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BIOTECHNOLOGY-BASED DEVELOPMENT

Opportunities and Issues in Technology Transfer and Commercialization*

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* The views expressed in this document are those of the author and do not necessarily reflect the views of the Secretariat of UNIDO. This document has not been edited.

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Introduction

The Industrial Revolution marked the greatest change in human society with the access of very large power sources provided by the steam engine and later by the internal combustion and jet engines. Dependence on human labour and on animals is now obsolete in much of the developed world. The utilisation of the reserves of coal, oil and gas has been the key to these developments. Nuclear fission power is also making a substantial contribution.

Large land and water resources have been exploited in combination with such energy as well as with new machinery to produce food, fodder and a variety of other crops. The developments in energy conversion devices and advances in telecommunications and transport have provided the means to enormous improvements in standards of living, in reducing uncertainties and in improving health and life spans. World population is growing at a rapid pace and has passed the five billion mark and is predicted to reach 6.7 billion by the year 2000. Efforts are being made to extend the benefits of industrialization to the large proportion of the world's population in developing countries which is still subject to hunger, poverty, ill health and hard physical labour.

It is clearly recognised that such vast strides in development have been possible through the evolution of new technologies leading to new products and processes and to increasing productivity. High efficiencies in the use of natural resources of land, water, and minerals have been achieved through technology.

A further impetus to these has been made possible by the advent of semiconductors and particularly by the invention of solid state devices for application in electronics and computers. Further revolutionary advances are forecast through the use of information technology and with the introduction of new materials. Biotechnology has also been ear-marked as having the potential to influence major changes in the pace of development. It is proposed to examine, in this paper, the extent of such potential to contribute to the well-being and improvement of the quality of life and to indicate the many actions required to overcome constraints for the widest and most rapid application of biotechnology for the benefit of the vast majority of the world's population.

General Factors

Technologies arise from new knowledge of basic phenomena. The application of such knowledge for meeting a known need or even an induced need is termed invention. The invention becomes useful only when it is economically and socially relevant and represents an improvement over existing products and processes in some specific manner and it is developed to be reliable,reproducible,controllable and safe. When these are reasonably assured, a technology is developed for wide application.

Technology is only one component of a complex system to produce the intended benefit. New capital investment and trained manpower are required to produce improved goods or employ processes. Specialised knowledge and resources are required for operations, packaging, advertising, marketing, distribution, after-sales service, protection of technology and improvement by secrecy or patents, copyrights of trade marks, drawings and manuals. Requirements under local, national and international laws have to be met for reasons of safety and environmental quality and in manufacture, distribution and trading.

The recognition of the unique molecular basis of genetics of all living organisms and the increasing delineation of the mechanisms underlying the translation of the codes of genes into proteins for structure and as enzymes to catalyse and regulate the further production of a variety of other materials in life systems have been fundamental discoveries in biology. New knowledge is being accumulated rapidly in developmental biology,sexual reproduction, growth, immunology and cell biology. Cells, organs and tissues have been grown in culture under controlled conditions. In plants, such tissues have been developed into whole identical plants. Methods are available for transferring genes from one organism to another, even across species by genetic engineering, which then incorporates new genetic expression capabilities not previously available in the gene-receiving organisms. Microbial systems have thus been artificially endowed with specific genes of higher living organisms such as plants, animals or man and to produce appreciable amounts of hormones, enzymes, vaccines or bio-control actives, available earlier only in trace amounts. Such genetic engineering has been demonstrated in plants as well as animals by new techniques. Restoration is being sought of immune capability to counteract cancer in terminally-ill human patients by analogous methods. Therapy by gene repair in inherited diseases and malfunctions is an emerging possibility. Enzymes and cells are anchored to function for prolonged periods in chemical-type reactors and produce specifically desired antibiotics, vaccines or other bioactives on an industrial scale. Automated techniques of instrumentation are available to analyse the sequence of nucleotides in DNA and of amino acides in proteins. Such techniques are also being evolved for synthesis of fragments of DNA or of complex proteins required for research.

