Policy and Development of Biotechnology: Bangladesh Perspective

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Science Policy

One of the dictionary meanings of policy is the statement of aims and ideas. The other meaning is plan of action. I am not sure whether most of the policy documents state about the mechanism of implementations of aims and objectives outlined in the policy document. But to a common man policy usually is a nice printed bound volume of pious wishes issued by a government, government agency or even an NGO. A formal science policy was issued by the Government of Bangladesh in 1986. As a statement of policy its contents constituted broad based application of science and technology particularly modern science and technology including biotechnology for national development. At that time poverty alleviation, good governance and women empowerment were not catchy terms. However, economic and social development through application of science and technology were supposed to take care of all related problems. It mentioned about establishment of scientific institutions, upgrading existing institutions and human resource development

Science Policy and WCS

World Science Conference was held in Budapest in 1999. The 12-page document containing 96 paragraphs each of which issued at the end, had

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policy related recommendations distilled into the Para 55(section 2.6) that reads as follows:

National policies should be adopted that imply consistent and long term support to S&T, in order to ensure strengthening of human resource base, establishment of scientific institutions, improve and upgrading of science education, integration of science into national culture, development of infrastructure and promotion of technology and innovation capacities. Interestingly many of the recommendations of WCS coincided with recommendations of our national science policy made 14 years earlier.

Policy and Action-contradiction

The question may arise then why we did not make a significant growth in the S&T sector, what to speak of biotechnology in Bangladesh? The answer is that the broad recommendations in the policy document did not have the adequate analytical framework or implementation strategy for addressing the nature of problems faced by the S&T sector and the recommendations were not based on expenditure, benefits constraints, etc. Science and technology enjoyed rhetorical support from all the successive governments. There were encouraging utterances for S&T development from time to time from political leaders but there were little or no follow up actions to match the words. I believe the political wishes were genuine but there was lack of conscious or unconscious synergy between political will, administrative set-ups and the scientific community. Even ignoring the earlier years, the 5th plan (1999-2002) size was TK. 19590 million of which allocation in S&T was only 8000 million, i.e. 0.41 per cent and only 0.106 per cent of GDP. Thus, in spite of pronounced political commitments when budgetary resource crunch due to short-term shortage arose the first casualty was S&T sector. In fact, S&T Division was upgraded to a ministry once and then downgraded and then a full-fledged ministry was created in 1993. Prior to that it shuttled to different ministries such as education, energy, industry President's Secretariat, etc. All these happened due to one reason, i.e. lack of confidence in the minds of the policy makers that S&T can play an effective role in national economic development. Many economists and

planers thought that S&T is a commodity that can be purchased from the international market when needed.

The situation has of course changed over the recent years. The S&T ministry has been given a new shape and name. Now it is called the Ministry of Science and Information & Communication Technology. Allocations have been increased significantly and thrust has been given on IT and BT. In the backdrop of what has been mentioned so far let me discuss situation about biotechnology.

Definition and Prospects

Biotechnology has been defined as the application of scientific and engineering principles to process material (organic or inorganic) by use of biological agents to provide goods and services. The Convention on Biological Diversity defines biotechnology as 'any technological application that uses biological systems, living organisms, or derivatives thereof to make or modify products or processes for specific use'.

The technology based on biological systems-plants, animals and microbes-has been practised for thousands of years through conventional methods and conventional biotechnology still plays a dominant role in providing goods and services. Genetic engineering is the pivot of modern biotechnology. It has opened up wide opportunities for development in different areas of biological sciences and last 15-20 years had been the golden age for biotechnology. Within this short span of time recombinant DNA technology that was hitherto considered a primarily fundamental subject has proved beyond doubt its applicability in many areas of human welfare. Apart from medicine, now biotechnology has been playing vital role in plant improvement, animal health and development, fermentation technology, environment protection and waste management. In medicine its development is spectacular. By now more than 200 newly engineered human pharmaceuticals have been approved for testing in USA alone. Many more are awaiting FDA approval for marketing. Similar is the case for transgenic crops. In USA more than 2000 have already been released for cultivation including soybean, cotton, sugar-beat, rice, wheat, etc. In areas of human

health and environment new and significant improvements have been achieved. More and more investments are being made.

In agriculture biotechnology has helped increase in productivity in crops, livestock, fishery and forestry. This technology has helped in controlling pests and diseases through enhanced genetic resistance, improved diagnostics, new vaccines and use of bio-control agents. It thus provides effective tools for enhancing and sustaining food security and poverty alleviation. Excellent prospects exist for improving health of much low-income community by engineering nutritional quality of food, bioremediation and genetic conservation.

Global Scenario

Genetic Engineering Based Products

The following genetically engineered pharmaceuticals are already marketed in US:

a) Blood factor VIII: C
b) Human insulin
c) Human growth hormone
d) Tissue plasminogen activator
e) Alpha interferon
f) Hepatitis B vaccine and
g) Monoclonal antibody to prevent kidney transplant rejection.

New Products Marketed/Under Marketing

1. *Tissue Plasminogen activator (t-PA):* Used for heart attack patients for commercial use. The annual expected sale is about $150 million.
2. *Erythropoiethin (EPO):* Used for cancer.
3. *Interleukin-2 (IL-2):* Used for cancer.
4. *Monoclonal antibodies for detecting and treating Cancer Cells.*
5. *Monoclonal antibodies against septic shock:* The antibodies are destined to eliminate toxic products of infectious bacteria, which persists even if the bacteria are killed. Septic shock is a common cause of death of patients who become infected with antibiotic resistant bacteria in hospitals.

