Chapter 1

Exploiting Developments in Science for New Bioscience Enterprises

> *"We are now starting the Century of Biology.... Just as information technology undergirds today's booming economy, biology may drive tomorrow's,"* says J. Craig Venter, President of the Institute for Genomic Research and pioneering gene finder.
>
> *"We have a chance to achieve incredible economic benefits,"* says Henri A. Termeer, President and CEO of biotech company Genzyme Corp. (GENZ).
>
> — John Carey
> in http://www.businessweek.com/1998/35/b3593020.htm

The 21st century has been accompanied by great expectations of knowledge and wealth creation. In response to these rapid evolvements, many prominent scientists and public figures have dubbed the 21st century as the "Biology Century" (Woese, 2004). How has this come about? Part of the answer lies in the myriad advances in science during the last half of the 20th century, especially in molecular biology, and in the transformation of knowledge into technologies that give rise to products.

However, the use of biological knowledge to serve human needs is not new, and neither are the enterprises associated with exploiting that knowledge. Human society has tapped biological knowledge for millennia to produce food, feed, beverages and fiber, but the advent of modern technologies and new biological knowledge has vastly expanded the applications of biology. Our early ancestors domesticated plants and animals, and, with the selective breeding of preferred species, they formed the biological foundation for today's plant and animal varieties, many of which are vastly different from their original parents. Indeed, few of today's crop plants are unimproved or harvested from the wild.

The extent and speed of new bioscience applications have caught the general public, and even some scientists, by surprise. The sequencing of the genomes of entire species, such the small flowering plant *Arabidopsis* (in 2000) and rice (*Oryza sativa* in 2005), means that humankind is literally unraveling the "Books of Life" of major organisms, and consequently gaining the potential to alter some very basic elements in these books. Genetically modified organisms (GMOs) have become a lightning rod for those who fear the rapid changes birthed from the acquisition of new knowledge. GMOs have also come to illustrate how basic science can be turned into a multi-billion-dollar growth industry in less than a decade. Promises and fears are the "yang" and "ying" of the new products from biotechnology. Many have warned that society is barely seeing the tip of the iceberg for bioscience products, and if this is the case, then tremendous opportunities for value creation in biology still exist, and with that, the certainty of more controversy.

In this chapter, the reader will be introduced to the basics of bioscience and the enterprises that have been created from bioscience. This chapter provides an overview of the main groups of applications from various branches of bioscience, and the context set for the markets associated with their products and their demand. In today's society, any value created from knowledge requires protection, both locally and internationally. This chapter will also discuss the important issue of value protection and its relationship to technology transfer for less developed countries, which collectively constitute the world's largest potential market.

1.1 What is "Bioscience"?

Several terms need explanation. *Biology* is the study of the life sciences, with two main branches (botany and zoology) and many disciplines (e.g., physiology, genetics, morphology). *Bioscience* includes all the sciences devoted to an understanding of life, while *biobusinesses* are enterprises based on utilization of biological knowledge.

BIOLOGY — Study of the life sciences; science of life, with two main branches (botany and zoology) and many disciplines (physiology, genetics, morphology, etc.)
BIOSCIENCE — All the sciences devoted to an understanding of life
BIOBUSINESS — Business enterprises based on utilization of biological knowledge

Modern bioscience, and indeed what is generally considered modern science based on verifiable research using internationally accepted standards, is only several centuries old. Our use of nature and its products has evolved through a long history of "trial and error" and experience. Much has been written about this local, indigenous knowledge, the basis of which is still being unraveled today using current concepts and modern tools. Chinese traditional medicine, the Indian ayurvedic approach to health, Egyptian and Tibetan sacred texts all attest to how various human civilizations in different parts of the world have accumulated their knowledge base of the life sciences.

It is not possible to pinpoint accurately when modern bioscience started. Scientists generally accept that the publication of *The Origin of Species* by Charles Darwin in 1859 has been a key influence on bioscience development since the 19th century. This, in turn, laid the serious foundations of experimental science, which has become a hallmark of today's modern bioscience. This is not to undervalue the remarkable contributions that earlier, mostly unknown scientists and farmers have made in improving crops and bioprocesses in several continents. Without the efforts of the early pioneers, we would not have today's rice or wheat, from which our major staples are derived.

Modern genetics underpins many aspects of modern biology, and with that, bioscience entrepreneurship. Modern genetics is considered to have started when Mendel's laws were rediscovered in The Netherlands in 1900 by Hugo de Vries. Subsequent to this, several decades of research followed. The first known commercial hybrid seed was developed by Henry Wallace in the USA, who also founded one of today's most successful seed companies, Pioneer Hi-Bred.

The first hybrid corn seeds were sold in the USA in 1924, sparking significant corn yield increases per hectare in North America. Due to the huge agricultural success of hybrid corn, all "natural" corn grown in the USA was replaced by their hybrid counterparts by 1960. The strategic shift from natural to hybrid corn subsequently snagged the USA the title of the "world's largest exporter of corn".

Parallel research and development (R&D) work on vegetables led to the commercialization of hybrid cabbage in Japan in 1951, while conventional breeding work markedly improved the yield and performance of important food crops such as rice and wheat. The "Green Revolution" of the 1960s bore testimony to the powerful impact of hybrid crops. The Revolution has been attributed to staving off famine in large parts of developing Asia then, and won for its chief architect, Norman Borlaug, the Nobel Peace Prize in 1971.

Bioscience has been tightly linked to agriculture, especially the growing of crops. Historians have shown that agriculture gave the stability needed for our nomadic foreparents to put down roots and develop the features of human civilizations. However, traditional agriculture aimed at supplying calories has today been supplanted by the "***New Agriculture***", in which crops have become "biofactories", converting the sun's enormous energy into a myriad of useful products.

Traditional "biofarming", or the growing of crops such as rice and wheat to meet basic sustenance needs, gave way to the rubber and palm oil plantations such as those in Malaysia and Indonesia, to produce value-added hydrocarbon products to meet the needs of a changing world. The plantations were early examples of the use of mass production techniques which treated plants as biofactories to produce rubber and palm oil. Biofarming has now evolved into "Biopharming", and has branched out further into "biofuels", "bioplastics", "biofertilizers", "biopesticides" and "bioremediation". Collectively, these constitute the New Agriculture, with significant opportunities for value creation.

The last quarter of the 20th century saw the emergence of multinational seed companies and the multiplication of smaller domestic seed companies as beneficiaries of the genetics revolution in bioscience. Much has been written about the role of public sector institutions in producing improved seed for poor farmers and serving the socially responsible role of food security. Much less has been written about the role that private companies have played in developing and making available improved seed material to move poor farmers away from subsistence to farming for cash. The cash generated from the agriculture of plantation crops like rubber and palm oil moved generations of people out of the poverty trap in Southeast Asia. Today, agriculture remains an important driver of economic development, premised on entrepreneurship, in this part of the world. This last quarter also evidenced the beginning of the second revolution in genetics, expressed through the so-called biotechnology revolution (see the Annex at the end of this chapter for a brief chronology).

1.2 What are "Bioscience Enterprises"?

A bioscience enterprise is any commercial activity which involves the application of biology and the understanding of life processes and creates economic value for its owner. This generally would include many activities in the biomedical industry, agriculture, food processing and environmental areas. For the purpose of this book, only plant and microbe-based activities are being considered, namely:

- Raw biocommodities
- High-quality seed material using hybrids
- High-quality seed material using tissue culture
- Biofermentation
- Biofertilizers
- Biopesticides
- Biofuels
- Bioremediation, and
- Biotech seeds.

