

Agricultural Biotechnology Research and Development in the Philippines: The Need for a Strategic Approach

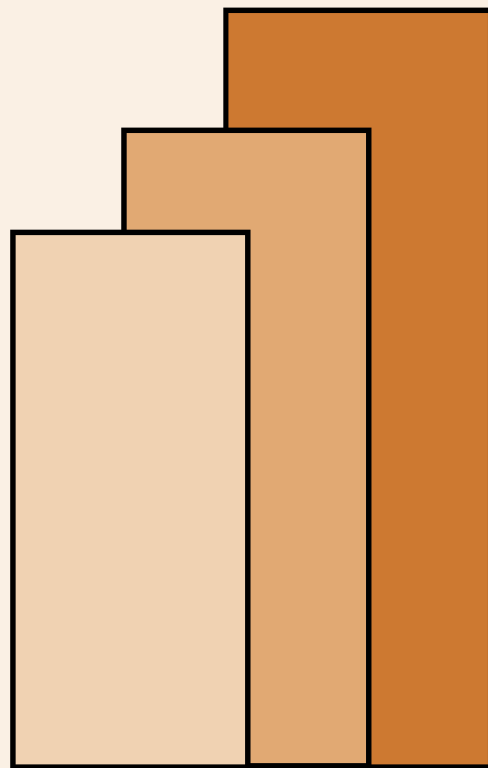
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Agricultural Biotechnology Research and Development in the Philippines: The need for a strategic approach¹

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Abbreviations:

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ASEAN - Association of South East Asian Nations
BAR Bureau of Agricultural Research
BIOTECH National Institutes of Molecular Biology and Biotechnology formerly
National
Institutes of Biotechnology and Applied Microbiology
Bt Bacillus thuringiensis
DNA Deoxyribonucleic Acid,
DOST Department of Science and Technology
GMO Genetically Modified Organism
IPR. Intellectual Property Rights
MTA - Material Transfer Agreement
PCARRD - Philippine Council for Agriculture and Resources Research and
Development
PhilRice - Philippine Rice research Institute
rDNA - Recombinant DNA
TPS - Technology Protection System
UPLB - University of the Philippines at Los Banos

Summary

Much has been written about biotechnology helping developing countries attain food security, increase farm productivity and profitability and yet minimize environmental damage from conventional agricultural practices. Current data from countries adopting modern biotechnology products particularly transgenic crops in agricultural production indicate that these goals are attainable. However, the diffusion of biotechnology to developing countries like the Philippines is not as rapid as the adoption rate in a few developed countries. Also, in some European countries, there is resistance to the adoption and use of crops developed through modern biotechnology. This paper examines the capacity of the Philippines to join and benefit from the biotechnological revolution. It reviews world trends and issues and Philippine agricultural biotechnology R & D contents, directions and management.

Modern biotechnology development involves two processes: the development of biotech products and the development of the regulatory framework for biotech products. The Philippines has in place a biotechnology R & D program since 1979 but the program has focused mainly on what is considered traditional biotechnology. R & D resources were expended on developing microorganisms to maintain soil fertility, protect crop plants, add value to agricultural by-products and improve traditionally fermented foods and rapid plant propagation by tissue culture. These programs appear to reflect the extent of available resources not only in facilities and maintenance funding but also on the existing manpower of whom few are trained in the molecular techniques required for modern biotechnology. Although these technologies are targeted for small farmers, their dissemination to this target group remains a problem. During the same period, advanced countries produced through rDNA techniques safer vaccines, more reliable diagnostic kits and genetically modified organisms (GMOs) such as corn requiring less pesticide, herbicide resistant soybean that allows zero tillage for soil protection, carnation with longer shelf life, virus-protected potato, tomato with better processing properties, and laurate canola with a novel use.

There is ambivalence towards GMOs. Genetically modified food plants are viewed with suspicion by some whereas microorganisms and animals modified for medical applications are not. Concerns on long term effects on the environment and human health are raised against genetically modified food plants. Yet, the USA and some developing countries have gone on to rapidly commercialize GMOs including food plants. On the other hand, pressure from consumers forced European governments to stall further commercialization of genetically modified food plants. There is on file in the Philippine Senate, a bill banning GMOs, in response not only to this world wide movement but also on the poor state of the regulatory framework for biotech products. Although the Philippines is the first ASEAN country to have in place guidelines for biotechnology research and development, there is no program to support implementation of the guidelines by

way of establishing the appropriate facilities required for research, of developing the scientific capability for risk assessment and funding biosafety research. No guideline for commercialization of biotech products exists. In addition, the new law on intellectual property rights has specifically excluded the patenting of animals and plants. Hence, the Philippine Congress is currently drafting a bill to protect plant varieties.

The secretary of agriculture recently stated that GMOs are advances that may be helpful to Philippine agriculture. The existing capability of the Philippine public institutions for genetic engineering applications needs strengthening. There are two laboratories with facilities for plant transformation and another four for DNA manipulations. Only one institution has the facilities and manpower for animal embryo transfer studies. There are about fifty individuals working in various institutions who are trained in the various techniques for genetic engineering. There is also the perennial problem of insufficient funds.

Given these limited scientific resources, there is a need to adopt a strategy in agricultural biotechnology development. A four-pronged strategy is proposed. One is to develop a sustainable system for the delivery of soil inoculants and biological control agents to small farmers. Two is to develop our risk assessment capabilities to enable us to access technologies elsewhere and to immediately test for possible commercialization transgenic crops already developed. Needless to say, we must put in place guidelines for the commercialization of biotechnology products. Three, is to implement a strong manpower development program especially in modern biotechnology that includes developing a local environment that nurtures scientific creativity. Four, is to confine molecular technique applications and genetic engineering work to species and problems important locally but not to other countries, e.g . bunchy top virus protected abaca.

Introduction

Much has been written about biotechnology helping developing countries attain food security, increase farm productivity and profitability and yet minimize environmental damage from conventional agricultural practices. Current data from countries adopting modern biotechnology products particularly transgenic crops show increased productivity with corresponding increases in profitability, with lower health risk to farm workers and with lesser environmental change¹. An analysis of the global implications of the various roles of the US, Europe and developing countries in the biotechnology revolution indicates a biotechnology-led growth for developing countries producing biotech products². However, the diffusion of biotechnology to developing countries like the Philippines is not as rapid as the adoption rate in a few developed countries. Also, in some European countries, there is resistance to agricultural biotechnology and the adoption and use of crops developed through modern biotechnology. On the other hand, biotechnology applications should benefit the Philippines where opportunities to increase farm productivity is apparent. Average farm yields are significantly low across major crops like rice, corn, coconut and sugar that occupy about 90% of agricultural lands. Also, the reliable production of some crops introduces more pesticides into the environment and/or results in soil degradation. The secretary of agriculture recently stated that GMOs are advances that may be helpful to Philippine agriculture.

This paper examines the capacity of the Philippines to join and benefit from the biotechnological revolution. It reviews world trends and issues and Philippine agricultural biotechnology R & D contents, directions and management using published literature, annual reports, symposia proceedings, thesis manuscripts, papers written by individuals, project listings provided by pertinent agencies, and limited field visits and interviews. This paper has three parts, part one presents the scope of biotechnology applications in agriculture, part two discusses world trends and issues in biotechnology, and part three presents the state of the art in and an analysis of agricultural biotechnology R&D in the Philippines.

I. The scope of biotechnology applications in agriculture

A. Definition and applications of biotechnology

Environmental changes most of them damaging are always associated with conventional agriculture. The doubling of agricultural production during the past 35 years was associated with a 6.87 fold increase in nitrogen fertilization, 3.48 fold increase in phosphorus fertilization, 1.68 fold increase in the amount of irrigated cropland and 1.1 fold increase in land in cultivation³. These changes have wrought havoc to some ecosystems causing lakes to die (eutrophication) and top soils eroded. Nitrogen fertilization of rice paddies has been associated with increasing

soil acidity and reducing crop productivity. Pest and diseases that cause an average of 30-40% loss in crop production⁴ are controlled by chemical pesticides. The decrease in wildlife populations, loss of beneficial organisms and impairment of farm workers' health due to pesticides have been well documented. Thus, technologies to minimize these changes are therefore necessary for sustainable agriculture.

Biotechnology is interpreted differently among different people. Official definitions include: 'Biotechnology is any technique that uses living organisms or substances from these organisms to make or modify a product, to improve plants or animals or to develop microorganisms for specific uses' (US Congress). Biotechnology is the application of science and engineering in the direct and indirect use of living organisms or parts or products of living organisms in their natural and modified forms (Canada)⁵. Agricultural biotechnology is modifications of any living organisms in ways that improve the efficiency, competitiveness and sustainability of food production (Ontario Agri-Food Technologies). The range of techniques in biotechnology require different levels of sophistication in facilities, basic science foundation and technical skills. The first level involves the manipulation of microorganisms and includes centuries-old fermentation technologies such as beer brewing, wine making mediated by microorganisms, production of organic chemicals like antibiotics and mushroom production. The second level involves the manipulation of tissues and cells from multicellular organisms such as plant tissue culture and mammalian cell cultures. The third level involves the manipulation and analysis of the genetic material, DNA, such as recombinant DNA (rDNA) technology, genetic engineering and applications of genomics, the study of whole genomes or the totality of the genetic material of a species at the molecular level. The first level is referred to as traditional biotechnology. Developed countries define biotechnology as the application of DNA manipulation techniques such as recombinant DNA and novel methods of using and manipulating cells to produce novel crops, animals and microorganisms generally referred to as genetically modified organisms (GMOs). In the Biosafety Protocol currently being framed under the Convention on Biological Diversity, modern biotechnology means the applications of in vitro nucleic acid techniques, including recombinant DNA and direct injection of nucleic acid into cells or organelles and the application of fusion of cells beyond the taxonomic family. (Plant) Biotechnology uses the disciplines of molecular biology, microbiology, genetics, biochemistry and plant breeding to translate basic biological knowledge into practical processes and products that have economic implications. It encompasses a range of techniques and technologies requiring different levels of investment. The techniques range from the simple, widely-used tissue culture to rDNA and genetic engineering techniques⁶.

Biotechnology applications in agriculture are numerous. Although research in the past two decades show differing emphasis by different countries. Developing countries in the ASEAN region particularly focused their resources on the use of microorganisms to maintain soil fertility, add value to agricultural by-products

and improve traditionally fermented foods and rapid plant propagation by tissue culture. Hence, research and development were on organic fertilizers, soil inoculants, protein-augmentation of farm produce, improved soy sauce production, mushroom production and the like. Plant tissue culture is mainly for the rapid propagation of selected planting stock. These technologies are targeted for small farmers and they appear to reflect the extent of available resources not only in facilities and maintenance funding but also on the capability of available manpower. Developed countries have produced through rDNA techniques safer vaccines, more reliable diagnostic kits and GMOs such as crop plants requiring less pesticide, allowing zero tillage for soil protection and acquiring longer shelf life, better processing properties, or novel use. A major application of modern biotechnology is the development of reliable, specific, novel genetic improvement techniques that shorten periods of breeding programs and attain objectives not previously possible.

B. The techniques of biotechnology compared with traditional methods

DNA manipulations comprise the most revolutionary of the techniques of biotechnology, developing products are not achievable by natural processes or if they are they could be the remote product of chance. As applied to crop and animal improvement, DNA manipulation and analysis as applied fall into two categories: those used directly modify genetic content (genetic engineering) and those used to dissect the genome to gather information and fast track classical breeding method.

Traditionally, an organism is genetically improved through hybridization that is, mating two individuals/populations with desirable properties to obtain a single individual or population having both desirable properties. Another traditional method is to produce genetic variation within a population by exposing the population to a mutagen or an agent that causes mutations followed by the selection for a desirable mutant. Both methods have their limitations. Hybridization allows recombination of properties only within species or with some technical difficulties among related species whereas mutations are random and limited by the genetic make-up of the target organisms. Genetic engineering aims to genetically improve an organism by introducing a foreign DNA coming from any species or synthesized in the laboratory. The properties of an organism is permanently changed since the DNA gets integrated into the genome of the recipient thus, such change is handed down to succeeding generations.

As a breeding method, genetic engineering broadens the germplasm base from which traits are transferred. Also, it enables the repeated transfer of new genes to existing cultivars without many generations of additional crosses, transfers specific genes without the concomitant transfer of other gene and enables the manipulation of genes to alter their mode and level of expression⁷. Genetic engineering involves transferring specific genes from one species to another whether related or unrelated. Only the gene of interest and other DNA sequences needed to indicate its presence and enable production of its product are transferred. Conventional

breeding produces a hybrid possessing traits of both parents whether desirable or undesirable. Hence, the process of obtaining the desired combination of traits often takes years of repeated selection and hybridization.

rDNA technology is the construction of a self-replicating DNA unit or DNA vector where the desired foreign gene is attached. The vector is then introduced into the host of interest where it may multiply independently or integrated into the genetic machinery of the host. The transferred gene comprise an ordered mix of DNA sequences with different functions affecting the expression of the gene and is referred to as a gene construct. The process wherein the gene construct enters a cell and gets to produce its gene product is called transformation. The recipient organism expressing the foreign gene product is called a transgenic or a genetically modified organism (GMO). A particular DNA sequence, gene or gene construct maybe used to transform different cultivars or different plant species. A widely transferred gene is the toxin gene of *Bacillus thuringiensis* which confers insect protection for the transgenic plant. This is often referred to as the Bt technology. Any crop containing this gene is referred to as a Bt crop (Bt corn, Bt rice, etc). A virus resistant transgenic plant is obtained from the transfer of a virus coat protein gene into the plant, this is referred to as the coat protein (CP) technology that falls within a more general technology - pathogen derived resistance. Another widely used technology is the antisense technology, also a DNA manipulation technique that turns off or prevents the gene from producing a product needed by the pathway that produces the unwanted trait. Hybridization technologies such as the PGS Seedlink(comprising of male sterility, sterility maintainer and restorer genes are widely used to facilitate the production of pure hybrid seeds⁸.