6. *AIDS treatment:* Recombinant alpha interferon, gamma interferon, IL-2, granulocyte macrophage colony stimulating factor (GM-CSF), tumour necrosis factor (TNF), EPO and CD_4 (a T-cell receptor protein to sop up AIDS treatment). More than ten vaccines against AIDS and AIDS related diseases are in various stages of development in the United States.
7. *Genetically engineered bacteria for agriculture:* Monsanto got good results with recombinant bacteria to protect wheat from a fungus. Genetically engineered N_2 fixing bacteria (Rhizobia) was found to contain within the test field. Recombinant insecticidal bacteria of corn showed up good results in field-testing.
8. *Recombinant products for health:* Recombinant beta interferon, gamma interferon, bloods clotting factor VII: C and GM-CSF and have reached market by 1990. By 1991 more and more recombinant therapeutics became commercial products. These include colony stimulating factor, epidermal growth factor, and insulin like growth factor, tumour necrosis factor and several new interleukins. Besides, a number of recombinant vaccines joined the race. Recombinant hepatitis B vaccine is already being sold. New vaccines for measles and pertussis (whopping cough) are on the way. So are for malaria, typhoid and cholera vaccines. Therapeutic human proteins are also on constant increase.
9. *Broadening goals of plant genetic engineers:* Insect and herbicide resistance was the primary goal of plant genetic engineering. New areas like improvement of oil seed crops are also being addressed. Tomatoes to reduce softening during ripening, improvement of key amino acids in forage plants, improvement of rubber production (engineering of rubber transferase gene) are the new avenues opened by genetic engineers working with plants.
10. *Protein engineering:* Recombinant DNA techniques are being used to produce genetically engineered proteins to study their three dimensional structures, effect of amino acid substitution on its shape and function. Big soap and detergent companies are using protein engineering to improve the detergent enzymes. It has its new application in medicine and starch hydrolysis. Knowledge of three dimensional protein structures has also opened up many opportunities

for designing smaller molecules that might act on the proteins. Compounds that block the action of viral proteins, cell receptor proteins, or specific enzymes become easier to design. Both the multinational companies as well as smaller companies are actively engaged in the area.

Transgenic Plants

By using genetic engineering methods more than 3000 plants have been developed with new characters. These are tolerant to freeze, resistant to insects, viruses, fungi, and herbicides. In addition, modification of ripening or softening of fruits shelf life increase of fruits and flowers; and modification of sweetening of fruits have been achieved. In USA, there are more than 2000 genetically engineered corns that have been released for cultivation. Other crops that have been released are Soybean (425), cotton (246), sugar beet (79), rice (54), and wheat (53).

Food Ingredients

Among the numerous microbially derived compounds as food ingredients amino acids, vitamins, sweetening agent (aspartame), organic acids (e.g. citric acid), antimicrobial agents, surfactants, flavour enhancers (e.g. monosodium glutamate) and various enzymes are important. The production of these compounds could be significantly improved through genetic engineering techniques. Vigorous researches are in progress in the advance countries. It is hoped in the near future ingredients derived from recombinant organisms will be available in the market that will balance the ever-increasing demand of the consumers around the world.

Starter Cultures

Saccharomyees cerevisiae (the bakers yeast) is the first genetically engineered starter culture to obtain regulatory approval in the UK in 1990. This strain contains enhanced level of two essential enzymes naturally present in baker's yeast, namely maltose permease and maltase responsible for the production of carbon dioxide that causes 'fluffying' of the bread. It is hoped in the near future more of such strains will be available to use as 'starter culture' in many of the fermented foods.

Peptide Growth Hormones

These are needed for increase milk and meat production. Growth hormone genes could be used to accelerate growth, improve feed efficiency and modify the nutritional quality of meat producing animals, poultry and fish. The peptide hormone bovine somatotropin (BST) has been found to increase the efficiency of dairy cows without altering the nutritional quality of milk. Approval by Federal Drug Administration (FDA) of USA is expected soon. A revolution in milk production is hoped to come with its application.

Improvement of Nutritional Quality

Nutritional quality of food supply could be improved through application genetic technologies. Potatoes with 30 per cent higher solid contents have been developed through gene transfer technologies. The ratio of essential amino acids in the cereal grains has been improved. The technology is contemplated to be used to improve the taste, texture, colour and processing characteristics of raw agricultural products. In future it is hoped that custom designed agricultural products with specific characteristics will be made available through genetic engineering techniques.

Transgenic Animals

Although controversial on ethical point of view, transgenic animals having new characteristics are being produced for increased meat, milk and pharmaceutical products. Human pharmaceuticals are being designed to be produced from animals through their milk, urine and blood. The gene for tissue plasminogen activator (an enzyme that dissolves blood clots in heart attack victims) has been cloned into sheep and cows and the gene is expressed in the milk of the animals. Such animals serve as 'bioreactor' to produce the desired pharmaceuticals and only a few animals would be required to produce the desired pharmaceuticals and only a few animals would be required to produce sufficient quantities for total worldwide use of the compounds. The milk from such animals will, however, not be consumed by human. But, the meat from transgenic animals will need to be consumed for making the process economically viable.

Antisense Technology

This is a very interesting and emerging area of genetic engineering that has been used for the selective inactivation of single genes coding for specific enzymes. The DNA molecule has two strands of which one is antisense or non-functional. In antisense technology RNA (Ribonucleic acid) is transcribed (synthesized) from the non-coding or antisense strand of DNA for a given gene. Antisense RNA forms a duplex with the normal messenger RNA (RNA which carries the message of protein synthesis from DNA) and renders the normal RNA non-functional and this inhibits the production of normal protein by messenger RNA. By applying this technology ripening of fruits cold be delayed and thus the shelf life of fruits could be increased. One product of such technology, i.e. delay in ripening of tomato, is now under review by FDA in the US. The technology will have extensive applications as it can be used for selective inactivation of specific genes involved in the production of natural toxic materials in food crops. These toxicants include caffeine, glycosides and various other materials present in many common foods.

Cancer Imaging Agents

Radioactive isotopes linked to monoclonal antibodies specific for cancer cells can be used as agents that form images of cancers. The monoclonal antibody portion of the immunoimaging agent attaches to the cancer cells when injected into the body. Gamma camera can capture the image formed by the gamma radiation's given off by the radioactive atoms. Monoclonal antibody imaging agents is hoped to be able to detect malignancies, which is not possible by the currently available procedures. Imaging agents will be able to confirm the cancer types and provide informations for selecting the best therapy. It is estimated that in the US alone there are 965,000 cases of different types of cancer per year and the monoclonal antibodies to detect these cancers will have an annual market of 400 million dollars. Companies like Centrocor, Cytogen, ImmunoMedics, NeoRX and Zoma in the US are currently working on imaging of different types of cancers.