Each of these will be previewed in the following sections of this chapter and described in detail in subsequent chapters.

Bioscience enterprises include more than those activities dealing with the production of specific primary (e.g., rice or corn) or secondary products (e.g., rice bran oil or corn oil). Ever since international trade regimes recognized the value of intellectual property (IP) through organizations such as the World Trade Organization and World Intellectual Property Organization, value creation through the commercialization of services, and through licensing of IP, has become common. In bioscience, the landmark decision in 1980 of the US Supreme Court to grant a patent on a microbial life form that could break down oil spills (see Annex) also meant that new opportunities were created for companies to invest in R&D that led to patentable processes and products.

1.3 Creating Value from Bioscience Through Entrepreneurship

The value chain in a bioscience enterprise (Figure 1.1) therefore starts with discoveries made during the R&D stage. In modern biotechnology applications such as the development of biotech seeds, some of the early transgenic plants were made using a process called particle bombardment, which required a special piece of equipment called a "gene gun". This particle gun was initially developed by Cornell University scientists, but later patented by DuPont company. Companies selling commercial transgenic plants made from the first transgenic produced using the patented gun have to pay to DuPont a percentage of any value created.

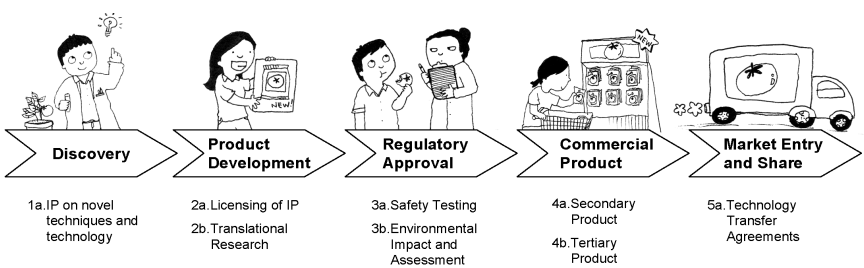

Figure 1.1. A comparative value chain in bioscience enterprises.

Figure 1.1 also shows the steps involved in developing bioscience-based products, many of which are regulated for safe use by government agencies. New industries have developed as governments (urged by a more enlightened and more demanding public) have put into place information requirements to support safety, to support traceability (i.e., where does a particular product in the market trace its origins from?), and to support consumer choice. Animal-testing laboratories for GM food products, detection systems for specific ingredients, and certification services for organic crops are examples of a growing industry aimed at providing more information on products. Collectively, they are valued at hundred of millions in US dollars.

Perhaps one of the biggest value additions in the value chain is further processing of raw commodity into secondary, tertiary and other products (Table 1.1). While a metric ton of rice is traded at between US$300–US$400 on the global market, a metric ton of rice bran oil (tertiary product) is worth about US$3,000–US$11,000. The extraction percent of rice bran oil is only about 0.9% of milled rice, so any R&D that gives rice varieties with higher

Table 1.1. Amplifying value through multiple secondary and tertiary processing for new products, exemplified by rice.

Plant Part	1st Stage Product	2nd Stage Product	3rd Stage Product
Panicle (Grains)	Milled rice	Human food staple Flour	Alcoholic drinks, etc.
	Brown rice	Fuel	Noodles, etc.
	Hull (husks)	Briquettes	Silica-based products
	Embryo and/or endosperm	Bran Bran oil	Tocotrienols Vitamin E Antioxidants
Leaves	Straw Phytochemicals	Fuel Paper Medium for mushroom growing Purified compounds	
Culms (Stems)	Straw	As above	
	Phytochemicals	As above	
Roots	Straw	As above	

oil content would create significant added value to the rice and the extraction process. Subsequent processing of a tertiary product like rice bran oil by extracting pharmaceuticals such as the compound, oryzanol (a known active anti-oxidant), would give even more value to rice. Organizations such as the National Innovation Agency, Thailand, have commissioned studies on how to add value to Thailand's rice crop beyond the traditional market niche of aromatic rice (NIA, 2006).

The new value chaining for a new agriculture strongly suggests that there can be different players in different countries to add to this chain. The company that owns the IP does not have to be in the same country that uses the IP to produce the bioscience product!

This is a significant, obvious fact that seems to have escaped the attention of so many national planners in countries that desire to be in the mainstream of the "Biology Century". Indeed, the new playing field argues strongly for the need to develop comparative advantages in some parts of the value chain for bioscience entrepreneurship.

Small countries with only human resources and knowledge economies can compete effectively in IP generation, provided investments are made to support R&D and effective IP protection regimes are in place. Of course, many countries have desired to do well in all parts of the value chain. This is shown by the number of science and technology parks that have mushroomed in Asia, even in countries which, analytically, do not have the comparative and competitive advantages to exploit their strengths.

1.4 Creating Value in Biotech Seed Enterprises

In the first paragraph of this chapter, reference was made to the "Biology Century", which is mainly due to the powerful discoveries and developments in genetics backed by computer power. The unraveling, literally, of the "Books of Life" (Ridley, 1999), means the ability to link specific gene(s) to specific functions and traits. The availability of technology and techniques for gene-splicing also means that novel plants or microbes with economically important traits can be created

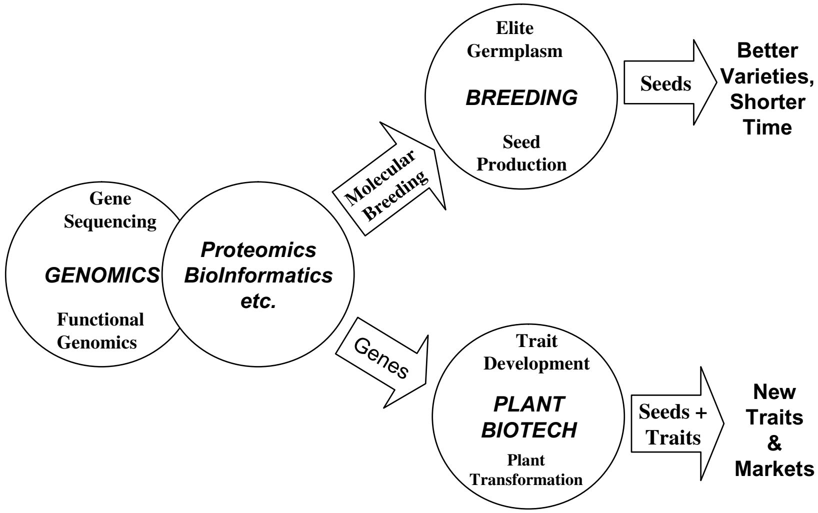

Figure 1.2. Schematic of a new biotechnology-based R&D to market chain (Courtesy: Monsanto Company, St. Louis, USA).

using genes from outside that plant's genome. Companies like Monsanto have put into practice a new biotechnology-based R&D to market chain to produce new plant varieties that meet specific grower needs for competitive farming.

Subdisciplines of modern genetics have evolved which are truly multi-disciplinary and require knowledge from traditional chemistry, biology and mathematics, to name a few. In Figure 1.2, only a few such subdisciplines are named — genomics, proteomics and bioinformatics. The net result, however, is to get competitive advantage by getting to market faster a particular new variety with the desired traits which is also protected by law.

A generic value chain for modern bioscience enterprises (Table 1.2) would show distinctions between activities aimed at value creation, value addition, value capture and value preservation. Important market development decisions to introduce a new product have been made based on the existence of value capture and value preservation mechanisms in a particular country.

Table 1.2. A new value chain in modern bioscience enterprises.