Molecular markers are DNA variations in plant and animal genomes. These are used in tagging agronomic traits and in selection in breeding populations (MAS or marker-assisted selection). Use of DNA markers associated with desirable traits reduces the time and guesswork used in the selection process. Selection is often the rate limiting step in plant breeding as it requires that the plants be sustained through out their growth cycle, allow them to express their genes at the right time and have them exposed to the conditions such as insect attack, drought, etc. that limit growth and yield in the field. Hence, selection is traditionally a long and laborious process. DNA markers are detected as early as the seedling stage without exposing the plants to their selective environments. Detection is highly reliable and rapid, one technical personnel can process at least a hundred samples per day. Molecular markers are also used to construct genetic maps, measure the genetic diversity of breeding materials and identify individuals, breeds, isolates or species. These include RAPD (random amplified polymorphic DNA) , RFLP (restriction fragment length polymorphisms), EST (expressed sequence tags) , microsatellites such as SSR (simple sequence repeat) and STR (short tandem repeat) and known genes. Genomics is an emerging research field of molecularly characterizing whole genomes or the total genetic material of a species. This follows the success of the Human Genome Project. Applications of genomics such as information about the structure of economically important genes, their locations relative to

each other, their products and the effect of other DNA sequences on the production and function of these products are considered the next revolution in biotechnology. These applications could offer technical solutions to the biosafety issues currently being raised against transgenic crops. Or, novel crops not yet imagined today could be developed.

In addition, DNA-based techniques have been developed for improved diagnostics and therapeutics. An appropriate, timely therapeutic regime can only be delivered after accurate diagnosis of the causal agent of a disease. DNA sequences specific to pathogenic agents are being packaged into diagnostic kits that are convenient and accurate. Safer, recombinant vaccines have been developed that totally removed the capacity of the attenuated organism to cause disease. A recent development are DNA vaccines. DNA vaccines are transiently expressed DNA sequences that produce the antigen thereby triggering the immune response of an animal to produce the corresponding antibodies against a specific pathogen. DNA vaccines can be so prepared that will require no refrigeration, and would have the advantage of better shelf life than current cell or protein-based vaccines in the market. It is expected that farmers in remote areas will have better access to these vaccines.

Genetically modified animal cell cultures have developed rapidly as a result of the inability of microbial cells to produce complex foreign proteins such as human proteins in culture. In addition to mammalian cell lines, insect cell lines especially those that support the growth of baculoviruses (insect-specific viruses) genetically engineered to produce human proteins are also developed. Obtaining a hybrid cell through fusion techniques in the laboratory have also found many applications. Hybridomas are cell cultures used commercially in the production of monoclonal antibodies which have applications as diagnostics, in identifying specific cells or tissues or in therapy. Hybridomas are derived from the fusion of spleen cell and a cancer cell. The spleen cell confers the ability of the hybridoma to produce a specific antibody and the cancer cell the ability to grow in culture indefinitely.

Techniques collectively referred to as reproductive technologies involve manipulation of the egg or sperm cell to modify mammalian reproduction. Included is in vitro fertilization (IVF) which allows the fusion of the isolated egg with a selected set of sperm cells outside the womb, allowing the fused cells or embryo to divide, implanting this to the receptive uterus of the female which then develop to term. IVF has led to the development of techniques that allows sperm cells to be stored and used later, to the selection of sperm that carries the male or female chromosome thereby allowing for the pre-selection of the gender of the resulting embryo and cloning. Gender pre-selection uses a very sophisticated technique called fluorescence activated cell sorting, has only been successfully used with pigs in 1998 and has been tested successfully in man early in 1999. Cloning is the production of new individuals without sexual union. In mammals, this is quite a feat reported since 1997 with the birth of Dolly, the sheep. Dolly was borne out of the union of an enucleated egg cell from a ewe and fused with a cell

from the udder of another ewe. The resulting fused cell behaved like an embryo and was implanted in the uterus of third ewe. Success with cows and mice have been reported since but various governments have adopted policies to prevent applications in cloning individual human beings. Reproductive and DNA manipulation techniques are also referred to as genetic technologies.

Plant tissue culture refers to the aseptic propagation of plants or plant parts. As the definition implies, it requires a highly controlled environment to prevent contamination and promote growth of plants/plant parts in confinement. Tissue culture is used either for micropropagation or as a plant breeding tool. Micropropagation results in the mass production for the rapid release of a new variety or selected cultivar with concomitant removal of seed borne pathogens and avoids the production of genetic off types. There are three generally used procedures: meristem culture, shoot multiplication and somatic embryogenesis. Meristem culture induces the actively dividing tissues of the plant to produce new plants. Shoot multiplication is the induction of a shoot to produce many shoots which are subsequently rooted into new plants. Somatic embryogenesis is a technique of inducing individual plant cells to develop into embryos. These embryos are encapsulated to produce artificial seeds. The method is hoped to produce cheaper genetically similar planting stocks compared with meristem or shoot cultures. All other tissue culture procedure are used in aid of plant breeding. Somaclonal variation with in vitro selection is a protocol for selecting desirable variants during tissue culture at relatively shorter period of time and lesser expense compared with traditional field screening and selection. In vitro selection allows for the use of more straightforward, rapid, objective selection procedures not feasible in the field. The selected variant maybe developed into new commercial lines such as reported for corn, tomato, papaya, apple, peach, and citrus⁷. Or the selected variants maybe used as parental stocks in breeding.

Another application is the reduction of the time needed to produce breeding lines for producing hybrids. Commercial hybrid seeds are produced from two isogenic lines, each line possessing the desired genes in pure form different from that of the other line. The traditional method of producing isogenic lines takes years but an intervening biotechnology is the production of haploid plant with subsequent diploidization to produce pure breeding lines or doubled haploids. Haploid plants are regenerated from anther, microspores or ovary cultures. These haploid plants have their chromosome number doubled to produce doubled haploids used like isogenic lines. This technique drastically reduces the time of producing isogenic lines by at least one half. For distantly related species, an intervening technique is embryo rescue which obtains the resulting embryo and let it grow in tissue culture. Embryo rescue and culture are used to overcome the incapacity of the ovary to support hybrid embryo growth. Somatic hybridization is the production of hybrids through fusion of cells from two selected parental lines. Techniques involving the isolation of single cells and their regeneration into whole plants are essential tools in the application of rDNA for plant genetic improvement.

On the other hand, plant cell cultures are being developed to produce specialty plant chemicals which cannot be chemically synthesized like the cancer drugs: vincristine and vinblastine from the tropical plant *Vinca rosea* (chichirica, Tagalog). One plant cell culture system already in commercial scale involves the production of shikonin, a red dye used in lipsticks. The system provides better control of production without regard for the vagaries of nature. A major technical drawback of the system is the inability to maintain a uniform genetic make-up of the plant cells in culture. The system is also more expensive to set-up compared with microbial-based systems. Hence, to this day no other commercial scale plant cell culture is reported. Cell fusion to achieve novel gene combinations have been tried with plants. Plant cells have their cell wall removed with enzymes to produce protoplasts which are then fused in the presence of agglutinating agent. Although new hybrids can be derived from this technique, so far a commercially grown plant hybrid derived by protoplast fusion has yet to be reported.

Fermentation technology is a production system designed to maintain microbes in a state that enables them to produce microbial biomass or substances of economic value. The industrial scale technology is a complex engineering system that requires large-scale aseptic conditions and includes a bioreactor or fermentor and the necessary downstream processing equipment that isolates the substance of interest. These systems traditionally manufacture high volume, low value products for various industries or for the consuming public. In advanced countries, such systems are several decades-old established capital intensive industries that currently supply the world with amino acids, enzymes, antibiotics, citric acid, vaccines and the like. In developing countries like the Philippines, fermentation systems are traditionally home scale using centuries old practices and vessels lacking any control on the process. Within the past decade, industrial countries have fermentation systems redesigned to suit genetically modified yeast, bacteria or mammalian cells to produce novel, high value substances such as hormones or human proteins.

The continuum of techniques comprising biotechnology requires increasing levels of scientific knowledge, technical sophistication, financial support and time to achieve desired results¹⁰. The development of microbial-based technologies and plant tissue culture requires conventional knowledge and laboratory skills such as aseptic culture techniques usually taught in most college biology curricula. The research facilities are relatively easy to procure and inexpensive. Mammalian/plant cell culture and attendant technologies require special training in laboratory skills as well as in-depth knowledge of physiology. Mammalian cell culture facilities and maintenance cost are relatively more expensive. rDNA requires extensive knowledge of genes and their mode of action in biochemical terms as well as sophisticated facilities of storing and growing cells, manipulating DNA and quite expensive reagents. Compared with rDNA, DNA variation analysis requires less expensive standard equipment, less reagents and more manageable techniques. DNA synthesis and sequencing services are now available at reasonable cost

which obviates the need to set up one's own expensive facilities. Hence, active rDNA research is done mostly in developed countries.

The development of a novel biotechnology product requires compliance to biosafety regulations - a set of special regulatory requirements due to the biological nature of the product. That is, a living organism multiplies, can become wild and can contribute its genes into the genetic pool and, thus, must be handled differently compared with a machine or a chemical compound. Research and development in as well as biotechnology products developed through genetic engineering must comply with biosafety guidelines. Most countries including the Philippines have adopted biosafety guidelines to cover research with GMOs.

It must be noted that the requirements for the dissemination or commercialization of a technology is not dependent upon the manner of development but upon the final product itself. For example, the commercialization of a traditional fermentation process such as antibiotic production is usually capital intensive as it requires a large infrastructure that must be kept aseptic whereas a transgenic crop plant simply has to be grown to produce the seeds for dissemination. Clearly, the form of the final biotech product sets the limitations to its commercial applicability. In a developing country such as the Philippines, the capital available for the commercialization of technologies and the small size of the market often limits the extent by which the private sector picks up technologies for commercialization.

II. Trends and Issues

A. Market trends

Antibiotics, alcohols, organic acids, amino acids, vitamins, industrial enzymes are some traditional biotechnology products, we daily encounter and use. Antibiotics, amino acids like lysine and methionine, vitamins and enzymes are feed components imported into the country. Some of these could be products of GMOs¹¹. Organic fertilizers is gaining acceptance locally and its rapid adoption is considered one of the success stories for sustainable agriculture internationally. Fungal-based and bacterial-based biocontrol agents against crop diseases are commercially available in many countries. Other microbial-based biotechnologies for agriculture being developed include genetically engineered baculoviruses for insect control and genetically engineered soil inoculants to promote plant establishment and growth. Monoclonal antibodies are used in many diagnostic kits as they provide the specificity, rapidity and ease required. Recombinant vaccines are also commercially available. Tissue-cultured ornamental plants, white potato, and banana plants are available from commercial and government laboratories in many countries with banana as the most tissue cultured crop in the world. Automated fermentation systems for the mass production of artificial seeds (gel-

encapsulated plant somatic embryos developed through tissue culture) are being developed to reduce the cost of tissue-cultured planting stock.

Transgenic crops were first grown in commercial scale in China (virus protected tobacco) in 1992 followed in USA (delayed ripening tomato) in 1994¹². Transgenic crops are being designed to possess traits not only addressing various impediments to crop production but also to avoiding post harvest losses, to improving product quality and to endowing novel capabilities (Table 1). Other traits that are currently being incorporated into crop plants are tolerance to abiotic stress such as drought, increased photosynthetic ability and improved nutritional qualities. In animal production, better diagnostics and safer vaccines have been developed. Higher milk production using a recombinant hormone has been achieved for some years. Leaner meat for hogs is being targeted by some research programs.

Transgenic crops are adopted by farmers at a rate greater than any other technology in the history of agriculture¹³. Planted areas have rapidly increased from 1995-1998 (Fig.1) as well as in 1999.

Multiple benefits reported by growers for selected transgenic crops include more flexibility in terms of crop management (particularly important for herbicide tolerant crops), decreased dependency on conventional insecticides and herbicides, higher yields and cleaner and higher grade of grain/end product(no worms, no mycotoxin-producing fungi in Bt corn), increased yields for pest protected crops due to avoidance of damage usually inflicted by the pest, decreased use of pesticide which redounds not only to savings in pesticide cost but also to reduction in environmental pollutant, reduced risk for farm workers as well as consumers, zero or minimal disturbance in the population of beneficial species and soil conservation, hence, over-all an increased profitability for the farmers and less disruptive environmental impact (Table 2).

The value of these benefits for the US and Canadian farmers ranges from a net return per hectare of US\$19.76 for herbicide tolerant cotton to US\$175 for Bt cotton¹. In fact, this first wave of transgenic crops are considered farmer-friendly. Contrary to charges by critics that biotech companies are the benefits more from the technology, farmer/company benefit ratio has been calculated at 2:1 for Bt cotton in the USA in 1996.

