaps has found a lot of appeal in recent years. The development of the product cycle theory by Posner (1961), where technical change occurred as a result of innovation in industrialized countries, and imitation in developing countries has now been formalized in economic theory. Differences in growth rates between countries are no longer considered as given but instead are attributed to technology "gaps". Most importantly, they no longer assume that production patterns based on national endowments remain static but instead, technology can be used to enhance or change these national endowments over time. Thus while initially a country begins from a position of comparative advantage in labour intensive products, there is no reason why it should remain in that position. Instead it may be possible for the country to use new technologies to enhance its basic comparative advantage or indeed in the more extreme case to change that comparative advantage.

The model of economic growth developed first by Japan and then followed successfully by South Korea and the other Asian NICs has given rise to a new branch of economic analysis, first put forward formally by Brander and Spencer (1983) and later given empirical support in a book edited by Krugman (1988) on the new economics. The identification of "strategic sectors" in the economy, for example automobiles in the case of Japan after the war allowed the Government along with industry to develop an infrastructure which would support and develop this industry. However the key here was an infrastructure which was flexible enough to adapt to changing needs and changing technologies (see Freeman 1987 for an excellent analysis of technological development in modern Japan).

Soete (1991 a,b) describes three types of strategic targeting. The first type is the most obvious, where certain sectors are considered to be strategic such as military technologies but also other areas considered to be important to the economic development of a country or a region. The microelectronics support programme of industrialized countries are included in this category; agricultural technologies in developing countries may also qualify. Nevertheless, even within this relatively narrow definition, the problem of identifying strategic and non-strategic sectors arises. The second category of strategic targeting is in trade policy. The "new trade" theory points to the existence of increasing returns in some products which are traded internationally. Here changing technologies make it possible for countries to reap economic rents from dynamic increasing returns. The final sector and probably the broadest relates more to industrial policy. The example used here is the automobile industry with its forward and backward linkages, pervading all aspects of socio-economic activities in a country. Here of course the danger is that such a definition can be used by Governments to justify protection on a very large scale, some of it perhaps unjustified.

In the following section we examine the impact of a new technology, namely biotechnology, on industrializing countries in southern Asia. The survey, based on a recent visit to six countries in south and South-East Asia, looks at developments in research, policies geared toward promoting biotechnology and the general research and development environment, including issues such as intellectual property rights and education which are relevant to the development of biotechnology. Through the survey we not only hope to provide a brief glimpse of the development and diffusion of a new technology in these countries, but also attempt to address some of the issues discussed above, relating to strategic targeting and technological capability.

3. Biotechnology in South Asia: A Survey

3.1. India

In India biotechnology research and development has been promoted within the framework of the more

general policy on science and technology. That the Government perceived biotechnology as important for fulfilling India's national development goals was evident when the Department of Biotechnology was formed in 1986 as a separate department within the Ministry of Science and Technology. The main reason for forming the department was the perceived need to coordinate biotechnology research already ongoing for some years in the country. It was felt that while the scientific capability to develop biotechnology based products existed, the research needed to be guided in a particular direction which would enable it to fulfil national needs. For this a central body was needed which could firstly ensure cooperation between researchers located in far flung areas of the country as well as act as an institution through which the Government of India could allocate funding for specific research projects or areas. The Department's major responsibilities include:

1. To evolve integrated plans and programmes

2. To identify specific research and development programmes and biotechnology related manufacturing

3. To identify and establish infrastructural support at the national level

4. To import new, recombinant DNA based biotechnological processes, products and technology

5. To evolve biosafety guidelines for laboratory research and production applications

6. To initiate scientific and technical research priorities

7. To initiate programmes of manpower development in biotechnology and

8. To establish the International Centre for Genetic Engineering and Biotechnology (ICGEB)

As is evident from this agenda, its priorities lie in research and training. This is done mainly by collaborative work with universities and research institutions who provide the infrastructure and the research and training while the Department provides the funding. In addition, there are advisory boards composed of both scientists within the country and foreigners. The latter category includes non-resident Indians who are represented in relatively large numbers. On a more specific level each project is supervised by a group consisting of members of the scientific community as well as personnel from the Department of biotechnology.

In agriculture, the emphasis lies on developing new, superior varieties of four crops, rice, brassica, chickpea and wheat; biological control of pests and diseases in crops such as sugarcane, cotton, pulses, oilseeds and vegetables; and biomass production for reforestation programmes through tissue culture; also special emphasis is being placed on sericulture biotechnology which is an important means of livelihood in the rural areas. India's rural needs have resulted in research in biofertilizers and have given way to a larger programme on environmental biotechnology. Six projects have been launched in the areas of bioconversion, fossil fuels, and for improving the quality of water.

Another area where India has made considerable progress is in aquaculture and marine biotechnology. Programmes include intensive carp culture using biotechnology, increasing the production of prawn and developing transgenic fish.

In medical biotechnology, emphasis is placed on recombinant DNA technology, development of diagnostic kits, drug delivery systems, DNA probes, vaccines for cholera, biosensors, prenatal diagnostics and genetic disorders. Diagnostic kits for a number of ailments such as amoebiasis, typhoid, tuberculosis, leprosy and hepatitis B are under advanced stages of commercialization. Two diagnostic kits, one for the detection of bancroftian filariasis and the other for pregnancy detection has been developed through private sector co.npanies.