These spectacular advances in the physico-chemical bases of biological systems and the controls on their development and interactions are combined with the knowledge and practice in biological chemistry, reproductive physiology, genetics, plant and animal breeding, fermentation and chemical engineering. The aim is to seek to apply them on a large scale in a variety of novel ways. The entire gamut of such techniques and controlled reproducible processes is described as biotechnology. Included in the broad term biotechnology are:

- Propogation of selected plants by asexual methods,
- large scale propogation of valuable animals from high breed parents through in vitro fertilisation and transfer of embryo for maturing and birth into a third non-high quality female,
- extension of embryo transfer for humans in cases of infertile couples,
- control of male and female fertility by birth control vaccines in man and animals,
- early detection of communicable disease by specific bio-sensors based on principles of immunology as well as the production of non-living high active bio-chemicals or industrial chemicals and bio-modification of properties of animal feed and human food materials.

Basic Factors

Nature with its vast bio diversity is the primary source for biotechnology. Only a very tiny fragment of living organisms have been identified and of this, very little of the broad chromosome and gene pattern and their relationship to expressed properties has been catalogued. The basic genetic structureconfers biological identity and expression providesbio-personality to each organism which develops in response to the environment and to nutrients. Slow changes take place naturally by selection depending on environment and interaction and competition among living organisms. There are also mutations of which a few survive.

Human intervention by selection of specific varieties in micro-organisms, animals andplants as well as by changing environment and nutrients has, in the past, evolved technologies which have proved beneficial. Big improvements have been made in agriculture, animal husbandry, food processing and industrial fermentation from such established processes. A specifically advantageous output of genetic potential is sought by selection, breeding, environment and nutrient. These developments, although relatively slow, have made extraordinary contributions to food and animal production, forestry and human and animal health. Pesticides and vaccines have provided a measure of protection, and drugs and antibiotics used for the control of disease. Fertilisers, vitamins and nutrients supplement natural availability.

The new techniques and knowledge described in the earlier section on biotechnology in this paper, have radically altered the rate of such developments. Genetic engineering and new types of bio-propogation provide entirely new means of exploiting bio-diversity and bio-potential of all species and varieties at will and at great speed. Bio-identity can be thus altered. Intervention is possible at every stage of development with the purpose of arresting it or directing it. Bio-personality is thus alterable by intervention with the environment for development and expression of identity. Even sex selection of progeny is possible by fractionation of sperms or by selection of the embryo of desired sex for further development to maturity. Bio-identity and bio-personality can be altered by genetic engineering. Inevitability in heredity can be replaced to some extent. Repair, even in developed life forms, is potentially feasible. Ageing, vigour, reproductive capacity and disease can be increasingly regulated and an active, healthy life and output can be prolonged. New knowledge and techniques are bound to increase exponentially in the future, offering new and widely varied technologies.

Special Features of Bio-technology Application

Biotechnology application can be characterised as primarily knowledge-based. The knowledge component is substantially high in investment for exploitation in biotechnology as compared to other technology-based industries. Capital costs in machinery and equipment would be comparatively smaller than in othertechnologies. Energy requirements are also a low proportion of the output value of products in biotechnology. However, substantial costs are involved in the generation of new basic knowledge and its application for a specific purpose. Further high costs are likely in the conversion of new application knowledge to a technology package in order to ensure reliability and reproducibility. Expert human resource inputs are required for strict quality regulation and a large number of scientific disciplines at high levels would be required to prepare a sound technology package. In certain types of products such as vaccines, hormones, bio-pesticides and bioactives, high costs are inevitable in toxicological evaluation and safety assurance, animal and clinical trials, field tests and in meeting requirements of Government Regulatory Agencies. Interactions between specialists in biology disciplines and those in design engineering, process delineation, instruments, sensors, controls, safety in operations, effluent treatment and disposal are particularly difficult to forge as there are very few design engineering project consultancy groups with adequate expertise, systems and experience suited to the special needs of biotechnology.

Patent, technology transfer and industrial intellectual property laws are not yet evolved adequately to cover biotechnology developments. There are widely divergent approaches to these. International agreements on these have to be evolved to encourage investments in technology development and transfer. Liabilities on any unforseen effects on safety may be a constraint. Since knowledge component is high and new advances are also being made, there are possibilities of a high rate of obsolescence of technology. Consequently, high prices would be demanded for transfer of technology. Risks in investment in industrial production may be sought to be covered by initial high prices for products, far in excess of the actual costs in manufacture.