The global value of the transgenic crop market was projected at US\$ 1.2-1.5 billion in 1998¹. The growth of this market was tremendous registering rates of 213% in 1996 and 185% in 1997. Provided that the adoption rate of transgenic crops continue to grow, this market is believed to attain an annual sales of US\$200 billion worldwide. Currently, large producers include the USA, Argentina, Canada and most likely China. Some plantings are also reported in Mexico, Spain, France and South Africa. Commercial planting of certain GM crops have been approved in the EU, Japan, Netherlands, New Zealand, Australia

and recently in Brazil. GM crops have been grown in several field trials in Malaysia, Thailand and Indonesia. Pending results of field trials, Indonesia is poised to deregulate commercial planting of GM crops. There is high acceptance of GM crop farming and foods in the USA, Canada and Australia as consumers believe that risks could outweigh benefits provided that appropriate regulatory framework in place.

B. Issues

1. Emerging trends in the development of agricultural applications of modern biotechnology.

Research and development in transgenic food crops are placing products in the market in four waves¹². The first wave targets farmers concerns in increasing productivity and profitability, promoting workers' safety and sustaining environmental integrity. The second wave targets processing and marketing concerns in reducing post-harvest losses and increased processing profitability. The third wave are transgenic food crops that provide nutrition as well serve as a prophylactic or therapeutic, a group of food called 'nutraceuticals' or 'functional foods' are being developed in various firms such as a banana that can deliver a vaccine when eaten. The fourth wave are transgenic crops that produce specialty chemicals for industry such as biodegradable "plastic" thereby using plants in place of microbial fermentation.

Techniques that enabled the transformation of mammals with rDNA and the high cost of animal cell-based fermentation systems led to research on the use of transgenic farm animals for the production of protein pharmaceuticals. Transgenic cows, sheep, goats are envisioned to secrete therapeutic human proteins like factor VIII for hemophilia, collagen II for arthritis, Pro542 for HIV, and others in the milk or urine with the objective of reducing the cost of producing these proteins¹⁴. Transgenic animals are themselves technical feats and a natural development of this feat is the multiplication of animals through cloning. Cloning produces organisms of similar genetic make-up and its widespread application in propagating transgenic farm animals will depend on whether cloning will be cheaper and more reliable than rDNA technology. Pharming or the production of human protein pharmaceuticals in transgenic farm animals is a specialized area of animal husbandry but will be limited and expected to be part of the pharmaceutical production chain. It should be noted, however that research results being more advanced in this area would find commercial applications in animal husbandry.

The first group of transgenic crop plants has acquired genes derived from nonfood organisms which made them unacceptable to some people. Controversy surrounding this first group of transgenic crops is putting pressure on the release of crops targeting consumer's concerns especially in markets where mistrust on transgenic food crops have started to take root such as in Europe. On the other hand, new uses for crop plants with their capacity to produce specialty chemicals will provide a management tool for a farmer. A farmer without changing his

practices and investments will be able to shift production from one market to another depending upon economic considerations.

A recently reported technology that has elicited much criticism is the TPS or Technology Protection System being developed by Monsanto from patents owned by the USDA and Pine & Delta Co. The TPS is a very imaginative use of genes and their controls that allows a seed producer to render seeds sterile when wanted. The system comprise of 3 genes and their control systems or promoters. Gene 1 codes for a protein that is toxic to the germination apparatus of the seed but leaves the rest of the seed normal. This gene makes the toxic protein only when placed adjacent to its promoter. However, between gene 1 and its promoter is a short DNA sequence block. Gene 2 codes for an enzyme that cuts the DNA block and allows the cells to produce the toxin. Gene 3 makes repressor proteins that prevent gene 2 from making the DNA cutting enzyme. The repressor proteins are inactivated by exposing the seeds to an antibiotic (tetracycline). The system is controlled by the seed producer who exposes the seeds to tetracycline. The plant produced by these seeds will then produce sterile seeds¹⁵.

The TPS is designed to protect the interest of the seed producer. It also prevents the transfer of a transgene to the wild, weedy relatives of the GMO. However, it has received much flak especially from the NGO, RAFI whose director dubbed TPS as the 'Terminator technology' because RAFI contends that pollen from the TPS containing plant could render non-GMO crops growing nearby also sterile. If the non-GMO crop is grown by a subsistence farmer, then the lifeline of the farmer is severed because he normally uses this year's seed for next year's planting. However, subsistence farmers usually grow crops in marginal uplands hence their plants would unlikely be fertilized by pollen coming from progressive farms which are usually located in more fertile areas. Researchers and the industry see much application of the genetic switch technology activating gene 3. Promoters can be designed to be controlled by chemicals commonly used by farmers who can now control the different traits of the crop depending upon the weather or market demands.

2. Genetic imperialism - the potential effect of the consolidation of life science companies ?

It is not the technology itself its who controls it and benefit from it that matters - Shand, RAFI, 1999.

The significant number, magnitude and extent of biotechnology-driven acquisitions, mergers and alliances of companies with complementing strengths in biotechnology R & D and global marketing resulted in an unprecedented consolidation in the industry¹. About 50 transactions have been recorded between 1995-98 and a selected 25 was valued at about US\$17 billion. These mergers effectively coupled the agricultural and pharmaceutical interests of these companies where biotechnology applications are enormous. The rapid rate at

which these transactions occurred were apparently driven by the desire to gain early market share of the fast emerging market of transgenic crops in both the developed as well as developing countries. Considering the huge volume involved, these transactions are expected to have far reaching policy and technology implications in developed as well as in developing countries. Mergers achieve cost reductions as a result of reducing administrative overheads, balancing of credit, debt and cashflow, streamlining of research functions, combining market forces to optimize coverage and efficiency of implementing a global market strategy, and finally lowering legal and regulatory costs associated with proprietary products that are becoming extremely expensive. Hence, there are now fewer companies with a larger market share in the transgenic crop market. These consolidations are expected to sustain agricultural biotechnology R & D which often need 10 years for product development. The strategy for deploying transgenic crops has become international in scope and scale coinciding with the implementation of world trade protocol. Thus, biotechnology is included in the agenda of the coming WTO negotiations. Various governments and the private sector has to work more closely in developing the regulatory framework for the adoption of transgenic crops.

These consolidations have elicited criticism from civil society contending that large companies will dominate the world seed supply making farmers too dependent on these companies. The term genetic imperialism has been coined to refer to this. The criticism has increased when the TPS was reported that upon activation seeds resulting from the crop are rendered sterile. Monsanto responded by proposing the conduct of an international review of the costs and benefits of the technology and related inventions and that subsequent actions taken only after such a review.

2. IPR issues

Most of the tools for genetic engineering are proprietary and in the hands of the private sector. The development of a GMO and the isolation and identification of desirable genes and of the various functional DNA sequences are intellectually creative endeavors and are subjects of intellectual property rights (IPR). Forms of traditional IPR systems used to protect biotech products include patents, plant breeder's rights, trade secrets and trademarks 16, 17. Proprietary materials or processes have restrictions put on their use. In addition to the GMOs, many proprietary materials and processes currently used in agricultural biotechnology research include selectable marker genes, reporter genes, promoters, genes of interest, genetic markers, transformation systems, genetically modified cells, research techniques, and diagnostic probes. Selectable markers are genes that allow the recipient cell to grow at the same time preventing non-recipients from growing hence enabling a researcher to obtain only the recipient cell. Promoters are DNA sequences that determine how much a gene will produce its protein product (gene expression). This is important especially in the Bt technology where the level of gene expression is essential for resistance management. Genes of

interest include genes that confer special properties to a plant such as the Bt gene which protects the plant from insect attack. Reporter genes indicate when a cell contains a foreign gene, the green protein gene renders the transgenic cell green, for example. Transformation systems are used to deliver a gene construct into a cell. The Dupont's biolistic system, for example, transform cells by bombarding them with gene-coated particles. Special genetically modified cells are commonly used to determine the activity of a cloned gene. Diagnostic probes are DNA or monoclonal antibodies that identify cells containing specific DNA sequence or substance. Use of these materials are either covered by material transfer agreement (MTA), technology use agreements, license or sublicense which impose certain obligations to the user.

2.1 Awareness of IPR among public research institutions and researchers

The increasing legal complexity involved in the supply of proprietary technologies may raise matters of contract law, intellectual property right, biodiversity and biosafety laws, technology transfer and competition law (where restrictive provisions are imposed). A research institution may not have clear knowledge regarding the type of IPR provided. This could lead to inadvertently infringing on legal conditions regarding the use of these inputs¹⁸. Lack of information leaves a researcher unclear as to his legal responsibilities, both to the owner of the technology and to other researchers. Hence, it is necessary for research centers to develop a system that ensures that the center fulfills its obligations in accordance with the MTA and informs staff accordingly.

Public institutions are often constrained by practice and mandate to apply patents on their new technologies. Defensive patenting in order to stake out a claim and ensure access is being considered to protect innovations from CGIAR institutions. Coordination in the access of certain research materials for efficiency is also considered to reduce problems of managing proprietary materials.

2.2 IPR and grower autonomy

In their effort to ensure protection, companies selling GM seeds enter into agreements with farmers for the latter to produce the crop using appropriate practices such as establishing a refugia in case of a Bt crop, refraining from using or selling the seed crop for next year's planting and allowing the company representatives to visit the field within the period and two years after the period of the agreement. Company representatives see to it that seeds from the crop are not used for planting not only within the farm but elsewhere. Although some farmers expressed resistance to this system, most farmers in North America do not oppose the system. The ethical issue raised is that the system promotes a culture of whistle-blowers, farmers telling on neighbors who use GM seeds without license. However, the new TPS technology can do away with the additional expense of monitoring technology users.

2.3 Current IPR laws disregard previous contributions to crop development

Many of the world's crop plants were developed through centuries of selection by farmers of developing countries. These plants were freely disseminated throughout the world. However, when these crop plants are modified by the addition of one or two genes and patented, they then become in essence private properties. Since the resources required to develop a product through modern biotechnology are beyond the means of developing countries, the IPR system favors rich countries. Critics argue against the patenting of GMOs primarily because of the failure of the IPR system to recognize the contribution of farmers of long ago. Also, civil society is actively promoting awareness of biodiversity in developing countries to stem the free flow of genetic materials to the developed countries as embodied in the Convention on Biological Diversity. Thus, there is need to design an international system of intellectual property that balances the private-property interests of the rich countries with the public good needs of the poor¹⁹.

A novel mode of sharing the benefits of commercialization has been developed by the University of California, Davis in connection with the patent of a wild rice gene, Xa21, which confers resistance to many crop diseases caused by the bacterium, *Xanthomonas*. Licensing fees are placed in a trust fund, the interest of which will be used by the University to provide scholarship to support graduate study at the University by a student from the source country of the species where the gene was derived. In this case, it is Malta.

3. Biosafety issues

Of the various genetically modified organisms, it is the genetically modified food plants that has raised controversy and may even result in a trade dispute between the US and its trading partners. Major issues raised against the widespread adoption and use of GM crops concern possible health risks and potential for ecological change or damage. Genetically modified crops often contains a gene or DNA sequence from a non-food organism. This foreign gene produces a foreign protein that could be toxic or allergenic to humans. A GM crop may contain a novel toxic/allergenic substance produced by a mutant gene resulting from the random introduction of the foreign gene in the plant genome. A GM plant may run wild and becomes a weed in itself. A GM plant may transfer its foreign gene to weed species conferring advantage to the weed and make it more difficult to eradicate (gene flow = genetic pollution). A GM plant containing an antibiotic resistance gene may transfer this gene to a microbe in the wild eventually into human pathogens. Bt crops may promote the selection of insects resistant to Bt which can no longer be controlled by insecticides. Bt crops may adversely affect non-target beneficial organisms. Regulatory bodies are inadequate to ensure that GM crops and their derivatives are safe for human consumption and to the

environment. The public are made into experimental guinea pigs for GMOs. The public are purposely kept ignorant about GMOs.

3.1 Possible allergenicity and toxicity of foods derived from GMOs

There is agreement among scientists that genetic engineering could produce a toxic or allergenic protein. Since virtually all food allergens are proteins, all food derived from genetically modified organisms must be tested for allergenicity. Even early in the development of a GM food plant, the production of a toxic or allergenic component due to genetic engineering is tested. The finding that the seed protein being transferred from the Brazilian nut to improve the protein profile of the recipient food plant is highly allergenic caused the termination of the research.. Countries permitting the sale and use of GMOs require these GM products to have undergone toxicity and allergenicity tests.

The random insertion of a gene construct in the plant genome may disrupt or modify the expression of an existing gene. Possibly, the gene construct may be placed adjacent to a sequence that can modify its expression. It may activate pathways or cause the fusion of genes thereby producing new toxins or allergens⁷. It should be noted that in traditional plant breeding the above-mentioned events are also possible. Furthermore, hybrids between crop plant and their wild relatives transfer blocks of genes that may also produce toxins and allergens. However, unlike transgenic food plants, hybrids of wide crosses are not subjected to the rigorous toxicity and allergenicity testing of GM crops. However, it should be noted that allergenicity is not unique to GM food plants. Common food allergens include milk, egg, fish, chicken, crustacea, and peanuts. On the other hand, it has been shown that genetic engineering can be used to remove toxicity, allergenicity or any other unwanted trait of an organism²⁰.

Presently, researchers are trying to do away with genes from non-food organisms. Genes are isolated from varieties or relatives of a crop or other food organisms. The bacterial resistance gene transferred to elite rice varieties, for example was isolated from a wild relative of rice²¹.