Although most of the researchers involved in biotechnology research are working in public sector research laboratories, private sector contributions in this field are rising. Beginning with the production and marketing of new seeds and varieties, companies are now moving into more sophisticated techniques such as tissue culture and genetic mapping. In the medical area, an increasing number of companies are working on vaccines and diagnostic kits for which India provides a large market. A number of these companies are working with the Department of Biotechnology in their projects. One such company is A. V. Thomas and Co. which has provided much of the basic research and the tissue culture of resistant varieties for the cardamom project recently initiated by the Department of Biotechnology. Supervision of the field trials is also being carried out by A. V. Thomas. A number of other private entrepreneurs have developed markets abroad. The two areas in which such private export oriented companies dominate are agriculture, especially tissue culture and cloning and pharmaceuticals. The Swedish multinational Astra has set up a research institute in South India which does research in the pharmaceutical field. An outcome of this investment has been the formation of another private company, Genei Limited which produces and exports indigenously designed recombinant DNA research tools and is presently exporting about six products to laboratories in the USA. Much of the technology used was originally acquired from the Astra Research Centre, although increasingly know-how is coming from private indigenous firms; local buyers are largely Indian universities and research centres including the prestigious

Indian Institute of Sciences. In addition, in recognition of the importance of private sector involvement in research, the Department of Biotechnology has helped to set up a Biotechnology Venture Company with participation from financial institutions and industry in 1990.

An important function of the Department of Biotechnology as mentioned earlier, is that of information dissemination and training. While India has a relatively reasonable pool of skilled labour, the interdisciplinary and hi-tech training that biotechnology research requires is weak or lacking. The Department has helped nineteen universities nationally to set up postgraduate teaching programmes in biotechnology. A few short term training courses (two to four weeks each) on new biotechnology techniques, as well as fellowships to study abroad are offered each year. To improve cooperation with other nations a visiting programme for foreign scientists and a few other financial support programmes at different levels of the educational system have been organized by the Department of Biotechnology.

The national infrastructure houses the Biotechnology Information System, a computer system which links nine information centres at universities and research institutes in the country; national facilities for animal tissue and cell culture; microbial type culture collection (MTCC), Blue Green Algal Collection (BGA), collection on plant tissue culture, biochemical engineering research and process development, oligonucleotide synthesis and enzymes and biochemicals, as well as four genetic engineering laboratories nationwide.

International research and development cooperation has also been listed as a priority and ongoing programmes include projects with Germany, Switzerland, the United States and the Soviet Union. Bilateral programmes with the UK, Sweden, Viet Nam, Poland, the Netherlands, China, Cuba, Brazil among others are currently being finalized.

Despite these efforts, India is facing a number of urgent new problems which it must respond to. Firstly the problem of biological diversity has been sharply highlighted in recent years and the upcoming United Nations Conference on Environment and Development (UNCED) has placed pressure on countries, especially those from developing areas to respond to the threat of the loss of biological diversity from these countries. While the UNCED meeting will influence international responses to conserving biological diversity, on a national level India has drawn up a detailed programme for the establishment of a facility for the conservation of germplasm to protect biological diversity.

Another issue which India must tackle is that of intellectual property rights. For a few years now, India has been placed on the US' "Special 301" list. This is basically a list of those countries who violate US patent laws. The US would like these countries to change their internal patent laws, bringing them more in line with US patent laws, so as to prevent present violations. In an attempt to persuade major violators to change their legislation, the US Trade Representative, Ms. Carla Hills travelled to a number of countries in south Asia including India in the winter of 1991. India has so far resisted making these changes but for a number of reasons will probably have to comply in the coming years. US threats to impose trade barriers on Indian exports for one is a strong enough reason at the moment when the country has just emerged from its worse balance-of-payments crisis. India will also have to change its laws if it is to successfully attract foreign investment, and already the new liberalization policy is being implemented. In biotechnology, the controversial "new seed policy" which allows duty free import of seed including new varieties on the condition that the mother plant be eventually deposited in India, has already been in force for a few years. India is not yet a member of UPOV but may indeed join if it alters its patent laws. There appears to be strong resistance on the part of the Indian scientific community to join UPOV or allow the patenting of biotechnological products, and the next few years will indeed bring about many interesting changes.

Internally, the diffusion of biotechnology faces a number of obstacles, mainly in the form of the infrastructure and market restrictions which have existed in India for so many years. Although biotechnology has developed in a relatively free environment, and a number of small and big private companies have also taken advantage of this environment to invest in this technology, cooperation between public and private sectors is still regarded with some suspicion.

In an interesting development, a number of biotechnology firms are being encouraged to produce their products for the external market. A large amount of trade now takes place with the Netherlands, which buys the tissue culture plantlets produced in India. The firms which are at the forefront of this trade are doing so successfully and appear to be competitive internationally. Thus there seems to be a shift away from across-the-board infant industry protection, although this is selectively practiced. In the medical sector for example, such firms are rare unless they are foreign holdings in which case the research patent is held with the foreign company. Nevertheless, these developments are encouraging, both for the scientific community which has easier access to biochemicals and enzymes needed from abroad, as well as for cooperation between private and public sector enterprises.