Value Chain	Activity	{Note}
Value creation	Gene identified & cloned, expressing protein to confer a trait	IP protection for novel gene discoveries
Value addition	Incorporating desired gene into popular local crop variety	Licensing trait to small seed companies
Value capture	Hybrid seed Non-reproductive seed	Commercial seed production and distribution system
Value preservation	IP protection system for seeds	Seed Law, PVP

1.5 Value of the Biosciences Product Market

Bioscience applications in the modern era (post-World War II) have been mainly in agriculture, fisheries and forestry. These industries, with their related bioscience applications, have been a source of employment for the majority of the world's people, as well as a significant contributor to the gross domestic products (GDPs) of many developing countries.

The overall picture is fast changing, with newer applications of the biosciences, such as biotechnology, fostering new sectors especially in the industrialized world. Modern biotechnology products, services and technology solutions were estimated in 2001 to have generated about US$40 billion of value worldwide.

While it is difficult to get comparable statistics because different baskets of enterprises are included under the term biotechnology or biobusiness or bioenterprise, the global value in 2006 was estimated at around US$60 billion for modern biotechnology alone (A. Ilaga at National Biotechnology Week, Philippines, July 2006). This is but a small fraction of the global value of bioproducts shown in Table 1.3.

These figures do not fully show the substantial value addition from secondary processing of bioproducts such as rice bran, from which rice bran oil is extracted, or the use of bioproducts such as corn starch for ethanol biofuel production. Needless to say,

Table 1.3. Relative contribution of various biobusiness sectors to economic activity (US$ billions and % GDP), 2001.

Biobusiness Sector	Global, US$ Billions (% of Global GDP)	South Asia, US$ Billions (% of Global GDP)	East Asia and Pacific Islands (Excluding Japan), US$ Billions (% of Global GDP)	USA, US$ Billions (% of Global GDP)
Agriculture, fisheries and forestry	2,611.4 (8.1%)	223.2 (28%)	362.1 (15%)	529.4 (5%)
Healthcare	2,933.8 (9.1%)	33.5 (4.2%)	108.6 (4.5%)	1,588.2 (15%)
Food sector (processing, manufacturing)	3,288.4 (10.2%)	100.5 (12.6%)	277.6 (11.5%)	1,016.4 (9.6%)
Biotechnology	40 (0.1%)	1.4 (0.18%)	4.1 (0.17%)	25 (0.24%)
Biobusiness related R&D	257.9 (0.8%)	2.4 (0.35%)	12.1 (0.5%)	105.9 (1%)
Other biobusiness	644.8 (2%)	15.9 (2%)	48.3 (2%)	211.8 (2%)
Total biobusiness	9,776.3 (30.3%)	376.9 (47.3%)	812.8 (33.7%)	3,476.7 (32.8%)
Estimated GDP	32,239.0	797.3	2,414.2	10,588.0
GDP as % of global GDP	100%	2.5%	7.5%	32.8%

Source: BioEnterprise Asia (2003); United Nations Statistics Division (2002); Food and Agriculture Organization (2002); and World Bank (2002).

the bioenterprise sector is growing in Asia at an estimated rate of > 10% p.a.

Research conducted by BioEnterprise Asia (www.bioenterpriseasia.org) showed that about 6,000 companies worldwide classified themselves as biotech companies in 2004. Within the Asia-Pacific region alone, the number of companies which classified themselves as biotech increased from 1,200 to over 2,500 from 2001 to 2004.

However, in Asia, most countries have tended to include both traditional biotechnology (e.g., tissue culture, biofermentation for food production) and modern biotechnology (e.g., drug production using genetically modified microorganisms), making it difficult to separate out the relative contributions of individual enterprises to the national economy. Countries like the Philippines and Vietnam, however, have identified specific niche areas in which to position themselves, such as in the production of natural food coloring or additives by extraction processes using plant material. Examples from the Philippines are papain extraction from papaya and a red dye from seeds of the anatto plant.

1.6 Why Excitement over Bioscience Enterprise?

Bioscience enterprises have only created a small fraction of the potential value that they are capable of generating.

Figure 1.3 is a schematic drawn from different sources to graphically show the unexploited potential of bioscience enterprises according to sector. The pharmaceutical (biomedical) industry up to today

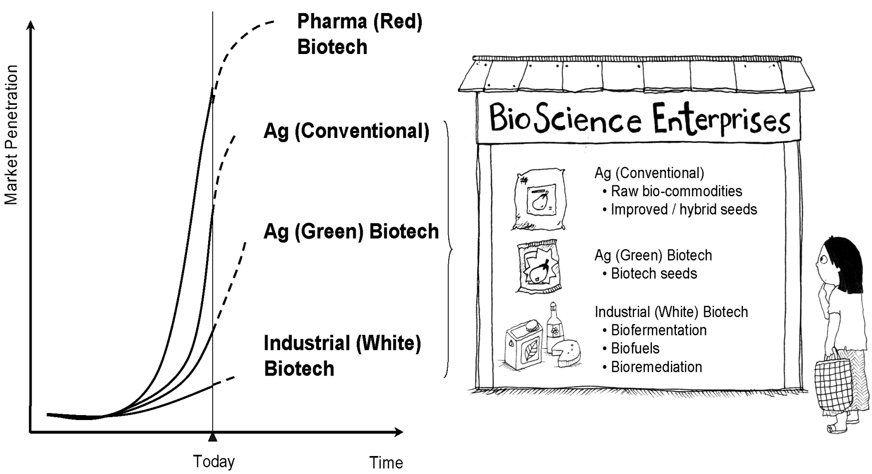

Figure 1.3. Relative market potential for development of various bioscience products.

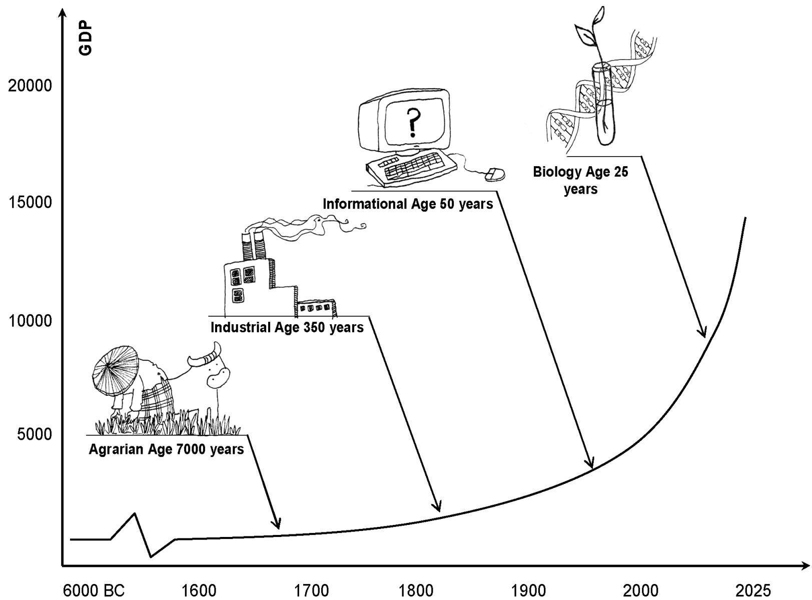

Figure 1.4. Comparison of economic impact of bioscience enterprises relative to other industries in history.

has created the most value, while agriculture (biofarming) is more matured than bioscience applications in industrial processes. Albeit a simple classification, it is meant to illustrate the growth potential and large market size of the bioscience entrepreneurship in industrial uses such as biofuel and bioremediation.

When compared with other significant global phases, modern bioscience enterprises have created much value in a relatively short time (Figure 1.4).