Recombinant Dairy Products

Recombinant DNA techniques have a high potentiality of improving starter cultures and enzymes used for converting milk into cheese and other dairy

products. Chymosin, a recombinant rennin obtained from microbial sources, already is used in commercial cheese manufacture. Other dairy enzymes like cheese flavouring enzyme and lactase is hoped to be produced more economically through genetic engineering. Another important area is the anticholesterol enzyme for lowering down the level of cholesterol in dairy products. Recombinant processes could produce commercial quantities of this enzyme for breaking down cholesterol in milk or milk products made for it. Companies like Dairy Food Laboratories (Waukesha, WI), Genencor (South Sanfrancisco, CA), Gist-Brocades (Chartotte, NC), Chr. Hansens' Laboraotry (Milwaukee, Wi), Lactaid (Pleasantville, NJ), Miles (Elkart, IN), Novo (Danbury, CT) and Pfizer (New York, NY) are actively engaged in this area.

Autoimmune Therapeutics

Infectious diseases as well as cancer cells are fought out in the human body by its defence mechanism called the immune system. But, sometimes the system fails to identify the intruders and may attack the normal healthy cells resulting in autoimmune diseases like rheumatoid arthritis, multiple sclerosis. These diseases are almost incurable at present. Recombinant DNA technology promises for the development of new proteins that will bring harmful and erratic activities of the immune system under control. Research work is in progress on thymosin-thymus gland hormones that modulate the immune system, Gamma interferon for the treatment or rheumatoid arthritis, Interleukin-1 and its analogs, Immunomodulators for treating rheumatoid arthritis, Cloned genes for Interleukin-1 (IL-1) receptor, D-glutamic acid/D-lysine polymer conjugates as cell receptor blocker for treating lupus, Protein A for removing excess antibodies from blood. Genetically engineered T-Cell antigen receptors are the target to treat autoimmune disorders.

Immunoassays for Pesticide Residue Tests

Like clinical diagnosis through antibody-based tests, Immunoassays offer possibilities for quicker, cheaper, simpler and more sensitive test for detecting synthetic organic pesticides. Synthetic herbicides, insecticides and fungicides are in great use both in advance as well as developing countries for the

protection of crops. But, many pesticides are the cause of various human diseases including cancer. So, strict regulations have to be followed so that not even trace amount of harmful pesticides carry over into food or end up in drinking water. Immunoassays will complement the present techniques like Chromatography and other analytical procedures for detecting low levels of pesticides in crops, food, water and environment. Several companies in the US are actively engaged in their development.

Diabetes Therapy

Human Insulin was the first recombinant protein approved for the treatment of diabetes. So long insulin was extracted from pancreatic glands of animals in slaughterhouses. But, this was a very tiresome job. Now, recombinant DNA techniques are used to produce Insulin by microbes like *E. Coli.* A number of companies are engaged in this field. Besides, several companies are using genetic engineering techniques to develop new approaches like Pancreas cell transplants and autoimmune treatment to cure diabetes. Diabetes is a very serious global disease. It originates from impaired capabilities to convert glucose into energy due to faulty secretions of insulin by the pancreas. Complications from high level of glucose could be severe coma, blindness, kidney diseases, high blood pressure and other serious disorders. With the availability of insulin from recombinant DNA techniques the future of diabetics for prolonging their life is really bright.

New Products of Promise for Chicken Industry

Recombinant DNA techniques have a good potentiality to improve the production of chickens and eggs. This is a huge industry and in the US alone value of chicken broiler production for meat is about 6.5 billion dollars/yr and that of eggs is about 3.5 billion/yr. Recombinant products that can improve growth offer the biggest potential market. Vaccines to prevent diseases and infestation with parasites have a significant market. Production of low cholesterol eggs is also a major target. Present researches are aimed at:

1) Development of multiple viral disease vaccines.
2) Production of recombinant chicken growth hormone.
3) Production of transgenic poultry with improved disease resistance and growth characteristics.

4) Cloning of DNA fragments from coccidiosis organisms.
5) Microinjection of embryos and use of retrovirus to transfer foreign DNA into cells.

Growth/Healing Proteins

Growth hormones like for dwarfism and others, healing hormones for burns, surgical, wounds, ulcers, etc. and also elderly and obesity hormones offer a good potentiality for their use in human welfare. Growth and healing hormones sometimes difficult to differentiate as the same substance can act in both the cases. At present, recombinant human growth hormone to treat the dwarfs has already been marketed in the US. Others are in the process of development at various laboratories. Some of the envisaged products are:

Epidermal Growth Factor (EGF): Stimulates skin growth. It is promising for healing wounds and burns, and hopefully for treating gastric ulcers.
Fibroblast Growth Factor (FGF): May heal surface wounds as well as stimulate development of blood vessels. May also be used for heart attack patients.

Human Growth Hormones (HGH): May stimulate both soft tissue and bone repairs. Could also be useful in orthopaedic surgical operations.

Interleukin-1 (IL-1): Stimulates secretion of growth hormone. More promising as a stimulant to the immune system.

Platelet Derived Growth Factor (PDGF): Could speed wound healing and soft tissue repair. It is already in pre-clinical trials.

Transforming Growth Factors (TGF): Appears in several forms like the Interferon's. Could both stimulate and inhibit growth of Cells. Promising for wound healing and bone repair.

Angiogenesis Factors (AF): Stimulates development of blood vessels. It has the potential for applications in healing of bedsores and other skin ulcers.