Biotechnology research and development in India is therefore still highly pre-competitive, and funded mostly by the Government. However, there is a distinct change in government policies regarding the development of this technology and in the environment for private investors. Private sector involvement both in research and development is considerable, especially in

agriculture and health, two areas where the size of the internal market is considerable. In agriculture, a number of specialized and relatively new firms have established themselves in the external market as well. For basic and industrial research, import of a number of materials such as enzymes and laboratory equipment can be imported relatively easily. Foreign multinationals have established research institutes in India, some of them consisting largely of local researchers, reflecting the relatively skilled pool of labour in India. In terms of strength therefore, India's investment in basic scientific research has proved an asset in the long run.

In terms of weaknesses, the fledgling technology faces an economy which is still dominated by cumbersome controls and weak linkages between the elaborate network of public research institutes and the private sector. There is some evidence to show that the public sector most notably the Department of Biotechnology, is collaborating with private sector firms in developing technological capability, but the atmosphere remains largely one of mistrust.

3.2. Thailand

Thailand first actively recognized the importance of biotechnology for its agricultural and industrial research in 1983 when the National Centre for Genetic Engineering and Biotechnology (NCGEB) was formed. The Centre obtains its authority directly from the Ministry of Science, Technology and Energy and is in charge of coordinating biotechnology research and development across the country.

The national biotechnology research network supported by the NCGEB consists largely of universities and research institutes across the country. At present the NCGEB funds research projects at Chiang Mai University, Chulalongkorn University, Kasetsart University, Khon Kaen University, King Mongkut's Institute of Technology, Thonburi (KMITT), Maejo Institute of Agricultural Technology, Mahidol University, Prince of Songkhla University, Srinakarinwirot University, Prasanmit Campus and the Thailand Institute of Scientific and Technological Research (TISTR).

In industrial applications of biotechnology, the research projects can be divided into two priority areas: one dealing with waste matter and pollution and the second for commercial production of a number of industrial inputs used by Thailand, formerly imported from abroad. In the first area the NCGEB has finalized projects in bioleaching, biogas production as well as pollution combating biotechnology. The research is currently supervised by Dr Morokot Tanticharoen at KMITT and includes a biogas pilot plant which will shortly be ready for commercialization and scaling up. A successful example of University-industry linkage is Spirulina. This bacteria which is used for wastewater treatment was initially a research project at KMITT funded by the NCGEB. In Thailand it has now been commercialized by a private sector company and is applied to the problem of starch pollution. Industrial biotechnology is relatively new and remains geared to developing some of the basic products and processes that Thailand lacks. Thus another research project at KMITT is aiming to develop a production process for bakers yeast for commercial purposes - a common input in a number of industrial processes but still not commercially produced in Thailand.

Pharmaceutical research priorities are geared to local problems. Two ongoing research projects are looking at the development of mosquito larvicide at TISTR and the production of 6-Aminopenicillanic acid (6-APA) using genetic engineering at Mahidol University.

Despite the considerable amount of ongoing research in industrial biotechnology, Thailand is still largely agricultural and this, believes Dr Amaret Bhumiratana of Mahidol University, is where the country's greatest potential lies. The country is relatively advanced in tissue culture and cloning technology and has built up a huge market, primarily in Western Europe in the export of orchids. A number of new projects which are still in the research stage are looking at a wide variety of areas ranging from improvement of dairy cattle through to genetically engineered growth hormones as well as research in embryo transfer technology, to tissue culture in horticulture and important agricultural exports such as rattan. In addition to this, the NCGEB has initiated several projects investigating tissue culture for oil palm propagation comparing its performance to oil palm seedlings derived from hybrid seeds, identification of disease resistance genes in rice and tissue culture of drought resistant strains of rice. In addition to these simpler technologies agricultural research is now aiming at genetic engineering. The research is mainly examining rice where a DNA probe is to be identified which will enable protein improvement in rice through direct gene transfer as well as RFLP mapping in rice.

In the area of public health biotechnology, research has concentrated on Thai health priorities and includes field trials of bacteria which are used for mosquito control at Mahidol University, research on viral insecticide at Kasetsart University, and genetic engineering in immunodiagnostics.

To conduct this research, a number of specialized laboratories have been identified across the nation and strengthened through funding provided by the NCGEB. These can be listed as follows:

1. Plant genetic engineering unit, Kasetsart University

2. Microbial genetic engineering unit, Mahidol University

3. Marine biotechnology laboratory, Chulalongkorn University

4. Biochemical engineering and pilot plant research and development unit, KMITT

5. Microbiological Service Unit, TISTR.

Despite a considerable amount of funding for research for the Government, Thailand still faces a number of problems in increasing its competitiveness world-wide in biotechnology. The two major problems which were identified lie in the area of capabilities and linkages between research and commercial sectors.

Thailand faces a shortage of skilled personnel in biotechnology. Dr. Yuthavong, Director of the NCGEB pointed out that the number of graduates each year who are able to do biotechnology research number about 200. A major objective of the NCGEB is to provide research grants to doctoral and master level students to improve basic research capabilities in the country. Three priority areas have been identified for students studying abroad, biotechnology being one of them. The long term objective is to develop M.Sc. and Ph.D. programmes in Thailand which can compete with similar programmes abroad. A number of universities have begun offering M.Sc. and also Ph.D. programmes in biotechnology.