In non-agricultural products, transfer of technology for production requires a high level of capability for absorption of technology in the investor and in manufacturing and marketing organisation. Such capability has to be evolved in many countries, if new technology has to perform with efficiency and safety. Specific steps are necessary to generate such capability through extensive education, training and retraining. Education is also required for the user of the bio-active products and devices.

Biotechnology Products

i) Health and Nutrition

Much attention is being paid to the production of several products and devices, which have special applications in human and animal health and nutrition. These include hormones such as human growth hormone used for correction of inherited dwarfism, bovine growth hormone and other products which increase milk production in cattle, human insulin for diabetes therapy, tissue plasminogen activator, streptokinase, enzymes and other very high value bio-actives with application in heart disease and cancer, vaccines, antibiotics for communicable diseases in man and animals and monoclonal antibody based test systems for early detection of diseases and of pregnancy. Sex determinationin very early detection of pregnancy may also gain importance. These are all produced by genetically engineered micro-organisms in culture very elegantly and in highly purified form. They are generally non-living, high-active products sold at high prices. There may be further additions to such categories of vaccines for bacterial, viral and fungal diseases. It is necessary to produce these in developing countries and make them available at modest costs. Technologies could be purchased from commercial companies by Governments or international organisations for such transfer and the products themselves should be made available at low, if necessary subsidised, costs for large-scale use in developing countries.

Millions of people in developing countries are afflicted by parasitic diseases, such as malaria, amaebic dysentry, tapeworm, and hook worm, for which there are no vaccines. There is, at present, far too little research work undertaken towards producing a vaccine. More extensive basic research needs to be done on the various stages of developmental biology of parasites themselves. Such information is essential for any development of vaccines. Drugs developed to combat parasitic infections are relatively toxic to humans and parasites develop resistance to drugs. Since parasites have mechanisms for adaptation, it may be necessary to evolve several different vaccines for each parasite. Such work is most economically and efficiently carried out in the regions and countries where such parasites are most prevalent.

Although cholera and small pox have been virtually eliminated, the currently available cholera vaccine is not very effective. It is necessary to concentrate research on developing genetically engineered cell-based vaccines in such cases also. There are many attempts being made to develop vaccines against leprosy and these should also be supported.

Vaccines for control of fertility in human males and females are being sought and these may be of considerable value in population control. There is also interest in application of these to animals to ensure low breed animals are not involved in further propogation during strategies for rapid upgradation of livestock with artificial insemination or in vitro fertilisation and embryo transfer. There may be interest in vaccines to permenently sterilise high quality male newly hatched birds for release for the broiler industry in order to protect the commercial interests of developers of high breeds. At present, in many cases, male chicks are culled and not released and only female bird chicks are sold for egg production. Stray dogs could also be sterilised in this way to control their population.

New hormones and bioactives may be developed to increase the productivity of milk, egg, fur, wool and fish in the animal feed industry. Amino acid and other supplements for increasing the nutritional value of animal feeds, through microbial production is clearly of considerable commercial interest. Likewise, application of safe enzymes and fungal culture to degrade cellulose and lignim in straws for cattle and other animal feeds and thereby increase their nutritive value is a major thrust. Transfer of technology on these to developing countries would contribute to substantial economic development and overall health and nutrition.

ii) Agriculture

The application of genetic engineering and biotechnology offers great scope in many areas of agriculture. New cereal, pulse and oilseed crops which are drought- and pest- resistant are urgently needed in many parts of the world to ensure self sufficiency in food. The optimal utilisation of scarce resources of land and water to maximise output per unit of land is the most pressing need. New techniques of cell fusion, protoplast fusion, shotgun firing of whole cells and the use of Agrobacterium tumificiens offer facile and simple means of genetic engineering to introduce desirable properties.

There is already much success in the use of tissue culture propogation for high yield varieties in plantation and forest crops such as oil palm, rubber, spices (cardamom, pepper, clove) and coconut. In due course, there may be developments in tea, coffee and cocoa. Virus-free sugarcane propogation by such a method has been demonstrated. Selected varieties of bamboo, eucalyptus, teak and other biomass trees and plants for use as fuel or timber, can be rapidly multiplied and grown in this way. Tissue culture is particularly valuable in hybrid varieties of all crops including cereals, fruits, vegetables and high quality nuts.