3.2 Possible creation of superweeds

The transfer of herbicide tolerance to crop plants has raised concern on the possibility of producing super weeds. The scientific community has yet to obtain proof that a GM crop can become weedy. No experiment has been able to show this possibility²². Probably because crop plants have been bred for thousand of years to remove their weedy tendencies and that weediness is determined by many genes. On the other hand, there is the possibility of a GM plant transferring its gene construct to a wild, weedy relative. In most groups of plants, related species regularly form hybrids and such exchanged genes tend to improve on each population²³. Wild rice are important weeds in direct seeded rice. It has been shown that wild rice and cultivated rice naturally exchange genes. Consistent gene

flow has been shown between the cultivated sugar beet and its weedy relatives²⁴. The transfer of a stress tolerant gene such as insect resistance or drought tolerance from a GM crop to its weed relative could make the weed more weedy. The weed may eventually become dominant changing the composition and structure of the plant community and the fauna that thrives on it. Hence, a major concern is the ecological havoc a GMO could create in the center of the crop's origin where most of its wild relatives exist.

The TPS system should be able to address gene flow problem.

3.3 Creation of new human, crop plant and animal pathogens

The transfer of a gene construct from one cell to another is very inefficient. Sometimes only 1 cell out of 10,000 would be transformed. Selecting for the transformed cell would have been costly and tedious without the technique of using selectable markers. Selectable markers are genes included in the gene construct that confer to the transformed cell an ability to grow in a special (selective) medium that kills cells without the marker. A selectable marker commonly used in plant transformation is the kanamycin resistance gene which confers resistance to the antibiotic kanamycin. Concern has been expressed on the possibility that during the disintegration of the GM crop in the field, some microbe might pick up the kanamycin resistance gene. Microbes are known to freely exchange genes in nature. Hence, the kanamycin resistance may eventually find its way into human, animal or wildlife pathogens. The planting of a GM crop containing an antibiotic resistance gene has been banned in Switzerland²⁵. Research testing for the possible transfer of kanamycin resistance during the degradation of transgenic plants in the soil did not provide any proof of the possibility²⁶. Response to this concern is the use of herbicide resistance as a selectable marker. If the herbicide is not applied in the field, there is no selection for herbicide resistance. Hence, no selective advantage is conferred by the herbicide resistance to the weed species into which it has been transferred.

There are reports on the creation of new, more potent viral pathogen between the coat protein gene and a wild infecting virus within transgenic plants^{27, 28}. On the other hand, this has not been observed certain viruses. This necessitates that tests for this phenomenon should always be made in the local area of introduction of a GMO.

A gene construct containing an antibiotic resistance gene may remain intact as the feed processes through the animal. It could be picked up by a gut bacterium. Since microbes freely exchange their genetic materials, this antibiotic resistance gene may find its way into human pathogens. Coupled with the extensive use of antibiotics in animal feeds, the development of antibiotic resistant bacteria could happen at very high rates. So far, experiments to test this possibility has not yet been reported.

3.4 Resistance management for insect resistant GM crops

Insects are known to overcome insecticides by developing resistance over time. The continuous exposure of the target insect to Bt crops could eventually develop Bt resistant insects. Organic farmers are very concerned because the microbial insecticide, *B. thuringiensis* is the only acceptable insecticide for organic farming that is highly effective for common insect pests. Development of resistance strains would leave them without an effective insecticide. Companies that own Bt crops have been required to develop insect resistance management (IRM) programs that farmer licensees must follow to prevent the rapid development of resistance in insects. This consists of planting a refugia in combination with the high expression of the toxin gene. Refugia refers to the population of nonBt plants planted alongside the Bt. The idea is to maintain a plant population where the insect may freely multiply. Without the Bt present, most of the insects that thrive on the nonBt crop will be sensitive to Bt. Whereas, insects that survive in the Bt crop will be resistant to Bt. Since there will be more Bt-sensitive insects, these will interbreed with the Bt resistant insects, producing hybrids that are susceptible to Bt. This idea is based on the assumption that insect resistance to Bt is recessive. However, a recent report indicated that insect resistance to Bt appears to be co-dominant rendering the refugia strategy ineffective. Hence, there is a need to develop a more effective strategy. Strategies being adopted include pyramiding or the incorporating several insect toxin genes in the gene construct. In transferring the Bt technology, it is necessary to determine the type of resistance to Bt that local insects can develop before a resistance management program can be adopted.

3.5 Possible deleterious effect of pesticide crops on nontarget, beneficial organisms

The farm is an ecosystem that supports a wide variety of life comprising of animals, various plants, and microorganisms. Critics of biotechnology have been contending that GM crops could disrupt the fragile ecosystem of farmlands. Genetically modified crops containing genes such as an insect toxin gene is considered a pesticide crop and must be assessed for properties similar to a chemical pesticide. Regulations require that the effect of a pesticide crop on nontarget, friendly organisms especially natural enemies of the various pest that infest the crop used in integrated pest management (IPM) is tested. Considering that there are probably hundreds of species that may come in contact with the crop during its lifespan, only representative organisms are tested. This approach has been seriously undermined with results of studies reported by a research group from Cornell University and another group in Iowa State University that monarch butterflies in the laboratory as well as in the field were killed or stunted in their growth after ingesting a Bt corn pollen. The monarch butterfly is regarded as an indicator of environmental pollution. Hence, the study has raised concern among

environmentalists about the possible deleterious effects of the Bt crops on the ecosystem.

However, others argue that agriculture is by its nature disruptive of the ecosystem. A rational approach to the debate is weigh possible risks versus the benefits of GMOs and similarly those of current agricultural practices.

3.6 Biosafety and the capability of regulatory bodies for biotechnology products

Specific decisions about permit applications for the use of GMOs in the environment, depend world-wide on the scientific assessment of what would constitute an adequate and sufficient biosafety test for that purpose. A biosafety test is a list of specified research questions that need to be posed and answered²⁸. These questions relate to human health and environmental risks. The novelty of GMOs has posed serious questions as to whether traditional tests for toxicity and allergenicity tests are sufficiently vigorous to detect possible toxic and allergenic substances in them. There are proposals to regulate GMOs containing genes from nonfood sources similar to nonfood substances added to foods like dyes. This would increase the cost of risk assessments and negate whatever cost advantages gained from developing the crop. There are doubts whether such added cost is at all warranted since only a single property of the plant was changed. Another issue is whether short term tests are predictive of long term environmental effects. Apparently, scientific experts do not agree on a satisfactory design of such biosafety tests. There is therefore doubt as to whether regulations based on these tests are sufficient. However, better testing methods are currently being developed. Also, an international group of experts has been proposed to convene to develop protocols for toxicity and allergenicity testing of GM-foods^{30, 31}.

3.7 The harmonization of biosafety guidelines

Most countries developing and/or commercializing biotechnology products have established a regulatory framework covering research, development and commercialization. However, there are differences on the methods and extent of tests. Also, the above discussions clearly indicate the need for an internationally accepted guideline on risk assessment of biotechnology process and products to accelerate the transfer of technology where these are needed most and to prevent the creation of trade barriers involving the movement of GMOs. Recognition of risks assessment results from one country by another would save resources on both the owners and users of the technology. This would save resources on both the owners and users of the technology. Several international efforts have been initiated to harmonize biosafety protocols. A call for the harmonization of biosafety guidelines in South America has been sounded especially so because these countries share common borders and ecosystems and that some are already growing in GMOs in commercial scale³¹. The Philippines is involved in two international initiatives currently underway to harmonize regulatory requirements

for transgenic crops. A Biosafety Protocol is being prepared in conjunction with the Convention on Biological Diversity. The ASEAN countries are also formulating similar guidelines for the region. The need for science-based regulatory procedures is strongly advocated to provide a stable atmosphere whereby research and development may flourish.

4. Increasing awareness and consumer perceptions

Public opinion regardless of how well experiments are designed is not based on scientific considerations²². Public attitudes are shaped more by history, culture and sociological factors than they are by scientific considerations. Based on the experience of Monsanto in the US market³³ public acceptance can be fostered by the presence of an appropriate, knowledgeable, science-based regulatory oversight that provides timely judgment and the flexibility to learn from experience, by a public awareness campaign among food supply providers and health professionals, policy makers, media and the consuming public to gain basic understanding of basic biotechnology products, their benefits, safety, and the regulatory oversight in place and be an understanding of consumer behavior to ensure that consumers will accept plant biotechnology products and will demonstrate their acceptance by continuing to purchase food they have in the past. The adoption of clear regulatory policy about GMOs has promoted acceptance. The concept of substantial equivalence is critical to the commercialization of many products of biotechnology. Substantial equivalence in this regulatory context means that there is no meaningful change in the nutritional value or composition of the improved crop variety. Scientifically sound principles in labeling requirement based on the concept of substantial equivalence. The US Food and Drug Administration does not require labeling of products that are substantially equivalent to their traditional counterparts. It should be noted that Monsanto's public relation strategy has failed in Europe where it is now regarded as a monster company ramming dangerous GM foods into people's throat for profit.

This year, the movement against biotechnology has gained momentum especially in Europe. The so-called Puzstai affair in the UK involved the premature public announcement of the results of a study claimed to show the toxic effect of GM potato on rats. This announcement was blown out of proportion by the media and caused the public suspicious of GMOs. Analysts claim that apparent loss in public confidence of regulatory and scientific bodies following the mad cow debacle and media frenzy resulted in the rejection of GM food crops by consumers. The effect was disastrous for the biotechnology industry as it caused large supermarket chains to withdraw from their shelves food preparations containing GM-derived ingredients. Field trials were also destroyed forcing one biotech company to stop them. Prince Charles expressed concerns that there is not enough information about GMOs, cautions about its adoption and the tampering of Nature. He further contends that the technology appears to benefit only the owners of the technology and farmers of industrial scale farms. Certain GM crops are banned in Austria and Luxembourg. Austria banned the cultivation of Bt corn-MON810 following the

publication of a study indicating the deleterious effect of Bt corn pollen on monarch butterfly larvae reported by a Cornell University research group. The same study prompted the European Commission to freeze further licensing GM crops for commercial planting. The Supreme Court of India banned the testing of genetically modified crop plants. Citing potential health risks, the British Medical Association called for an open-ended moratorium on the commercial planting of GM food crops. A fast food chain, Burger King, in Portugal has banned the use of ingredients derived from GM crops. A bill has been filed in the Philippine Senate proposing a ban against the entry of GMOs.

To address consumer concerns, negative food labeling to indicate that a product does not contain any GM-derived ingredient has been adopted by European countries to allow consumers to choose. The rapid development of consumer-friendly such as food plants containing cholesterol lessening substances is also proposed. Others believe the issue like that of other new technologies such as IVF shall blow over with time.

5. Ethical issues

Civil societies and religious organization have questioned the right of individuals and companies to patent life forms. Some contend that since life came from a more Powerful Being, man has no right to assign life forms to himself. Others contend that patenting life forms is similar to the industrialization or commercialization of life, that is life becomes a tradable commodity. Although it can also be said that agriculture and aquaculture are the commercialization of life forms. There is also a perception that traditional farming will be marginalized, although presently, traditional farming is already marginalized. The use of human, animal or microbial genes in crop plant is not acceptable to some people regarding this as a violation of the laws of nature. One opinion forwarded is that the ingestion of a plant transformed with a human gene is similar to the act of cannibalism. But if this food crop is sweet potato protein-enriched with the transfer of human milk protein genes, would that be cannibalism, too?

6. Biotechnology transfer to developing countries

Biotechnology is recognized as a major tool to improve agricultural productivity to feed a hungry world, a tool to ensure food security for all. However, the challenge remains in the transfer of this technology to the developing countries where the majority of the poor resides and where agricultural production is lowest. There are 43 international programs that aim to facilitate access of developing countries to modern agricultural biotechnology³⁴. These initiatives comprise of research programs, advisory programs, bilateral and multilateral donor agencies and regional and international biotechnology networks. Most of these programs offer opportunities for the application of biotechnology to suit a country's specific need. Furthermore, collaborating with these initiatives provide developing country scientists and policy makers with opportunities to benefit from the knowledge and

expertise gained from specific technologies and their applications, biosafety and technology transfer issues, and broader policy and planning implications in national research systems. However, to be effective, developing countries must also provide the necessary environment. International programs tend to concentrate on countries with relatively high levels of scientific and technological capability such as the Philippines. The presence of an effective biosafety system is a condition for donor-funded collaborative programs. Furthermore, to promote biotechnology-led agricultural development, policies are needed to stimulate private-public sector collaboration, transfer of public innovations for commercial production and stimulate investments in agricultural development.

A major issue is technology access by the sector that needs biotechnology interventions the most, the small resource-poor farmer. Following experience with hybrid seeds which are not affordable by small farmers, it is imperative that systems making biotech tools available to small farmers be devised. An improved seed is a very effective and powerful means of delivering novel technologies to the farmer. It is the core and the most familiar input to production. Farmers whether big or small appreciate the value of an improved seed. Unlike the seeds of the Green Revolution that requires a package of technologies, e.g. fertilizers, pesticides, to fully deliver its benefits, genetically modified seeds contain within themselves the new technologies and thus require less or zero additional inputs. This is the major advantage of transgenic crops over traditional biotechnologies currently being developed in the country such as biological control agents that represent an additional cost to the farmer. It is thus imperative for a developing country like the Philippines to develop the appropriate strategy to enable farmers access to genetically modified seeds.

The International Service for the Acquisition of Agri-Biotech Applications (ISAAA) has been purposely set to facilitate the transfer of biotechnology to developing countries to include capability building as well as the acquisition of specific genes and related technologies at equitable terms. ISAAA has been successful in arranging for the donation of genes from private companies to countries where the final product benefits the subsistence farmer and does not compete with the intended market of the company³⁵. Several countries have already benefited from the services of ISAAA. Malaysia, Thailand, Mexico, Brazil, Costa Rica developed local capability in genetic engineering and acquired genes through agreements facilitated by ISAAA. CGIAR centers also access the services of ISAAA for the acquisition of biotechnology tools. The ISAAA Asia-Pacific regional office is located at IRRI, Philippines and negotiations are underway for the transfer of specific technologies through PCARRD.