Hazardous Waste Treatment

Recombinant organisms offer the possibility of degrading recalcitrant compounds for which effective organisms have not been developed as yet by conventional techniques. Chlorinated organics, especially the aromatic compounds are at present the most recalcitrant chemicals creating major environmental problems. Polychlorinated biphenyls (PCBs) are the most dangerous among them. Research works in this area are aimed at finding for a gene/genes coding for an enzyme/enzymes that will break down the compounds easily. Some of them have already been found, cloned and multiple copies have been placed in bacterial hosts cells. The transformed bacteria are many times more effective than the conventional ones. Both specific as well as broad-spectrum enzymes are needed for the purpose. For the decomposition of pesticides residues recombinant bacteria have already been developed.

Recombinant bacteria like antifrost agents, insecticides and other purposes have already been released in the environments. So, use of ones for waste treatments becomes more feasible. Some researchers are now looking for 'suicide' genes that can be inserted into bacteria and at some later time be activated to kill the host organisms and prevent their further spread in the environment.

Genencor in America already selling huge quantity of enzymes like cellulases and hemicellulases for treatment of biomass waste. The company uses genetically engineered organisms to produce the enzymes in large quantities.

Human Genome

The last decade has witnessed a phenomenal progress in different fields of biotechnology. One such field is the sequencing of 'gene' called 'genome' project or in other words 'bio informatics'. A human being has 23 pairs of chromosomes in each somatic cell. In 1994 an ambitious project called 'Human Genome Project' was undertaken at a huge expense by a number of laboratories of the advanced countries. The objective was to identify some about six billion nitrogenous base sequences (Adenine, Guanine, Thymine & Cytosine) distributed among 100,000 or so genes located on 23

pairs of human chromosome and to utilize the knowledge for the treatment of congenital diseases for which there is no cure at present. And, by June 2000 this upheaval task had been completed by CELERA GENOMICS and a few other laboratories of the advanced countries. Gene sequencing which started in late 1995 with complete genome of a free living organism *Mopholis Influenza* that causes meningitis in children is now being done in many laboratories around the world and there has been an exponential growth of new information in genomics. By now complete genome of close to 100 microorganisms are known. Among higher organisms also quite substantial progress have been made with important agricultural plant like rice and also with the model plant like *Arabidiopsis.* The ultimate objectives of such studies are to utilize the knowledge for the treatment of genetic diseases in human being and also improve useful products of agriculture and industry.

Golden Rice

Professor Ingo Potrykus and his team working at the Swiss Federal Institute of Technology, Zurich, Switzerland genetically have engineered a Japanese rice variety (TP 309) by inserting into it as many as seven foreign genes enabling the rice grain to synthesise b-carotene - a precursor of vitamin A and an extra amount of absorbable iron. Potrykus group inserted four genes from the yellow coloured attractive Daffodil flower plant that gave rice grain the ability to synthesize b-carotene from the precursor present in it. The three genes for the synthesis of iron-storage protein came from French bean, Basmati rice and from a fungus respectively. Vitamin A deficiency causes blindness among children and lack of sufficient iron affects women being responsible for many anaemia related illness. This is the first kind of rice that is genetically engineered for nutritional enhancement and the humanitarian pay off from this could be enormous. Vitamin A deficiency affects some 400 million people around the world, leaving them vulnerable to infections and blindness. And iron deficiency afflicts up to 3.7 billion people, particularly women, leaving them weakened by anaemia. It is expected very much that with the availability of this rice strain around the world the potential benefits will be great. But, the success so far does not mean that the new crop is ready for market. Protrykus and his colleagues

used the *Japonica* strain of rice for their research work. But, the *indica* rice is the most common commercial strain. So, the scientists at IRRI have taken on the task of cross breeding the new strain with indica rice and field-testing the hybrid. It is expected that the results will be forth coming very soon.

Biofarming

Utilizing genetic engineering techniques the whole plants are now being used as factories for producing vaccines, pharmaceutical products, enzymes, drugs, antibodies and even biodegradable plastics. Plants have advantages over animal and bacterial cell cultures, since the plants, specially the annual types, can be easily grown and the product in question can be extracted after the plant maturation. In certain cases like banana the transformed fruit can just be eaten to get the desired immunization. And, in the near future one need to eat only a banana for protection from hepatitis B or potatoes to get immunity from colon bacillus (*E. coli).* Professor Charles Arutzen of the Boyce Thompson Institute of Plant Research and his group is the pioneer in this area of research. Likewise, industrial oil with a hydroxyl side chain has been produced in Canola corn oil by cloning and transformation of the corn by a gene from the California bay tree. Therefore, in the near future, it will be possible to produce oil of novel composition in existing oil producing crops by utilizing genetic engineering techniques. Extensive research works are also in progress to make plant synthesize polymers with plastic and elastic properties. Genes from bacteria that can produce Polyhydroxy alkanoates having plastic like properties are also being introduced into plants. Further research is in progress

Biotechnology, specially the industrial biotechnology, is expected to have a significant impact on the economy of the world within the coming decade, through the use of advanced tolls such as Genetic engineering. The enormous potential of biotechnology to provide diverse new products of therapeutic and industrial importance will usher a new era of development in the near future.

To date, major investment in biotechnology has been primarily in the health sector, the results of which are having a profound impact on medicine and

health care by providing improved approaches to the diagnoses. Although health related research must remain a national priority, future research work needs to be built on the common foundation in basic science to bring the power of biotechnology to bloom in other field. In this context the area of manufacturing and bioprocessing will get a major thrust in the near future.

But, biotechnology particularly the industrial biotechnology involving manufacturing and bioprocessing is a very capital intensive venture for which specialized capacity building is necessary. And, for that reason developing countries, specially the LDCs, are lagging behind in this area.

The Biotechnology Research Subcommittee (BRS), USA in its report has emphasized the need to develop biotechnology research in different areas and has set up priorities as follows:

1. Agriculture

Agricultural Biotechnology has the potential to increase food production, reduce the dependency of agriculture on chemicals, and lower the cost of raw materials, all in an environmentally friendly manner. It offers efficient and cost effective means to produce a diverse array of novel, value added products and tools.