Such work is possible only in the case of plants where a sufficient bank of genetic sources is available with information on their expressed characteristics. Much basic work is needed for collection of all cultivated and wild varieties and their maintenance and characterisation. In the developed countries, where technology can be protected by Breeders Rights, major commercial interests are in plantation crops or the supply of high quality seeds to large farms. There is also considerable activity in the rapid multiplication of cut ornamental flowers, as fashions alter demand with high frequency.

The propogation of potato and other tubers by microtuber is already a commercial success and this would be of much interest to most developing countries. This method substantially reduces the need for using 15 to 20 per cent of potato as seed material and also ensures high viability. In other cases, development of clones to plantlets in nursery bags, before planting, provides similar assurances of viability, helps to eliminate weeds and also save land upto six weeks, permitting multiple cropping each year.

Genetic engineering has allowed incorporation of pest resistance transfer from microbes to plants such as tobacco and elm trees and for the development of pest-resistent micro organism culture sprays with capabilities for pest control. There are unresolved problems on the safety of release of these for open field cultivations.

A major area of interest is biological nitrogen fixation. Microbial cultures with high capacity for nitrogen fixation can be produced on an industrial scale for spraying into fields. These are clearly valuable, in the case of oilseed and legume crops, and would help to reduce, to some extent,the need for chemical nitrogen fertilizers. In the present state of knowledge, such organisms - suited to cereal crops, sugarcane or tubers - do not appear to be available. Various forms of algae could be produced in ponds on a large scale and then applied as nutrients in agriculture. Special organisations have to be evolved for large-scale production of microbial and algal cultures in developing countries.

While there is research on the incorporation of such biological nitrogen ability to plants themselves by genetic engineering, success is not readily foreseen for several years. Nitrogen fixation, which is an energy-consuming process is highly complex and involves an estimated system of 2[illegible] genes. Newer techniques have to be evolved for such transfer of systems to plants from micro-organisms.

While the potential of biotechnology in agriculture is very high, applications may be more evident in developed countries with large farms, and where already excellent systems of integrated supply of high quality seeds, planting material, fertilisers, pesticides, agrochemicals and expert advice by commercial firms already function. These also supply company-owned plantations in many countries. Such systems have to be developed for small farms in developing countries as a pre-requisite for the introduction of biotechnology-based applications. There are also the questions of intellectual property rights and of safety and these are discussed later in the paper.

iii) <u>Industrial Products</u>

Fermentaion of sugarcane juice, molasses, starch from corn and tubers, provides the potential to produce industrial alcohol, butanol, citric acid, vitamin C and other chemicals and intermediates. These are only feasible in countries with surplus agricultural production as in Brazil, or North American and Western European countries. Sugar is, in any case, a surplus commodity in the world as it is being replaced by artifical sweeteners and fructose syrup.

There are programmes to produce protein by microbial culture for use in animal feeds and for the production of high-value products. Cocoa butter, industrially useful enzymes such as amylase, pectinase, amylo-glucosidase, pencillin acylase, cellulase, and proteinase will also be produced on a large scale. Anchored enzyme or cell-based culture for specific chemical transformations will clearly show an increase. It may be possible also to produce biodegradable polymers in industry - or the basic building blocks for these - through biotechnology. Modification of properties of natural polymers such as proteins, starches, cellulose, alginates through enzymes or micro-organisms would also be of interest. Waste disposal could be another area of considerable industrial importance for the application of biotechnology.

Opportunities in industrialized countries

i) Environmental Quality

Biotechnology will have an increasing role to play in helping to attain high environmental standards of waste disposal systems. These would include municipal sewage and garbage, animal waste from farms and abattoirs, wastes from dairy end-food processing, grain and oilseed processing, straws from agriculture, waste from paper and rayon factories and treatment of effluent and solid waste in chemical and petrochemical industry, agricultural affluents and drainage containing pesticide, fertiliser and agrochemical residues, removal of toxic metals from non-ferrous metal and alloy plants and from foundries, welding units and metal forging industries. Oil slicks from ships, refineries and pipelines could be controlled through new treatment. Disposal of packaging waste consisting of polymers, paper and metals may need new applications.

ii) Health

The main interest would be in retarding_ageing to reduce the effects of non-communicable diseases such as heart diseases, cancer and communicable disease such as AIDS. Efforts to retard ageing could be directed to factors such as, prevention of hair loss, improvement of skin condition and maintaining functional capacity among the old. Organ and tissue transplants, and genetic repair would become valuable tools. Use of growth hormone for increasing heights or for weight reduction through dieting without exercise are possiblilities. It would be possible to over-come infertility with the aid of biotechnology developments which would also help older members of the community to become more economically viable and active. These would reduce high costs in social medicine and care as life expectancy increases to 80 and above. New foods specially prepared for the aged will be developed. Similarly, special attention will be devoted to health products for young children, and for the cure of leukemia and other diseases.