With respect to research and development, Thailand is no exception to the major problem facing other developing countries, that of weak links between public research and private enterprises. Like in most other developing countries, research in biotechnology is funded largely by public organisations like the NCGEB and conducted by research institutes which do not have the facilities required for large scale commercialization. As a result the NCGEB has been trying to encourage private companies to invest in the research carried out by research institutes. There is some evidence to show increasing interest in biotechnology - the cases mentioned above of orchids and spirulina where the research initially began at public research laboratories but is now being produced by private industry on a large scale. In addition, projects are currently under way initiated by Thai industry, for example the case of soya sauce where researchers at public laboratories have been asked to do research on quality control and improvement, and fish paste - the Thai substitute for salt - where industry has approached research institutes for help on reducing time and improving efficiency of the fermentation process.

Thailand is presently under pressure like a number of other developing countries to change its patent laws. But this may soon change - as Thailand cannot afford trade retaliation from its main trading partners. Many researchers believe that although Thailand's present research will not be affected in a major way, it is likely that changing its patent laws may cost Thailand more in the long run as it moves to upgrade technology and its research capabilities. Thailand is therefore trying to do two things at the same time: (1) Build up capabilities in basic scientific research and (2) Develop an industry in biotechnology.

With its past tendency to rely on foreign technology imports, this may be more difficult for Thailand than for other countries in the region. However, its liberal investment laws and flourishing market may help Thailand to collaborate with and obtain foreign non-proprietary technology from foreign companies. In the long run however, improving the skills of its labour force appear to be the key to developing biotechnology.

3.3. The Philippines

The Philippines unlike India and Thailand does not have an official policy on biotechnology. Nevertheless, the Government has been actively engaged in promoting biotechnology research and development through various channels. As with most developing countries, this research appears to be largely "pre-competitive" or dominated by public sector research institutions and universities.

Within the public sector, research is largely concentrated in the network established by the University of the Philippines, and research institutes established by the Government. The work of these institutes includes its own research programmes as well as active participation in government policy-making in the form of recommending projects for funding. These institutes also participate in the technical panels that meet to recommend new policy areas in biotechnology. The University of the Philippines network includes a number of other colleges and universities with independent programmes in biotechnology. Many of them are primarily geared toward basic research and training in the natural sciences and any specific programmes on biotechnology usually take second place.

The priorities however remain geared to the needs of the larger community. In agriculture and industry, biotechnology is being used for the production of biofuels, microbial enzymes including amylase, cellulase and protease, organic acids, bioinsecticides, microbial-based fertilizers, microbial polysaccharides and plant tissue culture.

With respect to health biotechnology these are the priority areas which have been identified and where research is presently ongoing: drug research which is focusing on medicinal plants under what has been identified as the "herbal medicine programme". The Philippine pharmaceutical industry is heavily dependent on the import of most of its drugs. Having to import brand names and to make royalty payments for licensed products has largely rendered most drugs out of the reach of the majority rural poor. Research on medicinal plants as an alternative but also in addition to

conventional drugs has been ongoing at the Institute of Biological Sciences (IBS) at the University of the Philippines campus at Los Baños. They have developed extension and outreach programmes for rural areas and currently one of these programmes has been funded by the Government of the Philippines. In addition to this, several publications on Philippine medicinal plants have been circulated from IBS.

Similarly, in order to cope with local diseases and health problems, research in vaccines and diagnostics is currently examining schistosomiasis and malaria; biochemical characterization and disease patterns associated with microsporidia as well as the development of diagnostics to identify human and animal diseases prevalent in the Philippines.

Although work in biotechnology remains largely within the realm of the not-so-advanced technologies, some research has also been done using "new techniques" namely, the use of cell fusion in improving cellulose degradation, increasing alcohol yield, improving production of animal vaccines and the production of monoclonal antibodies for diagnosis of plant viruses .

Despite the research efforts, two major problems remain which are impeding the growth of the biotechnology programme:

1. Lack of skilled personnel:

2. Inadequate coordination of research and development activities in the country.

According to a recent report by Dr. W. G. Padolina, Chairman of the Sectoral Technical Panel on Biotechnology to the Government of the Philippines, there were in 1990 only 58 Ph.Ds. and 151 M.Scs. distributed across 20 institutions involved in biotechnology research and development. There needs to be a considerable increase according to this report, in R&D personnel if the Philippines is to progress along with other ASEAN nations.

The need for better coordination of research and development and an efficient pooling of resources to tackle the internal problems of the Philippines has led to new government policies. Five priority areas in biotechnology have been identified: agriculture, aquaculture, health, industry and environment. Within these broad priority areas, six projects have been identified for implementation between 1991 and 1996. These are:

1. Penicillin production

2. Diagnostics and vaccines

   - human diagnostics and vaccines
   - plant diagnostics
   - animal diagnostics and vaccines

3. Coconut tissue culture

4. Coconut tailored fats

5. Urban wastes

6. Reforestation

Coordination and implementation of these programmes is done mainly within the University of the Philippines network, with the University of the Philippines at Los Baños being a major contributor. UP Los Baños supports an infrastructure whereby both universities and institutes work together. Faculty and researchers are exchanged across institutes as and when required. In addition, providing support to the teaching system at the University are a number of autonomous institutes, such as the Institute of Plant Breeding and the National Institutes of Biotechnology and Applied Microbiology (BIOTECH) which contribute research skills and equipment to the system.