1.7 A Brief Description of Conventional Bioscience Enterprises

Conventional bioscience enterprises, which include agriculture, are collectively the world's largest employer! This is because much of the world today still consists mainly of rural communities, consuming what they produce, especially in Asia.

1.7.1 *Raw biocommodities*

Asia has been an important producer of some of the world's major biocommodities, such as rice, corn (maize), cashew nuts, rubber, palm oil and cacao. Asia is also the world's largest producer of natural timber and aquacultured fish.

While the commodities themselves remain important as food sources, increasing pressure is being put on their traditional role to supply calories for humans and feed for animals, especially on those commodities with potential for secondary exploitation such as conversion into higher valued biofuel or pharmaceuticals. This development is not surprising as plants have always been viewed as "primary producers" in the food chain because of their ability to capture energy from sunlight to make useful products. It is logical to expect that plants as "biofactories" will evolve in their role as human society evolves in its relative needs to use plants.

Asia is currently a net food importer despite its eminence in the production of raw biocommodities. As a region, it is self-sufficient in food commodities like rice, palm oil and fish, but is a large importer of corn, wheat, potatoes, soybean as well as various meats. Even with the food commodities for which there is sufficiency, such as rice and fish, the situation is a fragile one. Some countries are persistent net rice importers, either by design or by need (Table 1.4).

Most rice is consumed where it is grown and the global market for trade is a very "thin" market, with 5%–7% annually of milled rice being available for trade, such that any natural catastrophe has been known to dramatically disrupt availability and cause social consequences. Asia imports most of the surplus export corn (average 45%–50% of global surplus production) and because the global surplus is only 10%–15% of total production, it is projected that the market for corn will become tighter due to competing uses such as bioethanol production.

Furthermore, this region, which holds > 60% of the world's population, only has about 35% of the world's cultivable lands, with a significant area each year being degraded. The Food and Agriculture Organization, United Nations, has predicted shortages of usable land

Table 1.4. Production and trade in four commodities important to Asia.

Crop	Item	2004/ 2005	2005/ 2006	2006/ 2007
Corn (Maize)	Global Production Million M T (million tons)	714.0	696.0	698.0
	Global Exports Million M T (% of global production)	76.0 (11%)	82.7 (12%)	84.4 (12%)
	Asian Imports[1] Million M T (% of global exports)	35.5 (47%)	36.3 (44%)	43.3 (51%)
Rice (Milled)	Global Production Million M T	401.0	418.0	417.0
	Global Exports Million M T (% of global production)	29.0 (7%)	28.5 (7%)	29.0 (7%)
	Asian Imports[2] Million M T (% of global exports)	6.3 (22%)	6.2 (22%)	7.4 (25%)
Wheat	Global Production Million M T	629.0	622.0	594.0
	Global Exports Million M T (% of global production)	112.0 (18%)	113.0 (18%)	110.0 (19%)
	Asian Imports[3] Million M T (% of global exports)	22.4 (20%)	23.2 (21%)	28.8 (26%)
Soybean (For Meal)	Global Production Million M T	216.0	220.0	234.0
	Global Exports Million M T (% of global production)	46.6 (22%)	51.3 (23%)	53.6 (23%)
	Asian Imports[4] Million M T (% of global exports)	9.9 (21%)	12.1 (24%)	12.8 (24%)

[1]Top 7 Asian countries. [2,3,4]Top 9 Asian countries.
Source: United States Department of Agriculture, Foreign Agriculture Service (www.fas.usda.gov).

and water for farming if more action is not taken to use environmentally friendly technology such as bioremediation (discussed further in Chapter 7).

The 1971 Nobel Peace Prize winner, Norman Borlaug, warned in his address to the Asian Development Bank's annual meeting in 1999 that farmers in Asia will have to produce 50%–75% more grain if a food scarcity crisis is to be averted. The International Rice Research Institute has predicted that by 2020, Asia will need about 700 million tons of milled rice just to be sufficient, and this will require a doubling of raw commodity yields in some countries from the present.

The demand for proteins in Asia, especially from poultry and hogs, has also fuelled the demand for corn as animal feed. Corn is also used to make food products such as corn bread, corn chips and cereals, and as a vegetable, it is consumed as green corn and baby corn. Corn grain is a key industrial raw material used for making starch, glucose and oil. Corn syrup is widely used as sweetener for baked goods. Corn starch is used for a variety of purposes including making pills and sweeteners and for coating paper. Recently, corn has been diverted from these uses in large amounts to make ethanol for biofuel.

What does this all mean in terms of bioscience entrepreneurship?

The increasing demand for raw commodities with a potential to be converted into products in high demand — biofuel, animal and fish feed, etc. — suggests that investments in their efficient production will likely be relatively safe ones. Although there is value creation in the first stage and value capture as raw commodity, the value addition is through further processing.

While trading of the initial dried corn is a profitable business in view of the current high prices due to shortages from biofuel conversion, value addition is high from milling into animal feed and subsequent formulation for specific purposes. As a value proposition in bioscience entrepreneurship, however, experience has shown that companies that have entered into the intellectual property (IP) ownership of the genetic material for high-quality hybrid seeds are the ones that have outperformed their contemporaries in commodity trading, in terms of value capture.

1.7.2 *High-quality seed material using hybrids*

Seed for planting includes all plant material that can be used to grow new plants, from real seeds to plant suckers to cloned plantlets produced from tissue culture. The global seed market is valued at over US$30 billion per year, dominated by about ten multinational companies. Currently, no major seed company of Asian origin has yet to dominate the global seed trade, although Asia has the potential to be the world's biggest market for certified, high-quality seed.

Value capture in the seed industry is done through IP ownership of plant varieties protected by law and the offering of value to growers who purchase the seed material. Hybridization as a bioscience technical process is well-studied, but its use as an enterprise only started in the 1920s with corn in the USA. This led to the founding of one of today's largest seed companies (Pioneer Hi-Bred).

Hybrids offer a scientific means to preserve value as such seeds commonly lose their hybrid vigor (which confers 10%–15% yield advantage over non-hybrids) if the seeds from hybrids are reused for subsequent planting. The seed market includes hybrid and non-hybrid, improved seed.

Data from the United Nations Development Program shows that worldwide, the majority of growers are already planting improved crop varieties (> 90% of wheat is improved; > 65% of rice; > 80% of corn). However, crops like cassava and sweet potato are still largely unimproved. With the hybrids, there is a continual battle to uplift the traits which add to yield, such as pest resistance, and this is an area in which science can create value through new discoveries.

Without exception, all multinational seed companies have large R&D teams which use modern molecular biology and breeding techniques in their product development process. The value creation takes place when the scientific knowledge is translated into a new, improved crop variety which is able to be registered and sold. Companies recover their R&D costs through their own marketing and sales efforts or by licensing their technology to third-party seed companies without the capacity to do their own R&D. Almost a third of the cost price in a kilogram of seed may be from the technology licensing fee, passed on to the grower-buyer by the third-party seed company. However, in the context of bioscience entrepreneurship, this is an area where countries with significant R&D capacity but without the production capacity (i.e., land) can become key players. Good seed depends on good genetics, which in turn depends on basic advances in bioscience and solid R&D.

1.7.3 *High-quality seed material using tissue culture*

Tissue culture refers to a set of techniques and scientific knowledge which enables the growth of cells into tissues and whole organisms under artificial conditions. Tissue culture was among the earliest applications of modern bioscience to develop into a multi-million-dollar business for producing genetically identical seed material with the desired characteristics such as high yield, good eating quality or resistance to pests and diseases. The technique was also one of the earliest commonly included in biotechnology to create value for investors. However, even on its own, it has led to applications just as important as those of genetic engineering, for example, the selection and subsequent mass propagation of plant varieties showing resistance to specific diseases. Indeed, most of the large plantations of rubber and palm oil in Southeast Asia have their origins in tissue-cultured clones.