Research Priorities

- Continuations of mapping and sequencing of animal/plant/microbial genomes to elucidate gene function and regulation, and to facilitate the discovery of new genes as a prelude to gene modifications.
- Determination of biochemical and genetic control mechanisms of metabolic pathways in animals, plants, and microbes that may lead to products with novel food, pharmaceutical, and industrial uses.
- Extension of understanding of the biochemical and molecular basis of growth and development including structural biology of plants and animals.
- Elucidation of the molecular basis of interaction of plants and animals with their physical and biological environments, as a basis for improving the organisms' health and well being.

- Enhancement of food safety assurance methodologies, such as rapid tests for identifying chemical and biological contaminants in food and water

2. Environment

Bioremediation is the primary target of environmental biotechnology. This involves the use of living organisms or their products to degrade wastes into less toxic products and to concentrate and immobilize toxic elements, such as heavy metals, to minimize industrial wastes and rehabilitate areas fouled by pollutants or otherwise damaged through ecosystem mismanagement.

Research Priorities

- Development of an understanding of the structure of microbial communities and their dynamics in response to normal environmental variation and novel anthropogenic stresses.
- Determination of the biochemical mechanisms, including enzymatic pathways, involved in aerobic and particularly anaerobic degradation of pollutants.
- Expansion of understanding of microbial genetics as a basis for enhancing the capabilities microorganisms to degrade pollutants.
- To conduct microcosm/mesocosm studies of new bioremediation techniques to determine in a cost effective manner whether they are likely to work in the field, and establish dedicated sites where long-term field research on the bioremediation technologies can be conducted.
- Development of test and evaluate innovative biotechnologies, such as biosensors for monitoring bioremediation *in situ*; models for the biological process at work in bioremediation; and reliable, uniform methods for assessing the efficacy of bioremediation technologies.

Manufacturing/Bioprocessing

Bioprocessing- a type of advanced manufacturing that employs chemical, physical and biological processes employed by living organisms or their cellular components - will cater to the demands for new and improved

commercial products. Bioprocessing can provide products with unique and highly desirable characteristics and offers new production opportunities for a wide range of items.

Research Priorities

- To investigate methods to enhance the efficiency and expand the utility of upstream processing technology.
- To develop capabilities to recover and purify products from dilute bioprocess streams and develops predictive models to facilitate the design of down stream separations.
- To develop methods for monitoring and control of commercial bioprocessing including reliable and robust real time sensors.
- To expand the development of novel biomaterials, such as bio-mimetics and replacement tissues, through new tissue engineering and chemical systems methods.

3. Marine Biotechnology and Aquaculture

Although oceanic organisms constitute a major portion of earth's biological resources, yet most of these organisms (primarily microorganisms) have yet to be identified. Recent advances in molecular biology, biosensor technology, aquaculture, and bioprocess engineering now promise fundamentally new approaches and opportunities for identifying, using, and managing biological resources from the seas.

Research Priorities

- To develop a fundamental understanding of the genetic, nutritional and environmental factors those control the production of primary and secondary metabolites in the marine organisms, as a basis for developing new and improved products.
- To identify bioactive compounds and determine their mechanisms of action and natural function to provide models for new lines for selectively active materials for application in medicine and the chemical industry.
- To develop bioremediation strategies for application in the worlds coastal oceans where multiple uses – including waste water disposal,

recreation, fishing and aquaculture demand prevention and remediation of pollution's and develop bio-processing strategies for improving sustainable industrial processes.

- To use the tools of modern biotechnology to improve the health, reproduction, development, growth, and overall will being of cultivated aquatic organisms; and promote the inter disciplinary development of environmentally sensitive, sustainable systems that will enable significant commercialisation of aquaculture.
- To improve understanding of microbial physiology, genetics, biochemistry and ecology in order to provide model systems for research and production system for commerce, and to contribute to understanding and conservation of seas.

The BRS (Biotechnology Research Sub-committee, USA) has identified three overreaching priorities for biotechnology research in the areas examined:

Overreaching Priorities

(1) Expansion of research to discover, characterize, modify and control the genetics and biochemical products and processes of a broad range of terrestrial and marine organisms for application in biotechnology.

(2) Application of the tools of modern biotechnology to problems in agriculture the environment, and manufacturing to facilitate the development of new and improved products, processes and test methods.

(3) Strengthening and enhancement of facilities, repositories, databases, reference standards, and human resources to ensure the future vitality of the biotechnology enterprises.

Bangladesh like some other developing countries may take appropriate lessons and guidelines from this report and develop research programmes accordingly. Biotechnology is poised to make major contributions to the economic growth of the world at large in the 21st century through the coordinated implementation of these research priorities.

Present Status of Biotechnology in Bangladesh

Plant Biotechnology

The programme on Plant Biotechnology in Bangladesh was initiated in late 1970s in the Department of Botany, Dhaka University with tissue culture of jute. Thereafter within a span of 10-12 years tissue culture research laboratories have developed in different universities and R&D organisations like: Dhaka University, Rajshahi University, Chittagong University, Jahangirnagar University, Khulna University, Bangladesh Rice Research Institute, Bangladesh Jute Research Institute, Bangladesh Agricultural Research Institute, Bangladesh Council of Scientific and Industrial Research, Bangladesh Atomic Energy Commission, Bangladesh Institute of Nuclear Agriculture, Bangladesh Forest Research Institute and Institute of Post Graduate Studies in Agriculture. At present, a few NGOs like DEBTECH and PROSHIKA are also working on plant Tissue culture. As a result of intensive work on plant tissue culture protocols on plant regeneration and micro-propagation have been developed on different crops, forest plants ornamental and fruit trees as well as vegetables. These in vitro regeneration protocols are now waiting for commercial exploitation. It is expected that with the establishment of private entrepreneurs commercial utilization and expansion of tissue culture techniques will gradually find its due place in Bangladesh.

Animal Biotechnology and Aquaculture

In Animal Biotechnology Bangladesh Live-stock Research Institute (BLRI) and Bangladesh Agricultural University (BAU) have already taken modern biotechnology programmes. These include Embryo Transfer Technology, Multiple Ovulation Embryo Transfer and Artificial Insemination programme. But, the programme of animal gene transfer through genetic engineering technique has yet to be started. However, livestock biotechnology produced 11 types of veterinary biologics for the treatment of infectious diseases in livestock and poultry, vaccines for foot and mouth disease and rinder-pest. Biotechnology in fisheries induces Pawing in Carp, Pabda, catfish, Koi and others. With this technology 50,000 kg of different fish species can now be produced annually.