The Institute of Plant Breeding formed in 1975 aims to strengthen plant breeding research to develop new and improved crop varieties for Philippine agriculture. Since then, the Institute has established in Cellular and Molecular Plant Biology (CMPB) programme whose research goals include:

1. Development and application of in vitro technology,

2. Recombinant DNA technology for specific gene transfer, cloning, use of RFLPs and isozyme markers, and

3. Other non-conventional techniques involving somaclonal variations, *in vitro* selection and indeed mutation by chemicals and irradiation.

The Institute has developed and released more than 50 superior varieties of about 19 crops including corn, wheat, sorghum, cassava and sweet potato among others.

BIOTECH with its 13 laboratories and a pilot plant has a mandate to develop technology for goals and services which are cheaper alternatives to conventional products, safer for the environment and use local materials. Thus far BIOTECH has had a number of successes in commercialization of its products including the production of a superior yeast strain which is presently being used by two companies for increasing alcohol production; at the same time the development of thermophilic and mesophilic anaerobic fermentators produces biogas from distillery slops and reduces pollution and a process using local isolates decolorizes the distillery wastes; and the successful commercialization of inoculants for use as fertilizers in reforestation projects.

The presence of the International Rice Research Institute (IRRI) is also a tremendous resource in the Los

Baños region. Although not specifically part of the network at UP, IRRI with its team of highly skilled researchers and enormous capital resources, gives an added technological capability to the region. Its work on conservation and development of new rice varieties has benefited the Philippines and other rice growing countries enormously both directly through transfer of new varieties to the field as well as through training programmes for young researchers.

The benefits of such a system whereby institutes are obliged to use the skills offered by the University or as other research institutes are quite plain - ensuring greater collaboration as well as allowing a more efficient utilization of the skilled labour force which many have pointed out is rather scarce in the Philippines. The disadvantages of the system have been an inequitable division of resources between the specialized research institutes and the University and while students and teaching staff have access to the resources of the research institutes, a number of departments at the University have experienced a considerable loss in their resources as their research activities have been taken over by the Institutes. However, despite this it appears that the advantages are greater than the disadvantages and close cooperation between institutes and scholars may tip the scales even further in favour of the advantages in the long run.

Like most other countries in the region, the Philippines is presently debating a change in its patent laws.

Biotechnology products are presently not included in the country's patent legislation and there are strong feelings expressed on both sides, pro and con when the subject is mentioned.

Interestingly enough, of all the countries surveyed, regional cooperation, not only within ASEAN but also with other Asian countries, appears to be high on the list of priorities with respect to biotechnology. This may be because of all the countries, the Philippines still does not have a coherent policy on biotechnology and the need to cooperate with other researchers may be greater.

3.4. Taiwan

Taiwan in comparison with the countries discussed previously, is more advanced in biotechnology research and development. Taiwan's national policy on biotechnology was established in 1982 when biotechnology was declared one of eight programmes strategic to the country. Today the Government has built a strong infrastructure of public sector research and development which supports the private sector. In fact in contrast to many other countries promoting biotechnology research, Taiwan's emphasis is on promotion with comparative disregard to regulation of new biotechnologies.

The structure of biotechnology research in Taiwan consists of three levels. The basic research is conducted to some extent at the universities, but largely at the Academia Sinica, an institute of scientific excellence, devoted solely to academic research. The Academia Sinica originally established in Mainland China, was re-established in Taiwan after the formation of the Government of the Republic of China in exile. Divided up into separate institutes, each doing research in the different branches of science, the Academia is not involved in any application of its research output. Four of the institutes are specifically relating their work to biotechnology. The Institute of Botany is presently working on tissue culture of a number of crops including bamboo, passion fruit and papaya. Rice, an important staple crop in Taiwan, is being genetically mapped. At the Institute of Zoology, a national classification of insects has just been completed and published. The Institute is also working on aquaculture and studying the impact of growth hormones on varieties of fish. The Institutes of Molecular Biology and Biomedical Sciences are also involved in basic research, although the Institute of Biomedical Sciences is also funding clinical research at a number of hospitals in Taiwan. The emphasis is on vaccines for diseases such as hepatitis B and on diagnostic kits, a number of which are being marketed by Taiwanese industry.

The second level within the Taiwanese biotechnology research and development structure is the autonomous Government created and largely funded research institute, the Development Centre for Biotechnology. Established in 1984, its purpose is specifically to promote and upgrade biotechnology industry in Taiwan. This it proposes to do by linking up vertically the institutes which do basic scientific research such as the Academia Sinica and downstream biotechnology industry. For this it also has a pilot plant facility to develop technologies, enabling their transfer to larger scale industrial production. Horizontally, the Centre buys, adapts and develops new biotechnologies, facilitating their transfer to local industry. Its main research divisions include molecular biology, microbiology, cell biology and immunology, biochemistry, applied chemistry and agricultural biotechnology. The process development section includes facilities for scale up, fermentation, process scale up, recovery, separation and purification technology, large-scale cell culture technology, conceptual process design and economic evaluation and pilot and production plant engineering. The current projects which have reached this stage of development are a genetically engineered hepatitis B vaccine, monoclonal antibodies, process scale purification, bioinsecticide process scale up, mammalian cell and hybridoma scale up production and contracted production of biotechnological products. Examples of successful transfer of technology for larger scale production include aspartame and a number of antibodies.