The varieties of plants propagated by tissue culture in Asia and around the world are numerous and include herbaceous ornamentals, ferns, orchids, roots, tubers, tree species, tropical and subtropical crops. The benefits of propagating plants using tissue culture are manifold, apart from the uniformity in all the plants and the rapid multiplication. Plants grown in tissue culture are often disease- and virus-free. The economic value also is that tissue-cultured plants are easily exported in small lightweight containers. As plants are free of soil, disease quarantine problems are minimized.

With these advantages, export and import of tissue culture products are greatly facilitated. Tissue culture is a multi-million-dollar business in several Asian countries such as Singapore, Thailand, Australia, China and Taiwan. Taiwan alone exported over US$10 million of tissue-cultured orchids in 2003. Several tissue culture companies are now publicly listed companies and investors appear recently to have recognized the inherent value in this subsector. With the ongoing interest in biofuel, it is likely that tissue culture will be tapped to provide clonal seed material needed for the large areas planned in several countries of species like Jatropha.

1.7.4 *Biofermentation*

Biofermentation is a process whereby food and organic products are produced through large-scale fermentation in a bioreactor by organisms like yeast, fungi and algae. Some of the more familiar products produced through the process of biofermentation include natto and tempe. The process of biofermentation involves selection of a suitable microbial culture that has the metabolic potential to produce the desired end product. The medium in which the culture is fermented is carefully chosen.

The development of a suitable, economical medium is a balance between the nutritional requirements of the microorganism and the cost and availability of the medium components. The bioreactor in which the process of fermentation takes place should also be able to provide the culture with the optimal environmental conditions for growth. Producing products by biofermentation has been deemed advantageous as fermentation utilizes renewable feedstocks instead of petrochemicals. Also, the by-products of fermentation are usually environmentally benign compared to the organic chemicals and reaction by-products of chemical manufacturing. Often, the cell mass and other major by-products are highly nutritious and can be used in animal feeds.

There is now renewed interest in bioreactor technology for growing single-celled organisms such as algae which are capable of producing high yields of biodiesel. Algae are potentially the most efficient crop to grow for biodiesel as algal cells have high growth rates, and may have > 50% oil content formed when they convert carbon dioxide from the air and sunlight into energy. Studies suggest that algae are capable of yielding 30 times more oil per acre than the crops currently used in biodiesel production. Algae can create up to 32,000 liters of oil per hectare per year, far in excess of palm oil, presently considered one of the best crops for biodiesel production. The R&D to identify or selectively improve algal strains is in its early days. If the orders of magnitude in yield which have been gained from improving higher plants and microbes is any indication, then there is very high potential for significant improvement in oil yield of algal cells.

1.7.5 *Biofertilizers*

Fertilizers are needed to provide plants with the macronutrients for growth and development. In the modern era, high crop yields have been achieved because proper levels of fertilizer application have allowed the genetic potential of seeds to be expressed. Most of the fertilizer use today is made from petroleum-based products (i.e., synthetic fertilizers); some are organic. The high cost of synthetic fertilizers, coupled with concerns on sustainability, has led to the search for alternatives. Biofertilizers are organisms that enrich the quality of the soil through their natural processes and are commonly bacteria, fungi and cynobacteria (blue-green algae). Some of the more common types of biofertilizers include mycorrhiza, rhizobium and cyanophyceae. Natural soil already serves as a reservoir of millions of microorganisms, of which more than 85% are beneficial to plant life. Fertile soil usually consists of 93% mineral and 7% bioorganic substances.

Among the myriad of biofertilizers in use today, the use of mycorrhiza fungi to enhance plant health has been one of the most widespread. Mycorrhizal fungi are unique root-inhabiting fungi that colonize plants externally (ectomycorrhizae) or internally (endomycorrhizae). However, the mycorrhiza fungi and its host plant share a symbiotic relationship. The many benefits which the mycorrhiza fungus confers to its host are of much significance in its vast usage as a component of commercial fertilizers. According to Plant Health Care Inc., a leading manufacturer of biofertilizers, endomycorrhizae colonize the insides of plant root cells to benefit plants like fruits, grasses, most ornamental plants, hardwoods and fruit and nut trees.

The Biotech Consortium India Ltd. has been one of the main producers of BGA (Blue-Green Algae) biofertilizer in Asia. The BGA biofertilizer sold is a mix of different strains of BGA and carrier (cattle feed pulverized wheat straw). Elsewhere in Asia, fungi-based concoctions are commonly sold to augment synthetic fertilizers and have proven effective in maintaining high crop yields whilst reducing the overall cost of fertilizer per unit area. Several countries have, for environmental health reasons, launched campaigns to promote increased use of biofertilizers for food and plantation, commercial crops (e.g., palm oil in Malaysia), and to reduce dependency on synthetic, often imported fertilizers. The biofertilizer market is still a small one, but primed to grow in concert with increased demand for organic food, which is grown without synthetic chemicals including fertilizers. In Taiwan, the biofertilizer subsector was valued at US$4.2 million in 2003.

1.7.6 *Biopesticides*

Pests cause an estimated 20%–30% loss in production per crop harvest and the global pesticide market is a multi-billion-dollar one, valued at about US$39 billion in 2006. Almost every modern crop is produced using one or more pesticides and much has been invested in R&D to produce new plant varieties which can naturally resist pests and diseases. Most of the pesticides in current use are synthetic petrochemicals, hence their cost to growers has risen in response to the increase in oil prices.

Pesticides are regulated by governments, but often their misuse has had negative effects on human health and also on ecosystems. Biopesticides are considered a safe alternative and preferred in the growing of organic food. Biopesticides have received increased global attention from the late 19th and early 20th centuries and have sparked renewed attention in the 21st century due to current social issues surrounding their usage, notably, market globalization and sustainable development. Even before their commercialization, biopesticides have been prevalent in nature, with more than 2,000 plant species with insecticidal properties having been characterized.

The first generation of biopesticides essentially resulted from the use of readily available products, such as arsenic and its derivatives, animal oils and compounds from traditionally used plants. In the 19th century, a few compounds of plant origin were identified and used as repellents or toxins. This included alkaloids extracted from tobacco, nicotine and its isomer anabasine isolated from a plant growing in the Russian steppes and high plateaus of North Africa, and families of compounds represented by rotenone, rotenoids and pyrethrins. There are certain criteria for the selection of biopesticides for commercial use, namely, its activity, specificity, low mammalian toxicity, environmental acceptability and safety with regards to non-target organisms.

The value of the global insecticide market for 1998 was estimated to be approximately \$15 billion, of which agriculture made up 60% and industrial uses (including consumers) 40%. Estimates of the total market commanded by botanical insecticides are difficult to come by, but it is probably fair to say that botanicals hold less than 1% of the global insecticide market (i.e., < \$150 million). Among botanicals, pyrethrum enjoys a dominant place, likely constituting 75%–80% of the total. Neem insecticides are expected to challenge pyrethrum in the market. Pesticides based on plant essential oils are, in commercial terms, in their infancy. However, botanicals may well see annual sales growth of 10%–15% or greater, in contrast to the shrinking market for traditional synthetic insecticides. At present, registered products for insect control include 104 products on the market (mostly *Bacillus thuringiensis*), nematodes (44 products), fungi (12 products), viruses (8 products) and protozoa (6 products). Commercialization in developing countries is limited but growing.