There would be a large increase in simple diagnostic and health monitoring instrument devices, which could be used at home by sick and ageing patients, and so reduce the work load on medical services. Hospital services would also make extensive use of automated diagnostic and monitoring kits.

Special nutrient food formulations for those in stress conditions as in athletics, sports and the armed forces, especially those in unusual environments such as in submarines or at high altitudes, will be produced through biotechnology.

iii)Agriculture

Many of the applications and products resulting from biotechnology described earlier would be extensively incorporated in agriculture, animal husbandary, forestry, fisheries and in waste disposal. These could be undertaken by commercial companies. There are special interests, for example, in increasing the solid content of tomatoes, the sugar content of wine grapes or altering the fat composition of milk or meat. Nutritional requirements in crops and animals used for human and animal food will be met by biotechnology.

Requirements in Developing Countries

a) Human Health and Fertility

The developments of vaccines for the control of viral, bacterial and fungal diseases have been described and the wide use of these can alleviate much distress. The need, however, is to develop strategies to overcome a variety of parasitic diseases through vaccines. Another element of strategy would be to use biocides such as Bacillus thuringnesis cultures to control parasites in water bodies. Non-living biocide preparation could be made from bacterial cultures. Bioactive drugs and pharmaceuticals and its delivery to sites of infection would reduce dosage levels and the toxicity of drugs.

There is considerable potential for the use of biotechnology-based diagnostic devices for the early detection of diseases such as leprosy and for the preparation of vaccines against leprosy and various forms of infections such as hepatitis.

The most important requirement is the development of vaccines for control of fertility in male and female. These should be effective for one to two years providing temporary infertility without side effects. Oral vaccines would be ideal. There may be some opportunities for vaccines for long-term contraception.

High infant mortality rates could be reduced rapidly through the production of antibiotics and vaccines at low cost. As life expectancy increases in many developing countries, products to counteract old-age disabilities and to monitor the health of the elderly will be in demand. The costs of these, provided by companies from industrialized countries are abnormally high in comparison with incomes in developing countries. Innovations are necessary to make these available at modest costs.

b) Agriculture

Forests are being denuded rapidly, since fuel wood is the major source of energy for small-scale industry, post harvest drying in rural areas and for cooking. Quick-growing bio-mass trees for energy and timber could be provided by biotechnology. Bamboo and trees for paper production could also be provided in this way.

Pest and drought-resistant primary crops, such as cereals, pulses and oil seeds, are urgently needed. Micro tuber propogator of potato and other tubers can have large benefits. Improved varieties of cash and export crops, such as cardamom, pepper, ginger, nutmeg, cloves, safflower, cashew and special fruits and cut flowers, propogated by tissue culture, will increase productivity and exports. These also apply to medicinal and aromatic plants, plantation crops such as oil palm, arecanut, coconut, castor, linseed and rubber.

Biotechnology could contribute towards the improvement of livestock and the production of milk, egg, wool, fur and fish. Special attention should be paid to aqua culture, particularly shell fish, which have a high export value. Animal vaccines, animal nutrition supplements and animal growth and fertility regulation products will be very valuable.

Rural energy will benefit from the improvement of biogas production from municipal sewage, animal and agricultural waste. Advances in the process of fermentation for alcohol and other industrial products from a variety of biomass sources will be particularly welcome. The use of lignin and cellulose by-products of agriculture for such purposes or for animal feed will be of interest.

Biological nitrogen fixation techniques, which may be labourintensive,wouldbe of speical interest to developing countries. Systems for incorporation of these have to be organised.