Insect Biotechnology

Sericulture Research Institute, Rajshahi has been working for a long time for the improvement of sericulture production in Bangladesh. During recent past genetic engineering techniques have also been adopted for the purpose. At the Bangladesh Atomic Energy Commission low dose of gamma radiation to the silkworm has been employed for the enhanced production of silk. Significant progress has been achieved on Sterile Insect Technique (SIT) by utilizing gamma radiation. Besides, hormonal and pheromonal control of insects and also the Integrated Pest Management (IPM) programme are now being adopted for insect management. Isolation and characterization of *Bacillus thuringiensis* strains for the control of Lepidopteron insects has been initiated at the university of Dhaka.

Industrial Biotechnology

In the field of Industrial Biotechnology Bangladesh is yet to make real breakthroughs. Modern biotechnological programmes involving gene transfer technology have yet to be started in real earnestness. Whatever has been possible is through classical/old biotechnology methods. However, the results are quite encouraging and a good number of projects are in advanced stage that can be taken up for commercialisation. Some of these research programmes are:

(1) Bioconversion and bioprocessing have agricultural and agro industrial residues for feed, fuel and chemical.
(2) Genetic improvement of industrial microorganisms like: Citric acid production by *Aspergillus Niger* through gamma radiation.
(3) Mass scale production of Spirulina (reached commercial stage).
(4) Production of biofertilizer (Reached Commercial stage).
(5) Production of amylase and gluco-amylase for scarification of low cost starch.
(6) Production of microbial biomass protein and single cell protein.
(7) Production of tannery enzymes.
(8) Production of alcohol from agro-industrial residues – a few distilleries in the country are already utilizing more than 50,000 MT of molasses for the production of ethyl alcohol.

(9) Preservation of fruits, vegetables and spices by radiation and bioprocessing.
(10) Bio-enrichment of cereal food by microbial fermentation.

Bio-energy and Bio-conversion Technology

A significant achievement has been in the field of 'BIOGAS' production from animal excreta (cow-dung) and agricultural residues. The Institute of Fuel Research and Development (IFRD), BCSIR has been working since long in this field. As a result of research findings and its subsequent development in collaboration with Department of Energy (DOE) at present more than 10,000 biogas plants have been installed in rural areas. An extended programme to set up about 100,000 biogas plants throughout the country has also been taken up by the government that is now under implementation.

Environmental Biotechnology

In case of Environmental Biotechnology Bangladesh is yet to start its programme by utilizing modern biotechnological techniques. Whatever has been possible is through conventional methods. But, because of excessive population pressure and overall industrial activity environmental pollution is gradually increasing day by day which is causing a real threat to human health and ecological balance. Industrial effluents, municipal garbage and sewerage are discharged with minimum or no treatment at all into the surface water causing water pollution. The Department of Environment (DOE) of the Government of Bangladesh is doing some routine work only. Among the limited activities BAEC has installed advanced facilities to analyse harmful agrochemical residues at a very low concentration. Microbial technology could be a useful tool to minimize solid waste and effluents causing pollution. What is needed a broad-based 'Bioremediation' programme involving modern biotechnological approach including the development of microbes capable of degrading Xenobiotics and recalcitrant pollutants.

Genetic Engineering

Bangladesh is yet to start in real earnestness the techniques of genetic engineering for the improvement of plants, animals, and industrial microorganisms and also to combat with environmental pollution problems,

etc. Only a limited number of laboratories are now working at present to introduce and utilize the gene transfer technology for the improvement of crops like rice, jute and also for obtaining better strains of industrial microbes. Research and development of animal genetic engineering is particularly very limited at present. Below is given a list of some research works that are being carried out in different universities and research institutes:

(1) Agro-bacterium mediated genetic transformation of jute being carried out at the Institute of Food and Radiation Biology, AERE, BAEC, Dhaka and Bangladesh Jute Research Institute.
(2) Genetic transformation of pulses for fungus resistance initiated at the Dept. of Botany, D.U.
(3) Genetic transformation of rice and jute for salinity tolerance and fungus resistance being carried out at the Dept. of Biochemistry, D.U.
(4) Use of DNA probes for the diagnosis of diseases being initiated at the Institute of Nuclear Medicine, BAEC, Dhaka.
(5) Development of Food, Fibre and Energy through Recombinant DNA technology being carried out at the Dept. of Zoology, R.U.
(6) DNA finger printing of rice and jute at the Dept. of Biochemistry, D.U.

National Institute of Biotechnology

The concept of a National Institute of Biotechnology in Bangladesh was developed as early as 1984 and a Project Proposal (PP) was submitted to the government by the same year. In 1993 a feasibility study was conducted under World Bank finance at a cost of 3.2 million taka with a strong recommendation for the establishment of a 'National Institute of Biotechnology'. Thereafter, the matter was subjected to different examinations and evaluation by the government for several years. Subsequently in 1998 in a meeting of the National Council for Science and Technology (NCST) it was decided that an Institute of Biotechnology would be established in Bangladesh. Accordingly, a Project Proposal was submitted to the planning Commission. Based on this report a Project Concept Paper (PCP) was prepared by the Planning Commission in 1995 and submitted to the Pre-ECNEC meeting. This after many proposals, counter proposals

and revisions was finally approved by the government in a meeting of ECNEC held on 12.5.99 and accordingly a PP (Project Proposal) was prepared with an estimated cost of 20.21and then revised to a cost of 2768.24 lakh taka. The salient features of the institute are as follows:

1. Name of the Project: National Institute of Biotechnology.
2. Sponsor Organization/Ministry: Ministry of Science and Technology, Government of Bangladesh.
3. Estimated cost: 2768.24 lakh Taka (Revised)
4. Total aArea of Institute Building: 3700 sq. m.
5. Total floor space of the laboratories: 2250 sq. m.
6. No. of Laboratory: 6
7. Total No. of Scientists to work: 100
8. Expected year of completion: June 2004.