The future of the biopesticide industry seems to be bright. The industry is expected to grow 5.4% annually from 2005 to 2009, led by gains in the Asia-Pacific region.

1.7.7 *Biofuels*

Biofuels are fuel sources that utilize biomass to produce bioenergy in order to provide a wide variety of energy services and to produce biomaterials as substitutes for those presently manufactured from petrochemicals. Biofuels could be an integrating response to a number of global problems including equity, development, energy supply severity, rural employment and climate change mitigation. Biomass provides fuel flexibility to match a wide range of energy demands and is a renewable energy source that can be stored, which is an advantage over several other forms of renewable energy.

Two principal biofuels are currently in use — bioethanol produced from sugar cane, corn and other starchy grains; and biodiesel produced from oil sources such as palm oil, soybean and rapeseed.

The global production of biofuel is estimated at about 45 million liters for bioethanol (or about 3% of global gasoline needs) and 4 million liters for biodiesel (insignificant proportion of global needs). In 2005, Brazil, the USA and China, in descending order, were the top three producers of bioethanol, while Germany, France and the USA were similarly so for biodiesel.

Many predictions have been made about Asia's need for increased energy and fuel as countries in the region modernize and industrialize. As such, many countries are expected to turn to biofuels as an important source of energy in lieu of the current global shortage of fossil fuels. Brazil has probably the longest experience with blending bioethanol into fuel for motor vehicles, which, by some accounts, meets almost half the country's fuel needs.

In Asia, several countries have embarked on accelerated programs to produce biofuel, notably the giant countries of China and India, and also ASEAN countries like Malaysia, Thailand, the Philippines and Singapore. China has always been one of the major players in the Asian biofuel scene. The Chinese government has consistently attached great importance to new and renewable sources of energy development and utilization. Their 21st century agenda emphasized that renewable energy would be the basis of the future energy structure, and that renewable energy development should be preferred in national energy strategies. The government of India has also given high priority to the development of renewable energy.

Energy crops are important to long-term energy strategies because they can be expanded to significantly shift the pattern of world energy supply. Volumes of other forms of waste biomass available are limited as they are by-products of other processes. Plant species that can be grown as energy crops and used for bioenergy purposes are so diverse that they can be grown in virtually every part of the world. Representative energy plant species, apart from those currently used, that have been proposed for tropical and subtropical climates include: Aleman grass (*Echinochloa polystachya*), Babassu palm (*Orbignya oleifera*), Bamboo (*Bambusa spp.*), Banana (*Musa spp.*), Black locus (*Robinia pseudoacacia*), Brown beetle grass (*Leptochloa fusca*), Castor oil plant (*Ricinus communis*), Coconut palm (*Cocos nucifera*), Jatropha (*Jatropha curcas*), Jute (*Crocorus spp.*), Leucaena (*Leucaena leucoceohala*) and the Neem tree (*Azadirachta indica*).

As is the case with algae cultivation for biofuel, many of the proposed and current plant species for biofuel extraction have not undergone as much R&D to select for higher oil yields as has been done for the selection of other agronomic traits. Scientists have estimated that conventional breeding may lead to 15%–20% increases in oil yield in the mid-term, with higher increases possible with genetic engineering. This is a very promising arena with great potential for huge value capture.

1.7.8 *Bioremediation*

Industrial and farming activities have contaminated large tracts of land with toxic chemicals such as arsenic, mercury or high levels of salts, making the land uninhabitable or unsuitable for crops. Fresh water bodies have similarly been contaminated. While mechanical and chemical cures are known for removing the toxic or unwanted chemicals, governments are increasingly searching for environmentally friendly techniques to "clean up" polluted lands and waters. One such set of techniques is collectively called "bioremediation", or the use of microbes, plants or their enzymes to remedy contaminated land and water. An appealing feature of bioremediation is that the contaminated soil or water may be acted upon by organisms *in situ* (i.e., without removing them from their original site).

Several types of bioremediation techniques are in use; in the case where plants are used to clean up the environment, the technique is called "phytoremediation" — phytoextraction, phytodegradation, phytotransformation, phytostabilization and rhizofiltration (use of plant roots to reduce contamination in wetlands and estuaries). Phytoextraction is a popular technique, and much experience has been accumulated and shared within the scientific community to use specific plants for cleaning soil contaminated with heavy metals; the plant material is subsequently removed from the locale and incinerated.

About 400 plants have been reported to hyperaccumulate metals. The families dominating these members are Asteraceae, Brassicaceae, Caryophyllaceae, Cyperaceae, Cunouniaceae, Fabaceae, Flacourtiaceae, Lamiaceae, Poaceae, Violaceae and Euphobiaceae. Brassicaceae (this family includes cabbage) has the largest number of different genera known to accumulate different metals. Nickel hyperaccumulation is reported in 7 genera and 72 species, and zinc accumulation in 3 genera and 20 species. *Thlaspi* species are known to hyperaccumulate more than one metal. Specifically, *T. caerulescence*, a species of *Thlaspi*, is known to accumulate heavy metals such as cadmium, nickel, lead and zinc. Another species of *Thlaspi*, *T. goesingense*, is known for its accumulation of nickel and zinc. *T. ochroleucum* has been known to phytoremediate nickel and zinc, while *T. rotundifolium* has been discovered to supersede the former with an additional phytoremediation ability of accumulating lead.

Several common aquatic species also have the ability to remove heavy metals from water, e.g., water hyacinth (*Eichhornia crassipes* (Mart.) Solms) and duckweed (*Lemna minor* L.). Microbes that are known to degrade pesticides and hydrocarbons generally are exemplified by species like *Pseudomonas* and *Alcaligenes*, which use the contaminant as a source of energy and carbon. Even mushroom fungi such as *Phanaerochate chrysosporium* have been shown capable of degrading environmental pollutants. Laboratory studies in Singapore have shown that common ferns (*Pteris vittata* and *Pityrogramma calomelanos*) are able to bioaccumulate arsenic at levels significantly higher than those found in the environment. One by-product of phytoextraction is the recovery of valuable metals from the metal-rich ash, which serves as a source of revenue and offsets the expense of remediation, which often requires many cropping cycles to reduce metal concentrations to acceptable levels.

As a plant-based technology, the success of phytoextraction is inherently dependent upon proper plant selection. Plants used for phytoextraction must be fast growing and have the ability to accumulate large quantities of environmentally important metal contaminants in their shoot tissue or leaf. Genetic variation in metal-accumulating ability is known within populations of the same plant. In Asia, there is much ongoing R&D in countries like China, Pakistan and India where large tracts of land are unusable due to chemical contamination.

Bioremediation is not a new phenomenon, but modern science has made it a potentially powerful ally by improving the efficiency of the organisms concerned, either using conventional selection or through genetic improvement. Much "upside" has yet to be exploited and can be done only through further investments in R&D.