In addition, there is a division for industry and technology information whose objectives are to provide

updated information to industry and market surveys for biotechnology research and development projects in the private and public sectors. At present this division provides services which include product and market analysis, strategic analysis for product development and also maintains a database containing product and market information.

In agricultural biotechnology, the focus lies on microbial pesticides, fungicides, biofertilizers, transgenic technology, artificial seed technology, animal vaccines as well as antibodies for crop protection. The head of the agriculture division however voiced dissatisfaction with the general structure of biotechnology research in the country. According to him, there is no linkage with academic institutions such as the Academia Sinica who in turn do not show much interest in the application of their research for the country. Similarly, the Development Centre for Biotechnology has not been very successful at bridging this gap between research and application or at developing products which can be then marketed. Industry in turn has not shown as much interest as initially hoped in the products developed by the Centre. Indeed, the gap caused by this resulted in the formation of two new companies by the Centre to market products developed in recent years: one for diagnostic kits and the other for fungicide development.

On the international level, the Centre collaborates on a regular basis with a number of industrialized countries especially the USA and Germany and is also a member of the Asian Productivity Organization which consists, as the name suggests, largely of Southeast Asian countries. Biotechnology information is largely exchanged through periodic meetings consisting mainly of scientific but also policy and management representatives. The Centre is also represented at other meetings in the region such as the Third Pacific Rim Conference on Biotechnology scheduled for August 1992.

The Bioindustry Development Association (BIDEA) is a non-profit organization founded in 1989 and aims to promote cooperation between industrial sectors, government and academia in the field of biotechnology. Its members include over twenty organizations and companies and almost two hundred individual members in Taiwan. Its goals include the promotion of industrialization in biotechnology, as well as the diffusion of biotechnology in the economy. This it does by holding symposia and conferences, through international cooperation and information dissemination and lastly, by contributing to the development of human resources in biotechnology. It also publishes a quarterly journal entitled 'Bioindustry'. A venture capital funding system for funding new start-up companies in biotechnology has also been started. Government banks launched these financing schemes and special income tax benefits are available. The result has been the formation of 13 venture capital companies in biotechnology since 1986.

With regard to supporting infrastructure such as an intellectual property rights law, the Taiwanese Government whose recent changes in the national patent system will bring it more in line with that of the US, is encouraging researchers as well as private firms to file for patents. The Government goes as far as to pay for the costs of filing a patent and researchers who would previously not have bothered to file, as a result are now becoming more interested in obtaining a patent for their biotechnology products.

Taiwan is thus moving biotechnology into industry. The initial research phase of pre-competitive, government supported research appears to be on the decline now and there is more emphasis on industrialization. Although industry has been relatively slow at recognizing this, Taiwan appears to have left other developing countries in Asia behind and moved into the era of venture capital and full-scale commercialization of biotechnology.

3.5. Republic of Korea

The Korean programme in biotechnology and its achievements are by far the most notable of all the countries surveyed. Biotechnology was selected along with two other new technologies as the most important areas to be targeted for national R&D programmes by the Korean Government. Consequently, in 1984, the National Assembly passed a bill promoting Genetic Engineering. The Genetic Engineering Centre was established in 1985, the foremost research laboratory for genetic engineering and biotechnology in the Republic of Korea. The Centre is divided into research and development divisions and a technology service and is meant to perform a role similar to that of the Biotechnology Development Centre in Taiwan discussed briefly above.

The Genetic Engineering Research Centre has four major divisions: Division of Biochemistry, Molecular and Cell Biology, Division of Microbiology, Division of Bioresources and Process Technology and the Division of Technology Development and Services. Each division has a number of research laboratories. The division of technology development and services offers a gene bank, a bio pilot plant, biopotency evaluation, insect resources, plant development evaluation and regulation. The Centre is also involved in a human genome research programme. It is funded largely by the Korean Ministry of Science and Technology (MOST) and its main functions include the building up of national research and development infrastructure and leading the way in biotechnology, which it does through development and dissemination of new biotechnologies and products; through training and by contributing to the national policymaking structure; and functioning as a centre of excellence to promote cooperation between research and industry. The latter function is fulfilled through research and development assistance programmes including access to the gene bank,

biopotency evaluation and biomaterials, and by supporting bioindustries through the transfer of biotechnologies.

The training component of Korean biotechnology consists mainly of the universities. Seoul National University is the largest national university, and its divisions of biology, molecular biology, chemistry and medicine are mostly involved in teaching although some basic research is also being carried out. A new institute for Molecular Biology and Genetics at Seoul National University plans to have a total research staff of 200. Its objectives include basic research in the life sciences, development of genetic engineering technologies, graduate education in genetic engineering as well as cooperative research with other research institutes. The basic research divisions include three laboratories: molecular genetics, cell biology and biochemistry. Applied research is carried out by the Virus and Molecular Oncology Laboratory, the Microbial Engineering Laboratory and the Plant Molecular Biology Laboratory. Additional infrastructure includes a radioisotope room, a cell culture room, a cell and gene storage room and an animal breeding room.