The proposed six Laboratories/Divisions of the institute are:

1. DNA Laboratory
2. Plant Biotechnology
3. Animal Biotechnology
4. Fish Biotechnology
5. Fermentation and Bioprocessing
6. Bio-energy and Fertilization

The physical construction of the institute has already been started and the main laboratory building is expected to be completed by June 2005. Appointment of Scientists for the Project period is also underway.

NIB Objectives

The National Institute of Biotechnology, Bangladesh is going to be established with an aim to accelerate the research activities in the field of biotechnology in order to meet the ever-increasing demands in food, medicine, energy and industrial sector in the country. Overall, the institute may cater to the following areas in order to boost up the application of biotechnology in the country:

(1) Research work on priority problems in agriculture, food, industry, veterinary and human health.

(2) Networking of important national projects like genome project, field testing, etc.
(3) Human Resource Development – manpower training in biotechnology, capacity building, bio-informatics and holding of regular seminars and symposia in order to disseminate the up-to date knowledge on the subject.
(4) Policy Planning – act as a national focal point on biosafety, bioethics and bio-surveillance, and also technology alert and assessment system.
(5) Technology Resource Centre – act as national centre for making use of proven, economically viable biotechnology on the shelf for fostering remunerative employment and also act as a seat of Biotechnology Park

R&D Priorities for Biotechnology and Genetic Engineering in Bangladesh

In fixing the priorities in R&D activities in biotechnology the sectors that are considered important for our country are health, energy, agriculture, industry and environment. Biotechnology can play a great role in development activities in all these sectors if R&D programmes are taken up judiciously and such programmes are supported adequately.

i) Health Sector

Development of vaccines against viral, bacterial and protozoal diseases through modern genetic techniques. Vaccines for fertility regulation, production of drugs and pharmaceuticals, etc. call for proper investment in R&D activities in biotechnology and genetic engineering.

ii) Industry Sector

R&D activities should give priority to improvement of industrial strains of micro-organisms for production of those food supplements, drugs, vitamin, hormones, solvents and other chemicals which are now solely imported from abroad. Bioconversion of agricultural wastes into food, feed and fuels is another important area. Optimisation of process parameters for maximising productivity so as to efficiently convert raw materials to finished products call for inter-disciplinary approach to the biological process with heavy input from chemical engineering.

iii) Agriculture Sector

Priorities in R&D work should include programmes on development of high yielding, stress tolerant varieties of food crops through modern genetic engineering techniques, biological nitrogen fixation, bio-fertilizers, bio-insecticides, etc.

iv) Energy Sector

Emphasis should be given on the conversion of lignocellulosic wastes to bio-fuels, improvement of biogas technology from organismal and environmental (better bioreactor) point of view, development of energy plants, etc.

v) Environment Sector

Development of efficient activated sludge process for waste treatment, development of organisms for treatment of industrial pollutants, xenobiotics, etc. should get research priority.

Biosafety Aspect

With all the benefits, which accrue from the biotech revolution, it appears some of them are associated with potential risk as well as described below.

It is estimated that over the last three decades about half of the varieties of the world have been lost. One of the major risks in view there arises from the fact that novel varieties, which are commercially attractive, may replace some of the existing varieties unless proper attention is given to bio-conservation. Again, the genetic uniformity in plants and animals makes them vulnerable to pest and diseases. An epidemic caused by a mutant bacteria, pest or virus can cause havoc to a large number of plants or animals.

So far farmers in the Third World have been able to develop varieties, organise production and also were able to control the spread of disease as they were familiar with the indigenous plant or animals they were cultivating or breeding and the diseases which were likely to affect them, either by taking preventive measure or by providing the necessary treatment. With

the introduction of bio-tech seed the dependence of farmers on the supplier would increase, as the supplier alone would have the total information if any, on how to control disease problem. Because of the patent rights of biotech products the farmer would not be able further develop the variety, or experiment with it. This would turn the Third World farmers and breeders into mere workers. The problems of terminator gene have created serious controversy in this regard.

It is apprehended that biotechnology may also result in the substitution of a large number of natural products, such as flavours, added to beverage, food and other products. Their production, through cloning to increase the quality and quantity of a particular flavour may affect production of indigenous aromatic and medicinal plants. It may also affect the present genetic diversity, with consequent disadvantages, as mentioned earlier.

The genetically controlled animal produced in animal farms, would be cloned for increased quantities of proteins, but it may not suit the taste of consumers. The attempt to introduce casein gene in rice, though successful, may result in rice that taste like milk?

Again experiment on human genome has raised many ethical questions that deserve serious attention.

Finally environmental release of genetically manipulated products where one does not know the possible impacts they would have on other living forms, may result in disaster particularly when a large number of them are released for testing or for specific purpose, i.e. to combat pests, etc. without assessing other possible harmful side effect.

There is a tendency on the part of multinational companies to test biotech product without adequate safeguards over a period of time to know long-term effects. If the laws of the country do not permit and cannot be violated, then the tests might be done offshore or in the Third World countries unless those countries are guarded by strong bio-safety regulations.

Scientists in their desire to gain name and fame or to earn large financial benefits by undertaking research in manipulating genes to develop new forms of life tend to violate the laws of the country and undertake tests without considering the environmental impart.

For proper handling of genetically modified plant, animal and micro-organisms it is essential to have safety guidelines and for field application safety regulation is must to protect our environment from harmful effects if any of genetically modified organisms.

Biosafety Regulation

National 'Biosafety Guidelines' have been framed to be followed by the scientists working in the area of biotechnology.

The salient features of the bio-safety guidelines are:

(1) Procedures and guidelines on the introduction movement and field release of regulated materials.
(2) Physico-chemical and biological containment procedures and facilities.
(3) Guidelines for classification of micro organisms according to their risk assessment.
(4) Good laboratory practices.
(5) Good industrial large-scale practice.
(6) List of organisms according to different risk groups.
(7) The Universal Biohazard sign.
(8) Framework for risk assessment.
(9) Biosafety Committees.