Technology Transfer and Commercialization

The commercial_successes resulting from biotechnology are mainly in high-value health products of importance in developed countries such as insulin, growth hormones, enzymes for heart disease and new antibiotics and bioactives for cancer. The production of vaccine and antibiotics has become more efficient: tissue and microtuber culture have been applied widely; and transgenic systems in plants await safety clearance for open field use.

Large numbers of small biotechnology companies have been purchased by large companies unrelated to biotechnology. Only a very few are operating commercially. It is reported that only one company, engaged in heart disease products, has declared a dividend. However, expectation of future potential growth in some companies remains high.

Commercial biotechnology companies have been established in North America, Western Europe and Japan. There is interest in forming such companies in some countries of Central and South America and Asia including India and the People's Republic of China. Eastern European countries have also indicated an interest in commercial operations.

Obviously, most developments of benefit to society and national prosperity will come from investments by national governments, with support from international agencies and foundations. Such developments are clearly dependent on the capacity of countries to promote research, education and training in biotechnology. There are still unsolved problems on the safety and viability of technology which calls for basic research and knowledge to tackle such problems and to introduce regulation of activities.

There are high risks and high benefits in the adoption of biotechnology-based manufacture and these risks are substantial if there is no access to basic research. In developing countries high level consultants should be involved in such research which includes the selection, introduction and monitoring of biotechnology-based production and application.

Specialised engineering design, consultancy and project companies with adequate integrated systems of expertise of different disciplines, with local conditions in mind, should be associated with technology transfer and project implementation in biotechnology. However, biochemical and biotechnology engineers with relevant experience are not easily available.

Practical, relevant research has to be carried out in special multi-disciplinary research-development-technology units. These should have close relationships with other basic research scientists and with technologists of engineering design and consultancy groups.

New forms of risk-investment support have to be provided for biotechnology developments by large companies or by governments or financial institutions. There are also opportunities for creating special technology parks close to research institutions, and investments in these should be supported by special forms of financing as well as provision of common test and supply facilities.

<u>Forces, Motivation in Technology Transfer and Application</u>

The initial advances in technology in this sector have come from spectacular achievements in science. Opportunities for technology evolution and application have been largely identified by scientists, who are not familiar with commercial operations. Scientist groups have been able to generate financial support for investments by becoming entrepreneurs. Such activity is favoured in USA. Science-push rather than demand-pull has been the primary force in such technology development and commercial activity. The groups are sub critical in size and in varieties of engineering, manufacture, marketing and finance specialisations required for the total system. To meet the gap, the initial entrepreneurs have either joined or merged their company with others possessing expertise or have collaborated with large pharmaceutical companies or companies engaged in seed, fertiliser and pesticide production and marketing.

Scientists engaging in commercial activity tend to be enthusistic and optimistic but often lack adequate appreciation of constraints, high costs and efforts involved in demonstration pilot plants, technology package development for reliable, reproducible operation, and in large scale manufacture, marketing by brand names, advertising, promotion, distribution and sales. Large expenditure and complex procedures are involved in toxicology tests, clinical and field evaluation and safety clearance by regulatory agencies, all of which are mandatory for human and animal health products and bio-pesticides. The time scales involved are substantial. Similar clearances are necessary for all recombinant DNA based products, even if the end product is a non-living material.

Conditions for Successful Technology Transfer

Specialised agro-service companies engaged in certified seed, pesticide and agro-chemicals and which have extensive distribution and advisory service groups are the best suppliers of seedlings, micro-tubers, plants and nitrogen fixing cultures. They are likely to deal with large farms and plantations, which have, generally, an absorptive capacity for introducing innovations. The rights of major supply companies tend to be well protected against leakage and further propogation without payments. The provider and user of technology and new materials usually have shared long-term interests.

Companies engaged in antibiotics production will be able to absorb the technology required for production of enzymes, hormones and bioactives of high value. They are also able to market such products made by microbial fermentation, cell culture or enzyme action.

Organisations already familiar with the production of human vaccines derived from animal or organ culture systems are best suited to absorb the technology of vaccine production by cell culture, since they have experience in quality control, capsule filling, storage and distribution. Well trained staff with sound knowledge of quality standards and of systems of operations are absolutely essential. Animal vaccines from new biotechnology will have a greater probability of success than new human vaccines, and local production of such animal vaccines is possible, in develcping countries, when infrastructure exists.