III. Philippine agricultural biotechnology research and development

The establishment of the National Institutes of Biotechnology and Applied Microbiology (BIOTECH now National Institutes of Molecular Biology and Biotechnology) at the University of the Philippines at Los Banos (UPLB) in 1979

marked the formal start of a biotechnology R & D program in the Philippines supported by a grant from former President Ferdinand Marcos. Its mandate is to develop cost-effective technologies for the production of goods and services that are cheaper alternatives to conventional products but which are safe to the environment and makes use of locally available materials. Such mandate directs BIOTECH to be a generator of technology. With former and existing faculty members of the UPLB College of Agriculture as part time research leaders, the initial R & D program leaned towards the development of microbial-based technologies of agricultural applications such as food and feeds applications, nitrogen fixation and bio-insecticides. Research on plant tissue culture was implemented mainly by the UPLB CAS Institute of Biological Sciences, Botany Laboratory on macapuno embryo rescue, the UPLBCA Dept. of Horticulture on orchids and the Institute of Plant Breeding, UPLB on banana and white potato. VISCA Root Crops Research and Development Center also had at about the same time, research on tissue culture and protein enrichment of rootcrops. UPNSRI had a project on protein enrichment of Cavendish banana waste.

Biotechnology was identified in the late 80's by the Department of Science and Technology as one of the leading edges of science for development. And between 1990-1995, a biotechnology R & D program for agriculture is prepared as a component of the sectoral plan prepared by the Philippine Council for Advanced Sciences and Technology Research and Development (PCASTRD) of the DOST. The Council defines the scope of research projects for funding by the Council and selects priority projects. For 1995-2000, the Council listed the development of 3 groups of products, 7 groups of processes and establishment of database in the agriculture, forestry and environment sector and one selected or so-called vanguard project. The vanguard project is selected based on its social or economic impact: if service-oriented, it must be a response to a need, its target population must be wide, has a global market, and may incur savings for the government. If profit-oriented, the product must be better than the one existing in the market, must be patentable, has a ready market or its market can be developed and its development cost-effective (considering developmental time vis--vis patentable time). It must be timely. The project must be doable, that is, the local infrastructure is adequate, local resources e.g. expertise sufficient and must have technical and scientific merit. It must be environmental friendly. All projects except the vanguard project for 1995 were research using microbial -systems. The vanguard project was genome mapping of mango and coconut with molecular markers. However, there is no integrated agricultural R & D program and when taken over-all, the directions were set more by the ability of senior scientists to access funding from various agencies.

Between 1977-96, about 75% of agricultural biotechnology research projects were on the production of biocontrol agents, soil amendments, food and beverages and development of tissue culture methods (Table 3), about 15 % on other applications of microbial systems (feed additives, enzymes/cells for agriprocessing, farm waste management, vaccines) and about 10% in the applications of modern techniques

such as monoclonal antibodies, molecular markers and rDNA. Biocontrol agents are introduced natural enemies of a pest and are components of integrated pest management (IPM) strategy. The biocontrol agents being studied include mainly bacteria (*Bacillus thuringiensis* against diamondback moth), fungi (*Paecilomyces lilacinus* against nematodes, *Metarrhizium anisopliae* against several insect pests, *Trichoderma* spp against root rot pathogens) and baculovirus against coconut insect pests which are identified and produced using traditional microbial techniques. Soil amendments include organic fertilizers and inoculants that enable the plant to use atmospheric nitrogen, the nitrogen fixers or to increase a plant's capacity to use nutrients efficiently, the mycorrhizae. Soil amendments cause significant reduction of fertilizer requirements, better survival and higher yields.

Bio-organic fertilizers are compost supplemented with nitrogen fixers or mycorrhizae. Composting studies delved on hastening the process using local isolates of *Trichoderma* spp. Inoculants studied are *Rhizobium/Bradyrhizobium* for legumes, *Azospirillum* for rice and corn and mycorrhizae for peanut, cassava, sweet potato, mungbean and sugarcane. Production of these agents use conventional fermentation processes.

Microbially-derived foods and beverages studies included nata de coco, mushrooms, food flavorings like soy sauce-equivalents, coconut based yoghurt, the traditional rice wine of the Mountain provinces and the like. Other microbial system applications include studies on producing feed components e.g. protein enrichment of root crops and farm wastes, lysine and methionine, feed enzyme (phytase), use of mushroom compost as feed component, animal antibiotics (tylosin) and probiotics. Application of enzymes/ cells delved in reducing toxicity of aflatoxin and sweet potato weevil metabolites, in food processing such fruit juice clarification, in improving digestibility of copra meal, in farm waste management and in producing vaccines against hemorrhagic septicemia in cattle and carabao. ELISA-based diagnostic kits for *Pasteurella multocida* and *P. hemolytica* were developed based on antigens from microbial cells and cell derivatives. Similarly, production of these agents use conventional fermentation processes.

Tissue culture methods were developed for micropropagation, as aid to plant breeding and for metabolite production by cell cultures. Micropropagation techniques using meristem and shoots were developed for native cultivars of bananas, potato, ubi, shallots, garlic, cassava, sweet potato, abaca, papaya, strawberry, durian, mangosteen, passion fruit, rambutan, pummelo, avocado, Derris, Mussaenda, orchids, and other ornamental crops and using somatic embryogenesis for banana, calamansi, papaya, longan, lychee, avocado and coconut. In vitro selection methods were developed for tomato, rice, corn, calamansi, kalanchoe, banana, and sugarcane. Haploid cell regeneration were developed for coconut and rice and embryo rescue techniques for macapuno (mutant coconut) and wide crosses of papaya. Cell regeneration techniques, a

method essential in plant genetic engineering were being developed for coconut, rice, mungbean, mothbean, orchids, tobacco, ramie and coconut.

Monoclonal antibody techniques were applied for the production of vaccine against hemorrhagic septicemia caused by *Pasteurella multocida* and diagnostics for the red toxin in mussels and for plant pathogens. DNA markers were identified for banana, mango, coconut, mungbean, abaca, corn, rice and carabao. DNA markers are used to assess genetic variation in rice, mango, and coconut, characterize rice, mango, coconut cultivars, zooxanthellae of the giant clam and tuna, diagnose the tungro virus, detect food and water contaminants, analyze the coconut genome, determine the origin of local rice cultivars and aid in selection and mapping of resistance genes in rice, mungbean and potato.

Apparently, the direction of agricultural biotechnology research is determined by how the research system defined the scope of biotechnology which is very broad from traditional microbial systems to rDNA, the prevailing economic policies and the available resources. The nature of biotechnology research reflects the national policy directions of the early '80 when the emphasis was to develop technologies for import substitution. Hence, projects on biocontrol and soil inoculants are justified on the amount of pesticide and chemical fertilizer that could be saved from their use. Feed components such as protein enriched root crops or banana peelings are proposed to substitute for imported soybean and fish meal. Other microbially-derived feed additives like lysine and tylosin are to be locally produced rather than imported. Also, BIOTECH was established when biotechnology was a newly emerging industry. At the time, the trend was the development of fermentation systems for genetically modified microorganisms. Hence, there was an emphasis on fermentation systems and the development of technologies that could be commercialized.

Furthermore, the nature of biotechnology research reflects the expertise, level of funding, facilities and infrastructure support available during this period. Fifty-three (53) of the 59 senior scientists involved in these projects have been trained in the agricultural sciences (Table 4). It also reflects the very limited funding available. Research using microbial and plant tissue culture techniques is several times cheaper compared with the reagents needed for DNA manipulations. In fact, until 1997, many projects at BIOTECH are being funded at the rate of P12,000/yr, just enough to buy one or two of the multitude of reagents needed for DNA manipulations. Also, the infrastructure support is very poor. Frequent electrical outages have killed mammalian cell cultures and DNA libraries. Essential reagents took months to procure or lost their efficacy at the Customs. Prior to 1995, only the NSRI had the facilities to undertake rDNA work with nonpathogenic organisms. On the whole, however, the scientific community is very responsive to policy directions despite the limited funding. During this period, BIOTECH researchers developed 14 technologies for commercialization (Table 5), 9 technologies were awarded patents and 7 more have patents pending (Table 6).

Our current human and physical resources for modern agricultural biotechnology is modest but could be managed to produce significant work. There are 50 Ph. D holders trained in DNA manipulations and an additional 15 in biochemical and serological methods connected with 13 institutions located in various parts of the country(Table 7). However, only 7 of these institutions are equipped for DNA work with 3 equipped with a microprojectile bombardment equipment for plant cell transformation. Only the Philippine Carabao Center is equipped for in vitro fertilization studies and MBB UPDiliman equipped for animal cell culture studies.

The Proposed National Biotechnology Research and Development Program for Agriculture, Forestry and Environment (PCARRD)

In 1996, PCARRD initiated the formulation of a national biotechnology program for agriculture, forestry and environment. The program was developed along seven criteria : STAND priorities, application of modern biotechnology (70%), accommodation of domestic concerns and basic sciences (30%), market rather than supply orientation, environmental concerns, availability of human resource and infrastructure and provisions for social marketing and technology transfer. The general objective is the application of biotechnology on the improvement of present yields of selected crops, trees and livestock, the improvement of the quality of products e.g. delayed ripening of mango and papaya, the bioremediation of the environment and the development of policies, social marketing and technology transfer. To fast track results, strategies include the direct transfer of available foreign technology, procurement of gene constructs through MTAs, development of own technologies and gene constructs when feasible and adoption of foreign technologies when feasible. The comprehensive agricultural biotechnology program for agriculture, forestry and environment approved in 1998 has five components, crop biotechnology, livestock biotechnology, forest biotechnology, .microbial biotechnology and policy and social marketing and a proposed budget of P2.310 billion from the DOST and PCARRD in ten years. The crop biotechnology component gives priority to 7 crop commodities, coconut, fruits: mango, banana, papaya, durian and pili, ornamentals, rice, corn, cotton, abaca; livestock biotechnology to cattle, carabao, goat, sheep, swine and poultry; microbial biotechnology to biofertilizer, biocides and bioremediation. Program allocation of the proposed budget is 32.2% crop biotechnology, 23.4% livestock biotechnology, 21.2% microbial biotechnology, 19% forestry biotechnology and 4.2 % policy/social marketing component. Since the microbial biotechnology program addresses mainly crop production, the total proposed budget for crops is about 53.4%. However, funding for this program is not yet assured mainly due to the change in administration. Only P5 million of the P60 million needed for the first year of implementation has been allocated which accordingly will all be expended on the crop biotechnology program. In the prioritization of projects, heavy emphasis was placed on the application of modern biotechnology in line with the new policy of the DOST on the promotion of advanced sciences. In crop biotechnology, the probability of success, availability of external funding and

collaboration with foreign research groups were also considered. Still the program is very broad and all encompassing.

Recent information indicates that only five projects will soon be implemented: development of papaya with delayed ripening, papaya resistant to papaya ringspot virus (PRSV), applications of molecular markers in breeding corn and genetic engineering of coconut with increased medium chain fatty acids and of banana resistant to the banana bunchy top virus (BBTV). The papaya projects are apparently selected because IPB has already started the work with foreign collaborators and the probability of success is high. An IPB staff has been sent to Australia to train in the antisense technology and has already brought home transformed cultures. These types of transgenic papaya have already been reported by the same group of collaborators IPB is working with³⁶. The corn project was revised from the previous objective of developing Bt corn. Apparently, negotiations by CYMMT for the acquisition for the Bt gene is not progressing. Furthermore, three private companies in the Philippines have signified intention of introducing Bt corn provided that biosafety guidelines for field tests are clearer. Monsanto has already tested in the IRRI confined facilities Bt corn against the very destructive Asiatic corn borer. Its application for field tests is still being debated at the NCBP. The molecular marker technology although not as straight forward as directly transferring genes could be less expensive since it will do away with compliance to biosafety guidelines.

Developing a transgenic coconut with increased medium chain fatty acids would be a long shot. Although the technology for changing fatty acid patterns have been successful with rape seed, there are still too many unknowns with coconut fatty acid biochemistry. Regeneration of cell cultures to somatic embryos have already been reported at PCA Albay and elsewhere 37,38. Gene transfer experiments are yet to be reported. Early and rapid detection procedures for gene expression in coconut endosperm have to be developed. An early attempt at developing molecular tools at NSRI by the author such as constructing a cDNA library of coconut endosperm genes failed due to frequent electric outages that killed the library.

The development of a banana bunchy top virus resistant banana shall be assisted by INIBAP. Arrangements have already been made for the training of one IPB researcher in banana transformation. A transgenic BBTB banana is already available for testing for INIBAP member countries such as the Philippines.

Similar to previous experiences, the program is limited by the existing manpower resources in modern biotechnology techniques. Hence, positions for post-doctorals have been provided, however, with the devaluation of the peso, it is doubtful whether the program will be able to attract relatively well-trained individuals. Training for personnel is negotiated by individual institutions rather than being coordinated and assisted by a single agency. Yet there is a need to fast track a manpower development program in modern biotechnology with conditions that

will attract trained individuals to stay. There appears to be a high demand for well-trained individuals abroad hence conditions in the country should be able to compete. Monetary considerations is out of the question but programs that keep people in and within the international scientific mainstream might help.