Having set up the appropriate Biosafety Guidelines for working in the area of biotechnology, Bangladesh is now thinking to enact an 'Act' passed by the national parliament on the issue of 'Biotechnology'. The act to be named as 'The Bangladesh Biosafety Act-2001'is in its final stage of preparation prior to the submission to the government to be placed before Parliament as a bill for endorsement. The salient features of this 'Act' will be:

(1) Short title of the Act.
(2) Definitions of different terms/connotations.

(3) Formation of National Committee on Biosafety of Bangladesh (NCBB).
(4) Power and Responsibilities of NCBB.
(5) Risk Management of GMOs.
(6) Contained use of GMOs.
(7) Field Release of GMOs
(8) Public Deliberations Awareness.
(9) Restriction on certain activities related to GMOs.
(10) Working Principles for NCBB.

It is expected that after the 'Act' has been passed by Parliament, biotechnological research in Bangladesh will be done under more congenial atmosphere and bioethical problems will be taken care more diligently.

Bioethics

In response to 'Bioethics' Bangladesh recently is going to support the International Convention against human cloning for reproduction to be placed on the agenda of 56th UN General Assembly. Bangladesh strongly feels that human reproduction cloning is against the human dignity and in the long run it may also bring havoc to mankind. Universal declaration on the human genome and Human Right adopted in 1997 by the UNESCO specifies, "Practices which are contrary to human dignity, such as reproductive cloning of human beings shall not be permitted". In pursuance of this declaration any attempt to clone human being should be prevented through appropriate action/convention of United Nations, as it is contrary to 'Bioethics'.

Biotechnology Opportunities and Challenges

The opportunities of biotechnology are enormous in the field of agriculture, health care, industrial upliftment, energy development, environmental development or bioremediation. But this new and emerging technology is not without challenges particularly for developing countries. Major challenges include

- Capital intensiveness
- Specialized laboratory structure
- Commercialisation issues

- Private sector shyness
- Biosafety issues
- Bioethical issues

Bangladesh is in the threshold of entering into this modern area of science. Plant tissue culture was initiated in early 1970s, but not much progress has been made so far. As mentioned earlier, some initiation has been made in the field of animal biotechnology, aquaculture, insect biotechnology, industrial biotechnology, bio-energy and also genetic engineering. But in spite of all sincere efforts of the scientists, no breakthrough could be made because of lack of facilities and logistic support, research and development fund and incentives. However, during the last couple of years the government has given priority to the development of biotechnology

National Capacity building

Biotechnology, although a very promising technology, requires heavy investment at the laboratory, pilot scale and commercial level applications. For national capacity building the following areas need emphasis:

- Infrastructure development - laboratory building, ancillary facilities, specialized laboratories, etc.
- Manpower development - specialized expertise in the field of molecular biology, genetic engineering, protein chemistry, chemical engineering, etc.
- Equipment - for modern biotechnology work costly equipment like DNA synthesizers, protein sequencers, high-speed ultracentrifuge, pilot plant equipment for plant, animal and microbial technology work, etc.
- Fine chemicals - a regular supply of costly chemicals, enzymes, radio labelled compounds, etc.

Potentials and Requirements for a Biotechnology Development

Bangladesh has great potentials for development in the field of biotechnology. The potentials lie primarily in its rich fertile agricultural and biodiversity. Plant biotechnology, animal biotechnology, fisheries biotechnology or aquaculture, in every aspect Bangladesh has a great potential for

development. We have fertile alluvial soil; our masses are accustomed to different agricultural practices. What needed are a good variety of plant and/or a good stock of animal/ poultry/ fish, etc. that can be developed through modern biotechnology. For this the country needs a good team of well trained manpower for doing research in various fields of biotechnology like genetic engineering, cell culture, cell fusion, protein engineering, enzyme technology, etc. Bangladesh has good potential for development agro-biotech industry.

A 20-year Perspective Plan

Bangladesh is yet to start with biotechnology programme in real earnestness. Although scientists were concerned with its development from very beginning, because of lack of national policy planning the subject did not get due importance with the government for a long time. Though the situation has changed over the recent years, the National Institute of Biotechnology or similar other existing research laboratories and institutes will cater only to a small fraction of national need. Therefore, a 20-year perspective plan is deemed necessary to cater the future need with respect to:

- Manpower development
- Laboratory infrastructure development
- Building centre for excellence
- Identification of priority research areas like
  - Agriculture biotechnology
  - Healthcare,
  - Industrial biotechnology
  - Bio-energy
  - Bioremediation, etc.

Related Issues

Biotechnology although has revolutionised the subject of biology, it has also created new problems in the society the principal one of which is the transfer of genes from unrelated species. Although until now no havoc has been created, a danger is always there that 'it might be created'. Therefore, research work in this area has to be done under utmost care. Development of crop plants with new properties have created suspicion in the minds of

many. Again patenting and commercialisation of life forms has created new problems of intellectual piracy, monopoly business and bio-slavery. The related problems, which need to be addressed in harnessing the benefits of biotechnology, are as follows:

- Biosafety and bioethics
- Technology transfer and IPR
- Biodiversity
- Public awareness

Bangladesh, as mentioned earlier, has by now framed Biosafety Guidelines. Biosafety Act is under preparation. It is hoped that relevant issues will get serious attention from all concerned so as to reap the real benefit of biotechnology without harming present or future generation.

Conclusion

Biotechnology holds good promises for improved agricultural productivity and products. It ensures better management of agricultural echo system including water management, biofertilizers, biopesticides, biodiversity and bioremediation. In short, it can play a vital role in the socio-economic development of a country. The spectacular progress which has taken place in the last few decades indicate that we can no longer ignore the application of this technology for solving problems of agriculture, health, energy, industry and environment. However, a long term plan, adequate financial support for R&D in different areas of biotechnology, setting up of demonstration plant, etc. are necessary prerequisites for application of this innovative technology for our national development.