1.7.9 *Novel bioscience enterprises based on genetic engineering (genetically modified plants and biotech crops)*

About a decade ago, a significant new phenomenon emerged on the agriculture scene — biotech seeds (also known as genetically modified seeds), in which new traits had been introduced using the new tools of biotechnology such as "gene-splicing". Despite controversy over the use of such "gene-splicing" techniques, the uptake of biotech

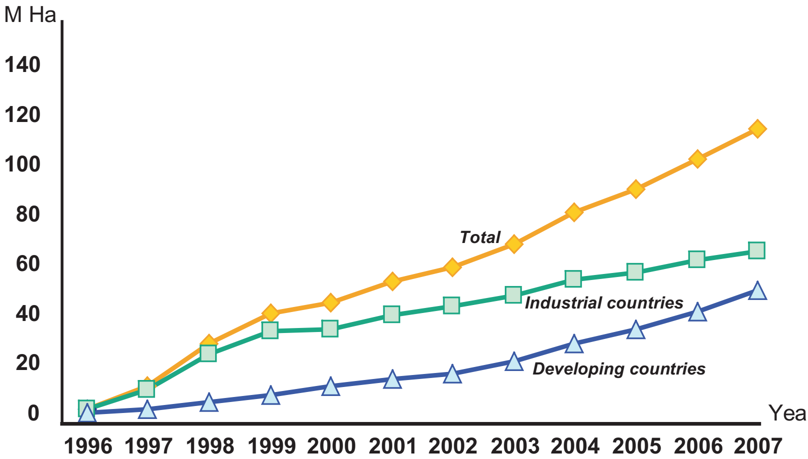

Figure 1.5. Global area of biotech crops, 1996–2007: Industrial and developing countries (million hectares).

Source: James (2007).

seeds has been remarkable and many independent academic studies have shown their value to poor farmers and commercial growers alike, as well as attesting to their biosafety and food/feed safety. The international non-profit organization based at Cornell University in the USA, called the International Service for the Acquisition of Agribiotech Applications (or ISAAA), has documented this remarkable phenomenon (Figure 1.5).

The global area with biotech seeds is now about 114 million hectares, a double digit percent increase each year since its first commercial planting in 1996. And this has been achieved with only four major crops — corn, cotton, soybean and canola — planted in 23 countries by over 10 million farmers. During that period, the share value of the leading biotech seed company, Monsanto, more than quadrupled over its IPO value. Worldwide, over 670 seed products have been approved by some 53 countries for safe use by consumers, including countries in the European Union! As a bioscience enterprise, biotech seeds have created much wealth for many companies and individuals. However, the potential has only been marginally tapped.

Many private and government-funded institutions are actively researching applications of biotech for plants, creating traits such as the following in new varieties:

- Agronomic Traits for
    - Biotic stress
        - Insect resistance
        - Disease resistance viral, bacterial, fungal, nematode
        - Weed-herbicide tolerance
    - Abiotic stress
        - Drought, cold, heat, poor soils
    - Yield
        - Nitrogen assimilation, starch biosynthesis, O2 assimilation
- Quality Traits for
    - Processing
    - Shelf-life
    - Reproduction: e.g., seedlessness
    - Nutrients (Nutraceuticals)
        - Macro: protein, carbohydrates, fats
        - Micro: vitamins, antioxidants, minerals, isoflavonoids, glucosinolates, phytoestrogens, lignins, condensed tannins
        - Anti-nutrients: phytase, allergen and toxin reduction
    - Taste
    - Architecture
    - Fiber
    - Ornamentals: color, shelf-life, morphology, fragrance
- Novel Crop Products for
    - Oils
    - Proteins: nutraceuticals, therapeutics, vaccines
    - Polymers
- Renewable Resources: biomass conversion, feedstocks, biofuels.

Various estimates put the untapped potential in US$ billions of new value creation to those who take out the IP protection. Again, in this arena, the countries and their institutions which exercise the most innovation are those most likely to reap the benefits.

1.8 Who are the Players in Bioscience Enterprises? (Private versus Public)

The range of bioscience enterprises has seen differential roles for the public and private sectors. Raw commodities such as rice, wheat, soybeans and corn initially saw much public sector investment. But this has gradually been replaced by the private sector, especially with soybean and corn. There is almost no public sector investment in corn or soybean R&D in the USA, the world's largest producer. Rice, because it is such a sensitive crop for food security in Asia, remains much in the hands of the public sector, with some companies entering into hybrid seed production only relatively recently. The other bioscience enterprises, from tissue culture to biotech seeds, are dominated by small-medium enterprises (SMEs) and MNCs. It is noteworthy that in Asia, governments have belatedly invested more into R&D than the private sector, and in crops which companies have ignored because of difficulties with capturing value. These crops have sometimes been called "orphan crops", for example cassava and sweet potato.

Biotech seeds have grown significantly in total value since their commercial introduction a decade ago. About 90% of the total number of approved biotech seed products today are owned by a handful of private entities which have been able to capitalize on their "first-entry" advantage arising from investments in R&D and market development — Monsanto, Bayer CropScience, Aventis Crop Science, Syngenta Seeds, Dow AgroSciences, Pioneer (DuPont), DeKalb and Hoechst/AgrEvo. Data from various public databases such as AGBIOS (www.agbios.com) show that the remaining 14% are owned by nine private companies (Agritope Inc.; Bejo Zaden BV; Calgene Inc.; DNA Plant Technology Corporation; Florigene Pty Ltd.; Mycogen (Dow AgroSciences); Plant Genetic Systems; Vector Tobacco Inc.;

Zeneca Seeds) and six public institutions (Beijing University; Cornell University; Chinese Academy of Agricultural Sciences; Huazhong Agricultural University; Societe National d'Exploitation des Tabacs et Allumettes; University of Saskatchewan).

These companies have been willing to share their IP through technology licensing agreements with SMEs in different parts of the world and even with government institutions. The royalty fees arising from such licensing is substantial and although the price of seed is higher than the equivalent non-biotech seed, growers have been willing to purchase on the potential of higher and more stable yields. The total value of biotech seeds has increased by some 5,000% in one decade, and the share equity of some of the pioneering companies has seen similar spectacular increases, creating much wealth for some of the early investors.

1.9 The Issue of Intellectual Property Protection for Biological Material and Processes

Consolidations in the form of acquisitions, mergers and alliances have been a noted feature of the biotechnology industry. Since 1996, more than 25 major acquisitions and alliances valued at $15 billion have taken place among agrobiotech, seed and farm chemical firms (James, 2004). While these are expected to result in increased efficiencies for the private sector, it raises fears of dominance and of marginalization of the role of public sector institutions charged with helping the "poorest of the poor". The challenge to both sectors is on identifying common ground for action to benefit resource-poor farmers, based on the common vision of ensuring food security for both the rural and urban population.

One issue that epitomizes social and ethical concern about biotechnology is intellectual property protection. Multinational companies are increasing their ownership of biological material, which will be protected by patents, relative to the public sector. Supporters of patenting point out that if the private sector is to mobilize and invest large sums of money in biotechnology R&D for agriculture, it must protect and recoup what it has put in. This is especially so when the returns to investment in agriculture do not compare as favorably as with pharmaceuticals. On the other side of the argument is fear that patenting will lead to monopolization of knowledge, restricted access to germplasm, controls over the research process, selectivity in research focus, and increasing marginalization of the majority of the world's population (Serageldin, 1999).

The new developments in biotechnology and information technology have forced a reexamination of the traditional roles of the public sector relative to the private. This has affected crops which traditionally have been only of interest to the public sector, such as rice; opportunities for the private sector started with the introduction of hybrid rice but is now extending possibly into biotech rice.

When the US Supreme Court upheld a patent in 1980 for a genetically engineered bacterium, it probably triggered what is now called by some as a new "gold rush" to own genes. An illustration of the proprietary nature of future rice varieties is given for *B.t.*-rice with resistance to stemborers — an insect-resistant rice variety could have as many as seven patents associated with it. This new situation has caused much discussion within international fora with regards to its impact on plant breeders' rights (PBR) and farmers' rights protected by conventions such as UPOV. Most Asian countries as yet do not have patent protection for biological material, although plant varietal protection laws exist. The direct effect of intellectual property protection on germplasm exchange is likely to be the requirement for companies or institutions using proprietary material to acknowledge its use in some way. It is also likely that trade issues will become intermingled with development objectives, especially in resource-poor countries.