Industrial products such as alcohol, chemicals, vitamins, and food additives such as mono-sodium glutamate can be more easily produced by technology transfer to entirely new groups or comapanis. Monoclonal antibody-based diagnostic kits technology can also be absorbed by new organisations for manufacture. Marketing should be preferably undertaken by well established pharmaceutical companies.

Effluent disposal from fermentation is often difficult and expensive as it involves large volumes with high organic matter content and these should be taken note of in any investments.

Institution Evolution for Biotechnology Application

Developing countries need to establish national biotechnology promotion agencies or relevant government departments with a strong commitment for the support of manpower and basic research, training and education. There should be high-level political interest and widespread appreciation of developments, including the potential for application and of safety measures. This can be accomplished by seminars organized by agency and national science societies and by special presentations to members of legislature, media personnel, civil servants, financial institutions, regulatory authorities and agencies involved in the use of biotechnology in, for example, agriculture, health, medicine, chemical and the pharmaceutical industry. These should be supported by films, videos and illustrated brochures. Visits and lectures by local scientists and technologists and leading scientists in other countries could be helpful in creating awareness and would facilitate international cooperation and exchanges. A group of internationally committed consultants may be able to provide assistance and advice on developments and opportunities. A national bio-safety board should be established to formulate safety guidelines, training programmes and to take measures for safety at all levels and institutions involved in genetic engineering.

Pilot plant facilities set up for trials and demonstration and small-scale production should be established for the transfer of technology. They would be used by research groups representing government, university and industry. When transferring technology from outside companies, engineering consultancy project organisations should be associated. Extensive training in operations and quality control is highly essential.

Intellectual Property Rights

The age of information exchange, of free movements of scientists and new variety of genetic stock in agriculture and animal husbandary is now being replaced by restrictions and commercial considerations. Breeders' rights have been granted to those evolving new plant varieties and these restrict further propogation by purchasers. Such rights may not be enforceable in the small farms of developing countries which generally produce primary cereals, pulses and oilseeds and therefore, new varieties may not be made available. Governments and international agencies may have to purchase such desired varieties from companies for national use.

The prices charged for technology transfer in the case of hormones, new antibiotics, bioactives and vaccines for use in human and animal health may be rather high and here again, support from governments and agencies may be necessary for local production. Products may have to be made available at modest costs to obtain large national economic and social benefits. Patents have been granted in USA for genetically engineered microbial, plant and animal life forms and these may pose restrictions for wide use, subject to safety clearance. International discussions and agreements have to be evolved on such issues. These require detailed examination and new proposals for possible action. The objective should be to encourage research and innovation by all competent groups - national government agencies, universities and industry - and, where necessary, to provide returns, rewards and recognition for achievements and risk investments.

Safety in Recombinant DNA Developments

There are widely divergent views on safety in the application of R-DNA research products and techniques. The U.S. National Academy of Sciences, after a careful examination, has concluded that such work is safe, under good laboratory practice, conforming to accepted guidelines. However, large-scale release of live materials would require assessment. The US Supreme Court has ruled that discussions by the National Institutes of Health R-DNA Committee should be open to the public. DNA repair in humans has been proposed and this requires further discussion. There appears to be support emerging for use of this technique in terminally-ill patients. These are highly complex issues requiring constant monitoring of developments.

Future Concerns and Possible Remedies

As a result of rapidly growing populations and the need to provide food, fodder and other materials, it becomes essential to maintain high productivity in agriculture, animal husbandry and forestry for energy, industry and materials. There is a danger of valuable genetic material being lost through aggressive cultivation of selected varieties. Monoculture may pose a threat and there are risks of large devastation by new pests or temporary unfavourable environmental conditions. It is therefore most essential to preserve the large genetic resources for future use through the establishment of national reserves, banks of plants, animals, micro-organisms, and to catalogue collections and species. National governments and international agencies should provide support for these.

The agricultural revolution has been possible through use of high-yielding varieties, with inputs of large amounts of fertilisers, pesticides and agro chemicals. The costs are rising after the oil crisis of 1973 and the subsidies for such production cannot be sustained by many countries.Biotechnology developments should be accelerated to provide alternative less expensive systems which can meet needs.