South Korean industry has a strong tradition in "old" biotechnology. The food industry has now moved ahead from old fermentation technologies into specialty chemicals such as amino acids and enzymes. However, the most lucrative market in the new biotechnology is that of pharmaceuticals and drugs. Many of the large conglomerates that dominate the economy have branched into pharmaceuticals and have consequently made a commitment to biotechnological research. One such company is Lucky Ltd. of the Lucky Goldstar Group which has started a Research and Development Centre whose research activities include biotechnology. Among their success stories, human gamma interferon for the treatment of cancer and rheumatoid arthritis has now been commercialized. Protein engineering research started in the mid-1980s. Actively pursued with X-ray crystallography and molecular modelling methods, they are closely related to rapidly growing recombinant DNA techniques. In order to keep abreast of new developments in the field of molecular biology, Lucky has also started the Lucky Biotech Corporation near San Francisco in the United States which collaborates with US and other foreign genetic engineering companies. Its research activities include gene cloning and the development of vectors and hosts. In an attempt to harness some of the potential of private sector research in biotechnology, the Government devotes much of its biotechnology funding to the Korean Genetic Engineering Research Association (KOGERA). Established in 1982, its main purpose is to promote research and development, especially with respect to genetic engineering and industrialization in the field of biotechnology. This it does by increasing cooperation between companies and public sector research, by actively participating in the drive to improve investment and researcher skills as well as increased participation in policy impact studies. KOGERA at the moment has 18 member companies, principally involved in pharmaceuticals, chemicals, food and textiles. Its research and development activities include national research and development projects initiated by MOST, Bioenergy projects initiated by the Ministry of Energy and Resources (MOER) as well as cooperative projects between corporate members of KOGERA. In the national arena, thus far about 40 projects have been completed including the development of phenylalanine, hepatitis B vaccine as well as hepatitis diagnostic kits.

KOGERA's training and information dissemination activities include domestic and foreign training courses, organization of seminars and workshops, surveys of biotechnology as well as a number of publications including journals - *"Genetic Engineering"* (Quarterly) and *"Technology Information"* (Bimonthly), weekly newsletters and training manuals.

South Korea's patent law was changed in 1987 to include protection for chemical and pharmaceutical products and micro-organisms and now extends coverage for up to 15 years.

Despite these efforts however, there are some problems facing the biotechnology research community in Korea. The problem common to all the countries surveyed thus far, namely a lack of cooperation between public and private sectors, is not unusual in Korea either. The reason according to researchers at the Lucky laboratory, is that the priorities and goals of public and private sector are very different. The fact that most companies who are branching out into biotechnology are either pharmaceutical companies or are buying up pharmaceutical companies like Lucky Ltd., is no coincidence. This is where the short to medium term profits lie. Government priorities however are only partially geared towards the same profit making goals, thereby creating a conflict. Companies are therefore reluctant to join national research and development projects and when they do join, the projects are mostly those perceived to be beneficial to the company as well, such as those mentioned above.

Lucky researchers also point out that while public sector investment in biotechnology is rising, this does not appear to be the case with private companies, a large number of whom feel that the dividends of investing in biotechnology have been slow to emerge. The recent changing of the patent laws to bring them in line with US legislation on biotechnology has also led to wariness among biotechnology companies, many of whom now have to compete directly with US companies.

3.6. People's Republic of China

In the late 1970s, the Chinese Government began developing a programme which would introduce hi-tech into the country. In 1985, biotechnology policy formulation was begun. Two programmes specifically

dealing with biotechnology were launched: the "torch" programme whose goal is the commercialization and industrialization of biotechnology, and the "spark" programme which aims to bring biotechnology to the majority of the Chinese population which remains rural. Today there are three priority areas in biotechnology, agriculture, medicines and pharmaceuticals and protein engineering for industrial use.

In agriculture, there are at the moment about 50 projects, most of them involving genetic engineering. The main areas of research are the following: rice biotechnology where there is close cooperation with the International Rice Research Institute (IRRI) through the Rockefeller Foundation which is supporting rice research both at IRRI and in China, disease resistance, nitrogen fixation, animal genetic engineering especially in pigs and fish, and finally fundamental research in agricultural biotechnology.

In pharmaceuticals, genetic engineering is being used in the production of vaccines such as the hepatitis B vaccine and drugs to fulfil the needs of the large population. Here the Ministry of Public Health has been actively involved. The Shanghai Institute of Biological Products (SIBP) is one such institute. Supported by the Ministry of Public Health it is one of the state-owned large enterprises responsible for development, research and production of prophylactics, blood products, antitoxins and clinical diagnostics reagents. A number of drugs and vaccines have been produced and successfully commercialized. With economic liberalization in China, the World Bank has just granted a loan for the production, full-scale commercialization and dissemination of a new measles vaccine. A Dutch company is being employed to establish this production unit.

Since 1985, China's policy formulation has consisted of the following highlights:

1. Adapt new technologies to transform old, "traditional" industries;

2. Establish key technologies which the country lacks or is weak in, including purification and reactor technologies;

3. Strengthening of fundamental research in the sciences;

4. Strengthening of the national infrastructure supporting biotechnology research. This includes setting up a gene bank, developing tool enzymes and relevant capital equipment as well as improving animal breeding;

5. Cooperation with other countries including the USA, the European Community and the OECD. In addition, China has ongoing projects with developing countries, notably Thailand and India.