The concerns about private sector domination of the factors of agricultural production cannot and must not be ignored. Effective regulatory mechanisms and safeguards need to be universal so that the impact of biotechnology is both productive and benign. Intellectual property protection and private sector participation in research are keys to continued technological innovations, but there is also a moral obligation to ensure that scientific research helps address the needs of poor people and safeguards the environment for future generations.

It should also be noted that a small number of public institutions have taken out IP protection on their genetic resources as well. Protection of intellectual property rights encourages private sector investment, but in developing countries, the needs of smallholder farmers and environmental conservation are unlikely to attract private funds. Public investment will be needed, and new and imaginative public-private collaboration can make the gene revolution beneficial to developing countries (Serageldin, 1999).

1.10 Outlook on Bioscience Products for the Marketplace — A New Playing Field and the New Agriculture

Bioscience enterprises reflect not only the dynamic changes occurring in science and technology throughout Asia, but also the infective spirit of entrepreneurship spreading throughout the region. In the past decade, many Asian nations, notably the so-called "Tigers", have invested heavily in building science capacity in educational institutions at all levels, and leveraged that by similar investments in technology capacity. Countries like Singapore and Korea have purposely targeted specific sectors, such as the Life Sciences, for exploitation. The goal has been to broaden the base of the current economies through future diversification beyond current strengths like manufacturing and ICT.

As the demand for basic commodities such as food, fiber and fuel continues, so too will the need for creative solutions to their supply through bioscience entrepreneurship. Innovation in products and processes will likely increase as the creative pursuits in science and technology start showing results in more countries within Asia. Asia as a region currently accounts for only a small fraction of all the patents filed worldwide. Again, there are purposeful efforts to improve on this and on related indices of research performance.

Table 1.5. Relative investment effort for major bioscience enterprises in Asia.

	Small-Medium Enterprises	Multinational Companies	Government Public Institutions
Biocommodities	+++	+++	+++
Hybrid Seeds	++	+++	+
Tissue Culture	+++	+++	+
Biofermentation	+	+++	+
Biodegradation	+++	++	+
Biofertilizers	+++	+	+
Biopesticides	+++	+	+
Biofuels	+	+++	+
Bioremediation	++	+	++
Biodetection	+++	+	+
Biotech Seeds	+	++	+++

The outlook is for a tighter link between creativity, innovation and enterprises.

Asia has great need for the products arising from bioscience enterprises. The relative investments in different biosciences suggest that there is much opportunity for growth (Table 1.5).

Education to participate in the exciting opportunities from rapid knowledge change in the biosciences is likely to be a key factor influencing success. The outstanding performance of several Asian countries in international assessments (such as the "Trends in International Mathematics and Science Study" or TIMSS), and in the regular international science olympiads, augurs well for the future. Without this sound base of science and mathematics education, it will be difficult to imagine competitive ability in the global marketplace.

"Today's students need to learn Biology..."

"We have entered a time of continuous learning, and the biotech revolution will require more of that from more of us than at any time in history."

— Richard W. Oliver in *The Biotech Age*, 2003

Annex: Brief Chronology of the Biotechnology Revolution

(Adapted from www.abc.net.au/science/features/biotech/default.htm; www.isaaa.org)

- 1973 — The discovery that created modern biotechnology. *Herb Boyer and Stanley Cohen showed it was possible to take a human gene and put it in a bacterium that could then mass produce quantities of that gene. This immediately opened up enormous industrial possibilities by presenting an easy way to mass produce hormones.*
- 1975 — *The Alsilomar conference of 1975 was where the first safety regulations for biotechnology were hammered out.*
- 1976 — World's first genetic engineering company is formed. *Herb Boyer teamed up with a venture capitalist to form Gentech, with the goal of genetically modifying bacteria to produce human insulin. Gentech was the world's first genetic engineering company and Boyer became the first molecular multi-millionaire.*
- 1978 — Scientists win Nobel Prize for discovering biological "snips" for DNA. *The 1978 Nobel Prize for Medicine went to Dr Hamilton Smith and Dr Daniel Nathans of Johns Hopkins University in America, and Prof Werner Arber of Switzerland. The prize was awarded for discovering enzymes that are like biological scissors. The enzymes cut DNA into pieces, an essential tool in genetic research and fundamental for Boyer and Cohen's 1973 breakthrough.*
- 1980 — First biotechnology patent granted. *In 1980, Cohen and Boyer were awarded a US patent for gene cloning that allowed them to make human insulin from genetically modified (GM) bacteria. Also in 1980, a landmark decision by the US Supreme Court granted a patent for a GM bacterium that could break down oil.*
- 1980 — Genetically engineered vaccine created. *In 1980, a vaccine for hepatitis B was genetically engineered. Hepatitis B was a major cause of liver disease and the genetically engineered vaccine, along*

with genetically engineered drugs, were immediately popular. People could see the advantages of the medical applications of biotechnology and accepted the new vaccines and drugs.

- 1983 — Genetically modified organism (GMO) approved for environmental release. *In 1983, Dr Stephen Lindow from Berkeley in the USA was given approval to release the first GM bacteria into the environment. Bacteria living on potato plants made the plants sensitive to frosts. Lindow wanted to release GM bacteria, which did not make the plants frost-sensitive, to compete with the non-GM bacteria on the leaves of potato plants; the potato plants were able to withstand temperatures as low as minus five degrees.*
- 1984 — Scientists stumble upon DNA fingerprinting. *Alec Jeffries from the University of Leicester in the UK created the first DNA fingerprint while researching the evolution of genes. Also in the 1980s, Nobel Prize winner Kary Mullis came up with an idea leading to the development of a technique called polymerase chain reaction (PCR). PCR is a technique that replicates a sample of DNA and enables scientists to amplify or multiply DNA from a sample as small as a single cell. The potential of PCR and DNA fingerprinting were quickly realized and used for fighting crime as well as establishing family and evolutionary relationships.*
- 1987 — GM foods start to grow. *In 1987, Dr Mike Bevan, from the Institute of Plant Research in Cambridge in the UK, grew genetically modified potatoes. Genes were added to potato plants to make them produce more protein and increase their nutritional value. Research into other foods included supplementing rice with vitamin A and removing allergy-causing proteins from peanuts.*
- The 1990s — *In the past decade, GM crops became commercialized and spread to many countries through double digit percent growth in planted area each year. Dolly the sheep was cloned and scientists finished a draft of the human genome.*
- Early 2000s — *Several genomes of public interest are mapped, e.g., human, rice.*
- 2006 — *Biotech crops exceed 100 million hectares planted by farmers in 22 countries. More than 500 plant-based biotech seed products are approved by regulatory agencies in 51 countries for public use.*

References

James, C. (2004). Global review of commercialized biotech/GM crops: 2004. ISAAA Brief No. 32. Ithaca, New York.

James, C. (2007). Global status of commercialized biotech/GM crops: 2007. ISAAA Brief No. 37. Ithaca, New York.

National Innovation Agency (NIA), Thailand (2006). *Potential World Markets for Innovative Rice Businesses in Thailand*. NIA, MOST. (www.nia.or.th)

Oliver, R.W. (2003). *The Biotech Age*. McGraw-Hill.

Ridley, M. (1999). *Genome: The Autobiography of a Species in 23 Chapters*. London: Fourth Estate.

Serageldin, I. (1999). Biotechnology and food security in the 21st century. *Science*, 285: 5426.

Woese, C.R. (2004). A new biology for a new century. *Microbiology and Molecular Biology Reviews*, 68(2): 173–186.