Gradually, traditional technologies and varieties of plants and animals in developing countries are being replaced by imports of plants and animals. Traditional medicine is also dying out, with the disappearance of medicinal plants and herbs. Modern medicine involves expensive drugs. antibiotics and exorbitantly priced products for heart disease and cancer. Support for scientific assessment of traditional systems is urgently needed as well as assistance for making available new medical products at affordable prices. A combined international strategy should be developed for this purpose.

There is growing concern regarding the possible replacement of developing countries exports such as, cocoa, cocoa butter, spices, essential oils, waxes resins, alginates, oil seed cakes for animal feeds, special vegetable oils and medicinal extracts. These are being replaced in developed countries through genetically engineered micro-organisms. Many natural products such as rubber, cotton, jute, silk, leather, wool, skins, resins, and essential oils have already suffered through the technological advances in petrochemicals, synthetic fibres, polymers, surface coatings and adhesives. Biotechnology may pose yet another threat to traditional exports from renewable resources. The remedy lies in strengthening the productivity in agricultural activities in developing countries through rapid application of biotechnology suited to exports competitively.

There are also concerns on the accidental release of virulent toxic life forms of microbes or disease-carrying animals, as well as fears of their use in wars or violent conflicts. These can be overcome only by strict vigilance and international agreements. Overuse of vaccines and biocides may lead to the emergence of more virulent resistant pests, parasites and disease vectors. There is no alternative to continued research and development for newer products, and to the monitoring of any outbreaks.

The adoption of very strict standards of toxicity and safety may preclude the use of products from biotechnology developments in developing countries and many may continue to die from communicable diseases. Populations may grow to unsustainable levels. It is not clear if a damage to benefit assessment suited to each condition could be made. A thorough and detailed disclosure of all information on new health products, including effects of long-term use, is essential.

The residues from the manufacture of bioactives have to be carefully destroyed and rendered safe. Field trials and clinical tests are occasionally carried out in a developing country while elsewhere such tests may not be permitted. An international code of conduct has to be evolved to avoid disputes and mistrust.

There are ethical questions involved in the issue of human embryo transfer and legal problems regarding parenthood. The use of human ova, preserved semen and frozen fertilised ova for future development are linked to special ethical questions, as is also application of such techniques for breeding athletes or highly intelligent offspring. The use of human embryos for research or embryo tissues for repair are already banned but violations may occur.

Sex determination in the early stages of pregnancy and the abortion of unwanted sex embryo has become relatively easy, and may be used for altering sex ratios in animals, especially when a male is no longer required as draught animals and the meat is not consumed. In humans, such techniques may be used to assure the sex of offspring. International conferences on ethics have to discuss such moral issues.

Many international organisations could take initiatives in providing safeguards, preserving genetic resources and protecting the world's biological heritage by making available products for health and by developing systems of transfer of technology and engineering design consultancy. These include UN, UNDP, WHO, FAO, UNEP, UNIDO, UNESCO, HABITAT and UNCTAD and Regional Commissions and Associations. The Commonwealth Secretariat and the Commonwealth Science Council could play major roles. Development finance organisations, such as the World Bank and regional banks could assist in investments in biotechnology application. Scientific organisations such as International Council of Scientific Unions and International Scientific Unions, national science academies and the Third World Academy could evolve guidelines on the practice of biotechnology and help to create much awareness.

UNIDO has taken the initiative in its programme to study the potential of biotechnology for industrial development and in promoting the establishment of the International Centre for Genetic Engineering and Biotechnology. The Organization has maintained its interest in promoting the application of biotechnology as a new technological system. It is recommended that UNIDO may consider taking actions to facilitate technology development, technology transfer, technology absorption, investment in application and in the evolution of international agreements on Intellectual Property and Technology Rights, preparation of Model Contracts for Technology Transfer, modalities for formation of National Apex Agencies, Organisations for Engineering Design Consultancy and Projects, International Guidelines on Safety in R-DNA systems and in the preparation of manuals, films, videos to promote biotechnology potential by sectoral decision-makers and the media in different countries and in the monitoring and distribution of information. UNIDO could assist member countries in evolving national strategies and institutions for biotechnology development suited to specific needs and resources. UNIDO could evolve a coordinating role among UN and other interested international organisations, foundations and banks in identifying major needs of member countries for technology in this area and assist in meeting such needs.