Assistance in developing local capability can be accessed from international biotechnology initiatives. Of the 43 international biotechnology initiatives³⁴, about 20 can be tapped by the Philippines to serve as important source of support and collaboration for biotechnology planning and implementation. In addition are programs with the government of Japan such as the Japan Society for the Promotion of Science (JSPS), Japan International Research Center for Agricultural Sciences (JIRCAS), with the German government and the International Foundation for Science of Sweden which have identified biotechnology applications as a priority.

The commercialization of locally developed technologies

Of the various locally developed biotechnologies, micropropagation of banana, orchids, abaca and white potato have developed into routine procedures in commercial and government service laboratories. This reflects the success of training courses in banana and orchid tissue cultures mainly at various units of UPLB, BPI- Davao Station and Natural Sciences Research Institute, UP Diliman. On the other hand, following the Western model, BIOTECH has inked agreements with individual entrepreneurs in the commercialization of its technologies. Despite aggressive efforts at BIOTECH to find entrepreneur-partners for commercialization, only 3 of the 14 'commercializable' technologies have been assigned to private groups. These have yet to develop into sustainable commercial operations. As of today, only one is paying royalty to BIOTECH (De la Cruz, R Pers comm).

Presley³⁹ cited common characteristics of start-up companies and research groups in developing countries that make commercialization difficult. These ventures are normally centered around a few bright scholars with fresh ideas. They lack adequate funding. The group have little experience in scaling-up and commercialization of the product. They have difficulties in defending their patents. Home markets are too small to make production economical. Truly, these situations apply here. Commercial agreements between UPLB and a private entity have been forged to cover only a single product hinging the success of the company to this particular product. Since the product is considered unfamiliar, the private entity often lacks marketing experience of the product. A start-up company assigned to commercialize a particular technology has gone on to develop its own equivalent product. Most of these technologies being traditional fermentation technologies require considerable capitalization. Also, the high cost of money, unstable supply and high cost of electricity and poor communications infrastructure and a shaky marketing strategy would make commercialization difficult to sustain.

One reason for the non-sustainability of commercial operations are technical problems often associated with a new technology. Microbial-based technologies offered by BIOTECH for commercialization often needs further development⁴⁰. The stages in the development of a fermentation technology includes first a laboratory scale test, followed by a bench scale test, a pilot plant scale and finally the commercial scale. Most of the technologies for commercialization has yet to go through pilot scale tests, since this portion is hoped to be partly funded by the private sector. However, the private sector has misgivings on huge investments to research. For technologies developed by public agencies, the private sector sometimes has to compete with public agencies which sometimes provide the product free. There is a tendency among researchers to try to develop a complete technology by themselves refraining to involve individuals with the appropriate expertise. This stems from the incentive system that gives recognition and award to individuals rather than to research groups. For example, in the case of a microbial-based technology, the efficacy of the organism for a particular process is discovered by a microbiologist. However, to produce the organism in commercial quantities, a fermentation engineer must conduct the appropriate studies. Unfortunately, this seldom happens. Furthermore, no mechanism is in place to ensure that research results are submitted much less reviewed by a peer group. Most of the information are in the form of abstracts of research results found in programs/proceedings of scientific meetings. Only about one-tenth of results of completed research projects are published in peer-reviewed journals. This lack of an automatic review process may also explain the low rate of adoption of technologies. For example, a review of results of studies on the effect of organic fertilizer or compost to corn production indicates that organic/compost fertilization may or may not increase yields. Hence, the current recommendation of organic fertilization in the Masaganang Maisan Program does not appear to have a well grounded scientific basis.

Furthermore, upon transfer of the technology, no research fund is granted for further improvements on the technology based on feedback from the user. In general, the flow of information from research to extension to technology user is one way. Only the actual training of users is funded. It is often assumed that the technology needs no further improvement by the researcher. Nor, are users generally taught on how they can improve the technology by themselves or perhaps, identify problems of technical failure. Farmers are often made to feel responsible when a technology fails to deliver the expected improvements. Yet, what is observed are often modifications of recommended processes. In Davao, a commercial organic fertilizer producer refrains from composting crop residues because of the possibility of transmitting diseases and uses the Trichoderma technology developed for crop residues to rapidly compost cattle dung. In Manila, another organic fertilizer producer composts chicken dung for similar reasons aside from the difficulty of composting variable materials. Also, the quality of

organic fertilizer is best with cow dung and chicken dung is better than crop residues.

Another aspect that is not considered is how competitive locally developed technologies are to imported ones. Often, local researchers appeal to the patriotic sense of entrepreneurs for the adoption of their technology. A novel, patentable effective technology with a tremendous commercial potential does not often lack buyers in the international market. The fermentation technologies for tylosin or lysine are traditional biotechnologies similar to those commercially operated elsewhere. Given the several decades experience of these foreign companies with the technology, the limited experience and studies conducted by the local scientists, it is too much to hope that these locally developed technologies can possibly compete. Nevertheless, only one technology has been taken up by a foreign company on the basis that the core technology, the organism, is new. However, even this product has not been commercially sustained. Most likely, the lack of data on its health and environmental safety has deterred its adoption. Furthermore, the production of pure microorganisms and their products is sensitive to economies of scale that one must go beyond the Philippine market to make profit.

There is a general perception that a local isolate is safe. However, when a living organism is introduced into an environment in quantities beyond the normal, there are possible risks. It is then capable of changing population structures. Furthermore, biological agents often elicit allergic reactions, hence it is prudent to have any biotech product tested for safety. There are reports of unwanted effects of microbial agents. One farmer claimed that the *Trichoderma* inoculum he used for composting degraded the wood of his house, a scientifically valid effect. The nematocidal *P. lilacinus* is reported to infect the eyes. Unfortunately, only the introduction of new species into the environment is covered by the Philippine biosafety guidelines subsequently, biosafety testing of local isolates for introduction into the environment is not funded.

The international trend in the commercialization of biotechnology has changed. Previously, small start-up companies developed technologies and tried to market directly their products. Today, these companies either sell the technology, form joint ventures, assign the commercialization to or bought outright by a large established company that had been in the business for decades. Outfits that develop basic ideas and techniques from the laboratory into commercially feasible technologies are few in the Philippines. These are either small companies or entrepreneurs with limited capitalization or farmer cooperatives. Hence, they have not much resource to sustain a long gestation period. Technologies that are picked up from the research sector needs none or only a few refinements and that production proceeds along with technology improvements.

Nevertheless, entrepreneurs with limited capitalization can thrive as indicated by the experience of a small tissue culture laboratory (produces 3,000 banana

plantlets/month) in Mindanao. In this case, the market for the product is already established, the technology is reliable and reliable technical manpower can be so manipulated to make it inexpensive such as using daily contractual labor rather than monthly wage earners that must be provided with corresponding minimum labor benefits. The operation also relies on family labor. Reliable supply of raw materials, reliable technology requiring mostly non-technical labor and an established market appear to help make an organic fertilizer venture in Mindanao profitable. Difficulties in managing the technology appear to explain the failure of one commercial production venture in Trichogramma.

It should be noted that there are biotechnologies that by their nature of being site- and variety-specific must be produced in the country. These are the soil inoculants and biocontrol agents. Organic fertilizer because of bulk must also be produced in the country. Hence, it is imperative to develop suitable technologies that can be transferred and their operations sustained by the business sector. A major issue is the access by small, resource-poor farmer of appropriate biotechnologies. In the Masaganang Maisan and Masaganang Ani Programs for corn and rice, the inability of farmers to use the recommended biocontrol agent, Trichogramma and organic fertilizer is the lack of reliable supply. Also, small banana growers in Luzon and Visayas not like their counterparts in Mindanao do not have ready access to tissue-cultured banana. Tissue-cultured banana plants are now preferred as planting materials and are regularly produced in government and private laboratories in Mindanao. Large private laboratories produce only for their own plantations such as that of a Stanfilco subsidiary producing about 120,000 plantlets per day whereas small ones sell to the public in nurseries that they maintain or upon customer's order. With the trend towards annual cropping of banana, it is expected that private laboratories will become more viable. It thus appears that for banana tissue culture to become a commercial venture in Luzon and the Visayas, efforts must be expended to make tissue-cultured plants preferred and affordable to small farmers.

In the commercialization of locally developed technologies, it appears that there are questions that are best answered even before research is started. Will the technology pay? How much will the development cost be? Do we have the market? the capital? Will the technology be marketable? If the technology produces new products, how will these be marketed? If the market does not yet exist, can we develop the market? Who pays for market development? Can it compete with an alternative technology? Can we make it available? How do you make it available? How will its production affect the environment? How will the product itself affect the environment? farm workers' health? consumer's health?

Regulatory issues

An appropriate regulatory framework is essential in the development of biotechnology to enable us to legally acquire and safely release biotech products in the environment. Three regulatory regimes are required for biotechnology

products in the Philippines, biosafety, IPR and commercial product regulation which could be with the Fertilizer and Pesticide Authority (FPA) and or the Bureau of Food and Drugs (BFAD) for organic fertilizers, biocontrol agents and plants expressing pesticidal genes, e.g. Bt genes.

Biosafety

The need for biosafety regulations has been extensively discussed above. Maredia⁴¹ argued that biosafety regulations can be economically justified by the benefits that accrue from its implementation. These benefits include the reduction of possible human and environmental risks of biotechnology products and 'accidents' cost to society, increased predictability for a research organization of the expected time and money to get a new product on the market, making the products of biotechnology accessible to a country and the provision of certainty and stability to the social framework, necessary for the development of biotechnology R & D activities. However, biosafety regulation imposes increased research lag, production costs, transaction costs and marketing costs to research organizations and opportunity costs to society due to the diversion of technical human and physical resources needed for productive endeavors. Thus, a country has to balance the potential benefits with the increased tangible costs of biosafety regulation.

The Philippines is the first country in Southeast Asia that adopted biosafety regulations when the National Committee on Biosafety of the Philippines (NCBP), a multisectoral body overseen by the DOST was constituted by Executive Order No. 430, October 15, 1990. The NCBP formulates and oversees implementation of biotechnology policies. There are five major biosafety policies; one, that no work on biological and chemical warfare be allowed; two, that only genetic engineering work and the introduction of new species are covered; three, that any work covered by the guidelines must be approved first by the NCBP; four, that enforcement of the guidelines rests with the institutions and scientists involved and fifth, that monitoring is the institution's responsibility. There are 3 sets of guidelines, the first covers the conduct of small-scale laboratory research, the second covers large-scale contained work and glasshouse trials and the third planned release of genetically modified organisms (GMOs) and potentially harmful exotic species (PHES) (NCBP, 1998). Certain regulatory functions overlaps with that of other agencies such as quarantine, hence, the apparent position taken by the Committee is to regulate only GMOs and the regulation of non-GMOs left to the responsible bodies of the various line agencies. Guidelines on the commercialization of biotech products are yet to be formulated.

The current guidelines are revisions of guidelines made in 1991. De Guzman et al¹⁷. reviewed the current biosafety guidelines and found these to have improved. The guidelines are less restrictive, less vague and unnecessary conditions and requirements were removed. Application forms were simplified and the approval process streamlined. Between 1991-1997, the NCBP has processed 61 applications

for the importation of biological materials mostly from IRRI (60%) and 80 research proposals (NCBP, 1998) . Most research proposals described work under contained conditions. As of this writing, no permit has been granted yet for the field testing of transgenic crop plant of which applications have already been received. The review further stressed the need to critically assess a more effective structure of the NCBP and provide a clearer definition of its relationship to existing regulatory bodies to ensure proper implementation of guidelines and for administrative expediency. Improving quarantine facilities was also pointed out. The need for harmonization is partly justified on the fear that experiments not acceptable in other countries may be relocated to the Philippines.

However, there remains vague provisions of the guidelines that applications for field testing has yet to be approved. Whether risks assessment will be tested on a select list of model organisms and what these model organisms will be are still subjects of debate in the NCBP. Also, there is no program to support implementation of the guidelines by way of establishing the appropriate facilities required for research, of developing the scientific capability for risk assessment and funding biosafety research. Research institutions have to request funding elsewhere to support this type of work, yet these are expressed functions of the NCBP in the executive order. This could be another reason why there is virtually no genetic engineering work in the country before 1996. Also, the delayed formulation of clear guidelines in the field release of GMOs and the lack of facilities could also explain why to this day no field release of GMO has been approved.

A question that has yet to be raised is the issue of cost and benefit of the biosafety guidelines. Compliance to Philippine biosafety regulations requires a lot of documentation, long waiting period and more research data than those required by other countries⁴². With the size of the Philippine market, private seed producers may not be able to recoup their investments in biosafety compliance. Given the experiences of various countries, there is a need to examine whether all of the provisions of the guidelines apply. How much will the proper implementation of biosafety regulations costs vis--vis its perceived benefits? For pharmaceutical products, it is reported that about 90% of the total cost of product development goes to research in compliance with regulatory requirements. Biotechnology products for agriculture would probably require less but the time needed to produce the required data is just as substantial. China started without formally adopting biosafety policies until it has gained some experience in developing and handling GMOs. Although genetic engineering work started in 1986 and commercial planting of its own transgenic tobacco done in 1992, drafting of a biosafety guidelines started only in 1994⁴³. Four principles guided the drafting of the guidelines. (1) The guidelines should facilitate rather than hamper biotechnology development while ensuring human health and environmental protection. (2) A science/product-based regulation system rather than technology/process based should be followed. (3) Risk assessment should be conducted on a case-to-case basis. (4) Guidelines shall be revised step-by-step as

experience is gained as well as information from other countries builds up. Thailand on the other hand, is proceeding with caution on the Bt gene due to its possible deleterious effect on the silkworm of its silk industry.