Overall funding and coordination of biotechnology research in China is carried out by the China National Centre for Biotechnology Development (CNCBD). All funding for biotechnology is first transferred by the Government to the CNCBD. Following advice from its reviewing panels which include scientists as well as government officials and policy analysts, the CNCBD allocates its funds to deserving and priority projects across the country. At the present moment there are about 100 research institutes across the country which are involved in biotechnology research projects funded by CNCBD. The CNCBD only funds the research part of R&D. However, once a product has been developed and needs to be commercialized, China too is facing the problem of having to persuade industry to finance the scale up and marketing of the product. Industry is generally reluctant to invest in research and development and it is left to the Government to develop special incentives to improve this relationship between basic research and industrial development. This is especially so in agriculture where research results are available only after a longer period of research. In the same way as with other countries surveyed thus far, but to a lesser degree, Chinese industry prefers to invest in pharmaceuticals and industrial biotechnology. Direct government investment in research and development in agricultural biotechnology is therefore essential especially for a predominantly rural country such as China.

The China-EC Biotechnology Centre was created in November 1991 with the aim of promoting cooperation both in developing new technologies as well as in basic science, between research institutes in China and in the member states of the European Community. Managed partly by the China National Centre for Biotechnology Development (CNCBD), the Centre will promote research cooperation in medical and agricultural biotechnologies, two of the priority areas in China today.

The National Research Centre for Science and Technology Development (NRCSTD) which acts under the State Science and Technology Commission (SSTC) is involved in policy research on technology in general. Their research on technology assessment, forecasts and evaluations of biotechnology impacts often form the basis for science and technology policy in China.

The most serious problem however which is likely to face China in the coming years is the issue of intellectual property rights. The Director of the CNCBD predicts a change in the Chinese patent system to accommodate biotechnology within a few years. China plans to join the World Intellectual Property Organization (WIPO) as well as the General Agreement on Tariffs and Trade (GATT), both international organizations which are discussing changes in international intellectual property rights regimes. China will most likely have to change its patent laws to some degree, and by joining WIPO, recognize patents granted by a number of other

countries. It remains to be seen what impact this will have on the local capability and products that the country has developed in biotechnology. Academics seem to be divided, some arguing that because China's biotechnology programme is geared largely to fulfilling rural needs, processes and products used for this are old and no longer have patents in the West; others argue that in future, China is likely to be competing with the international community and therefore the change, although inevitable, will have considerable future impact on Chinese industry, and agriculture. In the area of pharmaceuticals especially, the West is likely to face the greatest resistance from China on the patent issue.

4. Biotechnology and Technological Capability: Some Conclusions

The countries surveyed have very different levels of skills in basic scientific research, different market structures and different priorities in their research. Yet we can identify a number of important similarities in biotechnology research and development between these countries. Firstly biotechnology research in all these countries began largely as pre-competitive research, i.e., government initiated policies based on national priorities and needs. This is not to deny the significant role played by the private sector in many of these countries, however in general it appears that major funding for biotechnology initially came from the Government and was then followed by private sector R&D at various levels.

Of the countries surveyed, China, India, Thailand and the Philippines have a greater proportion of government involvement in research and development than South Korea and Taiwan. Research priorities are also closely linked between countries within the two groups. Thus because companies in South Korea and Taiwan find themselves competing in foreign markets primarily in the OECD countries, their research priorities lie in similar fields, notably the pharmaceutical industry where potential for profits is highest. In contrast, agricultural research where economic rents associated with new innovations are relatively lower, appear to be largely in the sphere of public sector research. In the first group of countries, agricultural research tends to be dominant. However an increasing amount of pharmaceutical and medical research is also being seen.

Thus it is clear that scientifically there is an enormous potential for the development of biotechnology research. Technological capability has been described by Lall (1989) as having three main components, technical, entrepreneurial and managerial skills which would provide the environment for effective development and diffusion of new technologies. Thus it is not just the scientific and technical skills which are important to the development of biotechnology but indeed the economic and scientific infrastructure which ensure not only high quality research, but also that the linkages between research and development, between research and industry are strengthened. A strong background in basic research is indeed a first step but thus far a major obstacle faced by industrializing countries is getting research to produce tangible results.

As this survey has demonstrated to some extent, a number of these countries have both explicitly and implicitly acknowledged the importance of these three components of technological capability in their national policies on biotechnology. The ability of policy changes to bring about changes in practice is another question altogether. Nevertheless, the interesting feature of the development of biotechnology in these countries is the attempt to incorporate some elements of what we can call here the "South Korean" or "Japanese models" of technological development. Thus while much of the research is still initiated and funded by the Government, so called pre-competitive research, the importance of industrial involvement both at the research as well as the development stages is being encouraged and also, importantly, there is a recognition of the need for an economic environment which is conducive to research and investment in biotechnology.

It is therefore evident that biotechnology as an important new technology has been recognized by all these countries and is at various stages of development. The question remains therefore whether it is possible for the diffusion of this technology given the infrastructure in these countries. We would argue yes, given many of the changes in infrastructure that are being made in order to incorporate biotechnology into the national economy. The rates of these changes will determine the success or failure of the diffusion of biotechnology and other new technologies to come. The real challenge for industrializing and developing countries therefore lies in ensuring an infrastructure and an environment which allows close cooperation between public and private research and development as well as investment in new technologies. For this, simultaneous effort needs to be made at two levels if biotechnology is to succeed. First, the development of a basic technological infrastructure and an environment conducive to investment in new technologies which is absent in a large number of countries who nevertheless are pursuing the development of this technology. Some steps have been taken in this direction although much still needs to be done. Second, the connection between academic research and industry is still very tenuous and needs to be actively encouraged.

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