An awareness campaign has been launched by well funded groups eschewing to the European stand on GMOs. Yet no one seems aware that the soybean and corn imported into the country most likely contain GMOs, coming as they are from the USA where about 50% of soybeans and 30% of corn are GMOs. Hence, the early morning 'taho' and the 'tofu' in the market could have come from these soybeans. Also, the potato fries in fastfood chains, soya and corn oil in processed foods such as common snack foods and directly imported food items are partly derived from GMOs which the English have called 'Frankenfoods'. Furthermore, these imported feed corn and soybean may have the antibiotic resistance genes that are feared of being transferred into gut bacterium and then into the environment. Also, the Bt protein is a very stable protein surviving degradation at pH 2, the pH of the human stomach and temperatures of 90oC.

Notable is the stand taken by PhilRICE in developing its own GMOs. To avoid the controversy of introducing genes of non-food organisms, they are using wild rice genes to enhance the rice plant's resistance to pests and are using herbicide resistance genes as selectable markers to avoid the antibiotic resistance controversy. IPB is more or less dependent on its collaboration with foreign institutions under international programs, using genes isolated in or by these institutions.

2. IPR issues

The Philippines is signatory to the WTO-TRIPs agreement and must harmonize its IPR laws with provisions of the agreement. Recently approved is an Intellectual Property Code (Republic Act 8293), the implementing guidelines of which are being actively disseminated by the DTI. A pertinent provision is the patentability of life forms which specifically excludes the patenting of plant varieties, animal breeds, and essentially biological processes for the production of plants and animals but allows patenting of microorganisms, non-biological and microbiological processes. Hence, under this provision, transgenic plants and animals or processes for the production of metabolites or human proteins from plant or animal cell cultures will have difficulties in obtaining patent protection. Approval of patents will apparently depend upon the interpretation of the term 'essentially biological processes' or whether in vitro manipulation of DNA and cells of higher organisms shall be considered non-biological¹⁷. Other provisions of the Code that directly affects biotechnology development are the first to file rule and the 20 year patent protection period. The first to file rule is clearer than the previous first to invent rule. The 20 year protection extends from the date of filing of application which harmonizes with the TRIPs agreement. This also addresses complaints from local inventors who claim that the former rule of extending patent protection from the date of issuance of patent allows for the piracy of ideas

especially since the period from filing to issuance takes as long as 3 years. However, the Philippines has yet to comply with the TRIPs requirement for the protection of plant varieties of which it has a deadline to beat, January, 2000. Perhaps, another reason why companies hesitate to introduce transgenic crop plants to the country is this vagueness on plant variety protection which could be expensive for the company to obtain and defend. One licensing agreement for the production of cutflower varieties between a local company and a Dutch company is known but production is very well contained in greenhouses unlike Bt corn in open fields. Furthermore, implementation of the agreement is beneficial to both parties as it prevents the competition from accessing the same varieties. However, for compliance to the WTO, the Philippine Congress is drafting a Plant Variety Protection Act.

The University of the Philippines promotes patenting of technologies developed by its staff and the DOST has a program with similar intent. The University has established IPR offices in its campuses. Scientists are assisted by the various councils of the DOST in patent applications. PCASTRD provides funds for patenting technologies developed from its own research programs whereas TAPI provides funds to other scientists. Hence, most biotechnology researchers are aware of IPR and have patents to show. However, because most of these technologies are developed from commonly used protocols there has developed within the science community a practice of withholding information. Thereby, the growth of the science is retarded because researchers refrain from publishing results. Also, there are cases of research being duplicated in time and space.

On the other hand, world trends show that the main source of expense involving IPRs are litigation on patent infringements or challenges to broad patents. Policies to help protect patents held by scientists and inventors and subject of litigation are locally needed. Two cases of violation of commercialization agreements between the university and the private sector are described by the patent holders. The practice is similar in both cases. The University assigned the commercialization to a company, the company started production using the patented process, it then proceeded to develop its own process and eventually left out the University. In these cases, one Filipino and one Australian companies were involved.

Access to genes and other biotech tools for research and development is being provided through IRRI for rice breeding, CYMMIT for corn breeding, INIBAP for banana and ACIAR to papaya with or without the assistance of ISAAA. In these collaborations, research institutions need to develop expertise to analyze potential limitations of these agreements and to inform staff of its implications. Researchers sometimes freely exchange materials and may unknowingly break certain provisions of agreements.

Regulation of final commercial products

Guidelines on the commercialization and handling of agricultural biotechnology products are yet to be drafted. We have several regulatory bodies that have functions needed for biotech product regulations. In the USA, the Department of Agriculture, Food and Drug Administration, Environmental Protection Agency and state governments are all involved in biotechnology regulations. Standards for organic fertilizers are subject of current discussions by a committee formed by the Fertilizer and Pesticide Authority (FPA), involving researchers and producers of organic fertilizers. There is a need to harmonize with international standards to enable us to gain access to world markets as well as ensure our populace of the safety of imported biotech products.

The cost of modern biotechnology development

The government stand on biotechnology has been clearly enunciated by various DOST secretaries. The previous direction of development has been on novel uses of microorganisms. However, there is a need to take a critical look at how the Philippines should join in the modern biotechnology revolution particularly in crop biotechnology. Mareida et al⁶ identified 5 progressive steps in crop improvement where biotechnology could come in and analyzed the cost and benefit of adopting investment options along these step according to an economic framework that considers the cost of the research, the value of research spill ins, the value of the benefit from the research result and the size of the market for the research output. The first step does not cost anything since this involves the spontaneous diffusion of imported technologies without the benefit of local R & D (Table 8). However, from the second step to the fifth step, the cost increases with the introduction of sophisticated biotechnology tools. For example, Step 3 has the added cost of a conventional breeding program compared with Step 2.

Modern biotechnology development requires large investments in physical, human, institutional and organizational infrastructure⁴ in research and regulatory capabilities which are considered in calculating the cost of a particular technology. The local cost of establishing a molecular marker technology laboratory is between US\$100,000 (manual) - US\$200,000 (automated). Maintenance cost at maximum capacity is about US\$100,000, the grant amount of the Rockefeller Foundation to the PhilRice's rice biotechnology program. The cost of establishing a genetic engineering laboratory would require 50% more (US\$ 200,000 - US\$400,000) because of biosafety requirements. Maintenance cost would be similar. These costs are comparable to costs reported elsewhere⁴. Personnel cost includes the cost of training scientists with at least Ph.D degrees who are well-grounded in the foundation sciences, skilled in the required laboratory techniques, and capable of maintaining their creativity in running and working in a research laboratory in a place where basic reagents are not readily available, where the electricity may fail anytime and other problems due to a poor infrastructure support for advanced

research. Studies towards the Ph.D degree is better done abroad because of the rapid pace in molecular biotechnology. Current estimates range from US\$100,000 - US\$150,000 per Ph.D. graduate. Technicians trained in molecular techniques are also needed. An excellent curriculum for training such technicians is the BS Molecular Biology and Biotechnology at UPDiliman. The total cost of training is about P300,000 per BSMBB graduate. Depending upon the management capability of a scientist, 4-8 full time technicians are needed to optimally exploit the research creativity of the senior researcher.

Investments in establishing and implementing the regulatory framework adds cost to biotechnology R & D. The formulation and implementation of biosafety guidelines involve research cost as well as personnel responsible for implementation at the national and institutional levels. These personnel must be able to assess risks of GMOs and their products with different features (insect protected, virus protected, delayed ripening) and of different species (transgenic plants, recombinant vaccines, recombinant microbes). Currently, no field of specialization exists to build this capacity but expertise can be developed by closely working with experienced scientists in the developed countries. In addition, cost is incurred in building special biosafety features of the research laboratory, in additional infrastructure needed for contained trials and for field testing and in the generation of the required data for compliance. Opportunity cost is also incurred in the time lag from application to approval at various stages (laboratory research, contained trials, field trials, commercialization). The formulation of and advocacy for IPR protection systems, the acquisition of biotech products and processes and the protection of locally owned IPR involve cost. Measures to allay food safety concerns involve the formulation of food safety policies on food testing and standards, actual research to generate data for developing food safety policies and in compliance to food safety policies, opportunity cost from application to approval and monitoring costs.

Finally, there is the cost of technology diffusion which depends mainly upon the biotech product whether the user is familiar with it, whether its adoption entails substantial investment and other such factors that are yet to be identified.

Strategic plan for biotechnology development

As discussed above, investment in modern biotechnology R & D is much higher than conventional R & D as it includes not only expenditures for building and maintaining competitive research capability, more expensive reagents, but also the cost of instituting and implementing the regulatory framework. Given the limited research investments in agricultural research, limited manpower and facilities and multitude of problems requiring technological solutions, there is a need to adopt a strategy to identify the best mode of investing scarce research resources and prioritize research programs. In biotechnology, it is important to consider first the role of the private sector in accessing the technology since this sector is more efficient in bringing into commercialization new technologies. Policies needed to

promote private sector research should be adopted. Apparently, policies will be specific since there are different biotech products. For example, Bt seed corn developed elsewhere require adaptability trials as well as R & D for compliance to biosafety policies and FPA policies. Recombinant vaccines imported into the country require compliance to BAI regulations. Hence, there is a need to review relevant policies to determine their effect on the introduction and commercialization of biotechnology products.

A second consideration is the uniqueness of the problem to the country and its economic impact. Technological problems in coconut and abaca production could be considered unique since we are the number one producers of these crops and that the size of the market for the research output would be considerably bigger than anywhere else in the world. Also, we could not expect other countries to solve the problem for us since most likely we would be the only country experiencing the problem on a significant level.

A third consideration is the applicability of biotechnology to the problem at hand and the availability of alternative technologies. There has to be a comparison between cost and benefit that includes relative time lags between development, relative probabilities of success, regulatory framework and commercialization modes. For example, early programs in nitrogen fixation is the transfer of the nitrogen fixing genes to common crops. However, years of research has yet to bear success. On the other hand, there is a wealth of data and experience on the use of nitrogen fixing organisms to promote better growth and reduce N fertilizer needs. Field reports indicate that we should continue with research on bio-organic fertilizers. Davide's work with resource-poor corn farmers indicate the efficacy of nitrogen fixers as substitute for inorganic fertilizers in marginal lands. PhilRice has validated the use of a 1:1 ratio of organic fertilizer and inorganic fertilizer in the exogenous supply of nitrogen. The current European hysteria against GMOs and the trend towards organic/natural foods may give us competitive advantage in producing fruits for the international market using non-modified biological control agents and organic fertilizers.

Finally, given the very strong lobbying in Congress and the media blitz by anti-biotechnology groups, it would be prudent to start with a project that is of urgent need, attracts least controversy, of which the private sector may not be interested in investing and may have a high degree of success. Of the various possibilities, the development of a bunchy top resistant abaca is the most likely. Accordingly, all abaca in the Bicol region has been afflicted with the disease resulting in lower yields than the healthy plants in Leyte.

The above considerations could possibly be inputted in the economic framework developed by Maredia et al⁶ for quantifying cost/benefit and provide an objective prioritization process.

Conclusion : Integrating biotechnology into the agricultural research agenda

The Bureau of Agricultural Research is in the right direction in requiring the integration of commodity specific biotechnology projects within commodity RDE programs. It is a recognition that biotechnology is a tool rather than an end in an agricultural research agenda. Successful applications in genetic improvement or breeding work, in the development of safer, more effective vaccines, of reliable diagnostics and in the development of new production systems have been amply demonstrated elsewhere. However, since funds will always be limited yet biotechnology possibilities seem limitless, there is a need for project prioritization. AFMA has already set a minimum limit to biotechnology research investments to 4% of research expenditures.

But prior to project prioritization exercises, the BAR should decide how much of its funds should go to support DA development projects and where should it go. Previous dispensations have used substantial research funds to establish demonstration plots in support of DA programs. Although external evaluators have been hired to find out how effective the programs are in transferring technology to farmers, a more critical look is needed to determine whether the money invested in demo trials could be better spent in research for technology development or whether a more cost effective alternative for technology transfer could have been adopted.

Biotechnology prioritization within a commodity RDE should be based on how critical the problem that needs to be solved and how cost-effective will the biotechnology research be. Hence, alternative technologies should not be discounted outright but rather compared with a possible biotechnology intervention. Although it may seem prudent to use less expensive research techniques such as microbiological systems rather than DNA manipulations, our experience fails to show its wisdom. Also, there is a need to focus and take a risk on a particular research approach. Our practice in developing research programs appears similar to that of a small farmer who plants as many crops as he can in his farm so that if one crop fails he still have another left. So we have a long list of projects which is presented to donor agencies who then take their pick according to their own priorities. Or this could be reflective of our confidence in our mastery of the technology. Furthermore, there is a need to be more realistic in choosing projects that are doable or in trimming down expectations from the project. Given the existing biosafety policies, it might take us more than 10 years to develop our own transgenic crop from scratch. Hence, there is an immediate need to start testing the applicability of the guidelines especially field-testing guidelines to allow its evolution into a more realistic one. It does not help us to have very stringent biosafety guidelines which we have difficulties following ourselves and in effect retarding biotechnology development.

Aside from determining specific critical problems where biotechnology applications will be most cost-effective vis--vis alternative technologies, the

following principles should be adopted. 1. Molecular marker studies should be linked with breeding programs. 2. The Philippines being the major source of coconut in the world should lead in the applications of crop biotechnology in coconut improvement. 3. As much as possible international programs should be accessed as well as private counterpart funds for biotechnology projects of our own choice. Otherwise, inclusion in international programs not necessary to our development will only divert what little resources we already have. 4. Access to critical technologies as well as transgenic crops suitable to our farming conditions should be facilitated. A study of current biosafety rules is pertinent to this.

Risk assessment studies should take priority to enable us to access already existing biotech products. IRRI is ready to disseminate for field testing transgenic rice such as Bt rice and a variety resistant to bacterial blight. INIBAP has available banana bunchy top virus resistant and fungal resistant clones. Field testing Bt corn with private seed companies should be also be facilitated.

A decision also has to be made whether BAR should take a more active role in contributing to the design of development programs for the Department to pursue. Such a program should have a reliable, scientifically tested technology as a central core. Presently, an opportunity exists in the fruit industry. Trends in the epidemiology of the greening disease of citrus and several diseases of banana indicate the decline of these crops unless disease management programs are adopted all over the country involving communities, provinces and individuals in their own capacities. This type of program substantially reduces pest management costs which often are not affordable to small farmers who in turn by not adopting effective pest management practices promote the spread of the diseases. And so, the disease eventually wins. A concept paper on a program to save the demise of the citrus and native banana industries through a national stress management plan with the participation of LGUs, DECS and various units of the DA is included (Appendix 1). It indicates appropriate biotechnology applications and further biotechnology researches that are needed to support the program. Essentially, the intention is to show that research should not stand alone but should closely dovetail national agricultural development priorities.

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Table 1. Traits of some selected transgenic crops commercialized and for field test

| Crops | Traits already commercialized | Traits in Field Trials/Development |
|---------------------|--|---|
| Canola | <ol style="list-style-type: none"> 1. Herbicide tolerance 2. Hybrid technology 3. Hybrid technology and herbicide tolerance 4. High lauric acid | <ol style="list-style-type: none"> 1. Improved disease resistance 2. Other oil modifications |
| Corn | <ol style="list-style-type: none"> 1. Control of Corn-Borer 2. Herbicide tolerance 3. Insect protected/herbicide tolerance 4. Hybrid technology 5. Hybrid/herbicide tolerance | <ol style="list-style-type: none"> 1. Control of Asian-Borer 2. Control of Corn Rootworm 3. Disease tolerance 4. Higher starch content 5. Modified starch content 6. High lysine 7. Improved protein 8. Resistance to storage grain pest 9. Apomixis |
| Cotton | <ol style="list-style-type: none"> 1. Bollworm Control with Single genes 2. Herbicide resistance 3. Insect protected/herbicide tolerance | <ol style="list-style-type: none"> 1. Bollworm control with multiple genes 2. Control of Boll Weevil 3. Improved fiber/staple quality 4. Disease resistance |
| Potato | <ol style="list-style-type: none"> 1. Resistance to Colorado Beetle | <ol style="list-style-type: none"> 1. Resistance to Colorado Beetle+ Virus resistance 2. Multiple Virus resistance (PVX, PVY, PLRV) 3. Fungal Disease resistance 4. Higher starch/solids 5. Resistance to potato weevil/storage pests |
| Rice | | <ol style="list-style-type: none"> 1. Resistance to bacterial blight 2. Resistance to rice-borers 3. Fungal disease resistance 4. Improved hybrid technology 5. Resistance to storage pests 6. Herbicide tolerance |
| Soybean | <ol style="list-style-type: none"> 1. Herbicide tolerance 2. High oleic acid | <ol style="list-style-type: none"> 1. Modified oil 2. Insect resistance 3. Virus resistance |
| Tomato | <ol style="list-style-type: none"> 1. Delayed/improved ripening | <ol style="list-style-type: none"> 1. Virus resistance 2. Insect resistance 3. Disease resistance 4. Quality/high solids |
| Vegetables & Fruits | <ol style="list-style-type: none"> 1. Virus resistance | <ol style="list-style-type: none"> 1. Insect resistance 2. Delayed ripening |

Source: Clive James 1997

Table 2. Benefits reported from the commercial production of transgenic crops

| Crop/Country | Yield /income increase | Reduction in pesticide use | Other benefits |
|--|---------------------------------|--|---|
| Bt cotton/USA | Yield up to 20% Average - 7% | 0-1 insecticide application from 4-6 applications | no effect on nontarget beneficial species compatible with IPM |
| Bt corn/USA | ~ 9% | 0 insecticide application | -ditto- |
| Bt potato | US\$35/ha | reduced insecticide application by 1-2 | -ditto- plus improved size, shape and quality of tubers |
| <i>Herbicide tolerant soybean</i> | | 1-3 herbicide application | increased flexibility in management better yield dependability, improved soil and moisture conservation, compatibility with tillage conservation that reduces soil erosion |
| <i>Herbicide tolerant canola</i> | 9-20% | reduced to only 1 herbicide application, reduced herbicide use from 570 g to 160 g | -ditto- plus improved seed quality |
| <i>Virus resistant tobacco</i> | 5-7 % more leaves | reduced by 2 the usual 7 insecticide applications | |

From James, 1997

Table 3. Product target and techniques used in Philippine biotechnology research (1979-97)

| Product | No of Projects(%) | Techniques commonly used |
|--|-------------------|--|
| 1. Biocontrol agents | 55 (20.9%) | Fermentation |
| 2. Soil amendments (Inoculant, compost) | 44 (16.7%) | Fermentation |
| 3. Food/beverage | 43 (16.3%) | Fermentation Cell culture |
| 4. Tissue-culture methods | 52 (19.77%) | |
| Micropropagation | 31 | Tissue culture |
| Plant breeding techniques | 19 | Tissue culture |
| Cell culture technique | 2 | Tissue culture |
| 5. Feed Component (enzyme, antibiotic, improved material) | 20 (7.6%) | Fermentation |
| 6. Enzymes/cells for agriprocessing | 16 (6 %) | Fermentation |
| 7. Diagnostics | 7 (2.6 %) | Monoclonal antibody, DNA markers |
| 8. Farm waste management | 4 (1.5 %) | Fermentation |
| 9. Molecular markers ¹ techniques | 12 (4.6 %) | Molecular |
| 10. Vaccine antibody, conventional methods | 3 (1.1 %) | Monoclonal |
| 11. Animal reproductive technologies | 3 (1.1%) | Cell manipulations |
| 12. Genetically modified organisms | 7 (2.7 %) | rDNA |
| Total | 263 | |

Source: Compendium: Biotechnology Research in the Philippines, 1997.
BIOTECH, UPLB - PCASTRD, DOST

¹Includes 9 additional projects (mango, coconut, rice, carabao, microbes, zooxanthellae, tuna done at IPB, PCA , PhilRICE, MBB, MSI and BIOTECH) not listed in above source

Table 4. Fields of specialization of senior researchers in agricultural biotechnology¹ (1977-97)

| Field of specialization | MS | PhD |
|---------------------------|----|-----|
| Foundation sciences | | |
| Genetics | 0 | 3 |
| Cell biology | 0 | 0 |
| Molecular biology | 0 | 2 |
| Biochemistry | | 1 |
| Microbiology | 3 | 2 |
| Applied sciences | | |
| Plant breeding | | 4 |
| Animal breeding | 2 | 2 |
| Plant pathology | 1 | 14 |
| Entomology | 2 | 7 |
| Soil science | 4 | 5 |
| Food science | 3 | 14 |
| Other fields ² | 18 | 7 |
| Total | 33 | 61 |

¹Project leaders for projects in Table 1.

²Other fields: Veterinary sciences, animal nutrition, crop protection, agricultural engineering, fermentation/biochemical engineering, animal science, silviculture, chemical engineering, plant biotechnology, horticulture, environmental (biological) engineering, biophysical chemistry, crop science/physiology, agronomy, botany

Table 5. Technologies Developed at BIOTECH, UP Los Banos, 1979-98⁴³

| Commercial Name | Description |
|--------------------------|---|
| 1. MYCOVAM | Mycorrhizae tablets for reforestation replaces 60-85% fertilizer requirements Licensed to. Los Banos Biotechnology Corp Remits P10-15,000/month royalty to BIOTECH |
| 2. MYCOVAM | Powder containing mycorrhizal fungi for reforestation, agricultural and fruit tree crops P25/kg, Licensed to Los Banos Biotechnology Corp. |
| 3. BIO-GREEN | Bio-organic fertilizer with Trichoderma sp. and Azotobacter, P175/50 kg bag, <i>Licensed to 5 private companies</i> |
| 4. NITROPLUS | Bio-organic fertilizer for legumes with Rhizobium and replaces 30-50% N-requirement at 4 packs/ha of peanut P25/pk |
| 5. BIO-N | Biofertilizer for rice and corn, with Azospirillum P25/pk, licensing under negotiations |
| 6. BACTROLEP | Bioinsecticide, Bacillus thuringiensis preparation, effective against corn borer and diamondback moth of cabbage |
| 7. PELMICTROL | Bioinsecticide, Bacillus thuringiensis preparation against mosquitoes |
| 8. COCOGROE | Plant growth hormone preparation from coconut water, P250/L |
| 9. Plant diagnostic kits | Monoclonal antibodies for plant virus diagnosis |
| 10. HEMOSEP | Pasteurella vaccine against the deadly hemorrhagic septicemia in cattle and carabao, P10/dose |
| 11. LYSINE | Feed additive, an amino acid (lysine) preparation nutritional supplement |
| 12. TYLOSIN | Feed additive, antibiotic preparation, therapeutic and growth promotant |
| 13. MANNANASE | Enzyme preparation for conversion of copra to produce high quality feed supplement |
| 14. YEAST strains | Improved yeast strains for higher alcohol production |

From de la Cruz⁴⁴

Table 6. Technologies patented or patents applied for by BIOTECH, UPLos Banos, 1979-98⁴³

| Patent No | Inventor | Title | Date filed |
|-----------------|---|--|---------------|
| 14067 | EJ del Rosario | An apparatus for the continuous flow tower fermentation of sugar into ethanol by a flocculant yeast with automatically controlled feeding of sugar and yeast | Dec. 26, 1979 |
| 15246 | JC Mamaril, RB Aspiras | Process of producing rhizobial inoculum | Sept. 3, 1982 |
| 15247 | LE Padua | Bacterial insecticide, its composition and use | Sept. 3, 1982 |
| 15248 | PC Sanchez | Process of producing mungbean sauce | Sept. 3, 1982 |
| 15444 | RE dela Cruz | Process of producing mycorrhizal inocula | Sept. 3, 1982 |
| 26413 | CB Pham | Process of producing animal feed from cassava fiber residue | Feb 17, 1992 |
| 27274 | CB Pham | Bioprocessing of agricultural crop residues | |
| 27995 | CB Pham | Microbial production of l-lysine using homoserine auxotrophic mutants and repeated batch fermentation | |
| 29753 | JC Mamaril | Process for producing concentrated plant growth hormone and regulators from coconut water | Nov. 16. 1993 |
| Patents pending | | | |
| 47313 | FS Maslog | Production and development of monoclonal antibodies against hemorrhagic septicemia, | Nov 12, 1993 |
| 47312 | BM Espiritu | Bio-organic fertilizer, special compost inoculated with beneficial molds and nitrogen fixing bacteria | Nov 23, 1993 |
| 49333 | ES Paterno, FG Torres | Use of coconut shell charcoal as carrier materials of powdered and granular inoculants | Nov 9, 1994 |
| 49334 | ES Paterno, FG Torres | Use of soil and charcoal and wood ash mixture as carrier for microbial inoculant | Nov 9, 1994 |
| 49470 | AK Raymundo, TO Zulaybar, ES Luis, RD Ayo | Bioprocess of local tylosin production for feed additive | Nov 29, 1994 |
| 49471 | GD Reyes | A process to produce biodegradable plastic from Bacillus species isolated from soil | Nov 29, 1994 |
| 53009 | SM Mercado RR del Rosario | Process for the production of microbial rennet | May 8, 1996 |

From de la Cruz⁴⁴

Table 7. Research resources for crop biotechnology

| Institution | Facilities available for | | No. of Ph.D with training in | |
|----------------|--------------------------|----------------|------------------------------|--------------------------|
| | Mol.markers ¹ | Transformation | DNA | Biochemical ² |
| UPLB | | | | |
| BIOTECH | X | - | 8 | 12 |
| IPB | X | - | 8 | 3 |
| IBS | X | - | 4 | - |
| D Plant Path | - | - | 2 | 1 |
| D Horti | - | - | 2 | - |
| Inst Chemistry | - | - | 2 | 4 |
| NCPC | - | - | - | 1 |
| UPDiliman | | | | |
| MBB | X | X | 7 | 2 |
| MSI | - | - | - | 1 |
| NSRI | X | - | 3 | 1 |
| PhilRICE3 | X | X | 8 | nk |
| VISCA | - | - | 3 | nk |
| PCA Albay | X | - | 1 | nk |
| CRDI | - | - | 1 | nk |
| CLSU | - | - | 1 | nk |

¹Molecular markers ²Some are also trained in DNA manipulations

³From Sebastian 1999

Table 8. Five steps in a conventional crop improvement program

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1. Spontaneous diffusion of imported technologies without the benefit of local R & D
 2. Direct transfer of technologies after testing and screening by local R& D programs for adaptability to local environments.
 3. 'Adoptive' transfer of technologies whereby finished technologies from elsewhere are subject to local adaptation before local release (e.g. the use of imported varieties as parents of local breeding programs).
 4. Comprehensive applied research where imported knowledge from basic research is utilized in local applied research programs to produce home-grown technologies.
 5. Comprehensive basic and applied research which utilizes imported knowledge but also has the ability to conduct own basic or pre-technology research.
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