TRANSGENIC PLANTS AND WORLD AGRICULTURE

Report prepared under the auspices of the Royal Society of London, the U.S. National Academy of Sciences, the Brazilian Academy of Sciences, the Chinese Academy of Sciences, the Indian National Science Academy, the Mexican Academy of Sciences and the Third World Academy of Sciences.

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This report was prepared by a working group representing the Royal Society of London, U.S. National Academy of Sciences, Brazilian Academy of Sciences, Chinese Academy of Sciences, Indian National Science Academy, Mexican Academy of Sciences, and Third World Academy of Sciences. The individual members of the working group are listed at the end of this report. The co-sponsoring academies wish to thank the Royal Society of London for providing staff coordination, meeting facilities, and travel support for academy delegates. The Council of the U.S. National Academy of Sciences has discussed this report and commends it to interested parties.

The report also is available online at **http://www.nap.edu/html/transgenic**

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PREFACE

During the 21st century, humankind will be confronted with an extraordinary set of challenges. By 2030, it is estimated that 8 billion persons will populate the world—an increase of 2 billion people from today's population. Hunger and poverty around the globe must be addressed, while the life-support systems provided by the world's natural environment are maintained. Meeting these challenges will require new knowledge generated by continued scientific advances, the development of appropriate new technologies, and a broad dissemination of this knowledge and technology along with the capacity to use it throughout the world. It will also require that wise policies be implemented through informed decision making on the part of national, state, and local governments in each nation.

Scientific advances require an open system of information exchange in which arguments are based on verifiable evidence. Although the primary goal of science is to increase our understanding of the world, knowledge created through science has had immense practical benefits. For example, through science, we have developed a more complete understanding of our natural environment, improved human health with new medicines, and discovered specific plant genes that control disease or drought resistance.

Biotechnology can be defined as the application of our knowledge and understanding of biology to meet practical needs. By this definition, biotechnology is as old as the growing of crops and the making of cheeses and wines. Today's biotechnology is largely identified with applications in medicine and agriculture based on our knowledge of the genetic code of life. Various terms have been used to describe this form of biotechnology including genetic engineering, genetic transformation, transgenic technology, recombinant DNA technology, and genetic modification technology. For the purposes of this report, which is focused on plants and products from plants, the term genetic modification technology, or GM technology, is used.

GM technology was first developed in the 1970s. One of the most prominent developments, apart from the medical applications, has been the development of novel transgenic crop plant varieties. Many millions of hectares of commercially produced transgenic crops such as soybean, cotton, tobacco, potato and maize have been grown annually in a number of countries, including the United States (28.7 million hectares in 1999), Canada (4 million hectares), China (0.3 million hectares), and Argentina (6.7 million hectares) (James 1999). However, there has been much debate about the potential benefits and risks that may result from the use of such crops.

The many crucial decisions to be made in the area of biotechnology in the next century by private corporations, governments, and individuals will affect the future of humanity and the planet's natural resources. These decisions must be based on the best scientific information in order to allow effective choices of policy options. It is for this reason that representatives of seven of the world's academies of science have come together to provide recommendations to the developers and overseers of GM technology and to offer scientific perspectives to the ongoing public debate on the potential role of GM technology in world agriculture.

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SUMMARY

It is essential that we improve food production and distribution in order to feed and free from hunger a growing world population, while reducing environmental impacts and providing productive employment in low-income areas. This will require a proper and responsible utilization of scientific discoveries and new technologies. The developers and overseers of GM technology applied to plants and micro-organisms should make sure that their efforts address such needs.

Foods can be produced through the use of GM technology that are more nutritious, stable in storage, and in principle health promoting—bringing benefits to consumers in both industrialized and developing nations.

New public sector efforts are required for creating transgenic crops that benefit poor farmers in developing nations and improve their access to food through employment-intensive production of staples such as maize, rice, wheat, cassava, yams, sorghum, plantains and sweet potatoes. Cooperative efforts between the private and public sectors are needed to develop new transgenic crops that benefit consumers, especially in the developing world.

Concerted, organized efforts must be undertaken to investigate the potential environmental effects—both positive and negative—of GM technologies in their specific applications. These must be assessed against the background of effects from conventional agricultural technologies that are currently in use.

Public health regulatory systems need to be put in place in every country to identify and monitor any potential adverse human health effects of transgenic plants, as for any other new variety.

Private corporations and research institutions should make arrangements to share GM technology, now held under strict patents and licensing agreements, with responsible scientists for use for hunger alleviation and to enhance food security in developing countries. In addition, special exemptions should be given to the world's poor farmers to protect them from inappropriate restrictions in propagating their crops.

The Need for GM Technology in Agriculture

Today there are some 800 million people (18% of the population in the developing world) who do not have access to sufficient food to meet their needs (Pinstrup-Anderson and Pandya-Lorch 2000; Pinstrup-Anderson et al. 1999), primarily because of poverty and unemployment. Malnutrition plays a significant role in half of the nearly 12 million deaths each year of children under five in developing countries (UNICEF 1998). In addition to lack of food, deficiencies in micro-nutrients (especially vitamin A, iodine and iron) are widespread. Furthermore, changes in the patterns of global climate and alterations in use of land will exacerbate the problems of regional production and demands for food. Dramatic advances are required in food production, distribution and access if we are going to address these needs. Some of these advances will occur from non-GM technologies, but others will come from the advantages offered by GM technologies.

Achieving the minimum necessary growth in total production of global staple crops—maize, rice, wheat, cassava, yams, sorghum, potatoes and sweet potatoes—without further increasing land under cultivation will require substantial increases in yields per acre. Increases in production are also needed for other crops, such as legumes, millet, cotton, rape, bananas and plantains.

It is important to increase yield on land that is already intensively cultivated. However, increasing production is only one part of the equation. Income generation, particularly in low-income areas, together with the more effective distribution of food stocks, are equally, if not more, important. GM technologies are relevant to both these elements of food security.

In developing countries, it is estimated that about 650 million of the poorest people live in rural areas where the local production of food is the main economic activity. Without successful agriculture, these people will have neither employment nor the resources they need for a better life. Farming the land, and in particular small-holder farming, is the engine of progress in the rural communities, particularly of less developed countries.

The domestication of plants for agricultural use was a long-term process with profound evolutionary consequences for many species. One of its most valuable results was the creation of a diversity of plants serving human needs. Using this stock of genetic variability through selection and breeding, the “Green Revolution” produced many varieties that are used throughout the world. This work, carried out largely in publicly supported research institutions, has resulted in our present high-yielding crop varieties. A good example of such selective breeding was the introduction of “dwarf” genes into rice and wheat, which in conjunction with fertilizer applications, dramatically increased the yield of traditional food crops in the Indian sub-continent, China and elsewhere. Despite past successes, the rate of increase of food crop production has decreased recently (yield increase in the 1970s of 3% per annum has declined in the 1990s to approximately 1% per annum) (Conway and Toennissen 1999). There are still heavy losses of crops owing to biotic (e.g., pests and disease) and abiotic (e.g., salinity and drought) stresses. The genetic diversity of some crop plants has also decreased and there are species without wild relatives with which to cross breed. There are fewer options available than previously to address current problems through traditional breeding techniques, although it is recognized that these techniques will continue to be important in the future.

Increasing the amount of land available to cultivate crops without having a serious impact on the environment and natural resources is a limited option. Modern agriculture has increased production of food, but it has also introduced large-scale use of pesticides and fertilizers that are expensive and can potentially affect human health or damage the ecosystem. A major challenge faced by humankind today is how to increase world food production and people's access to food, which requires local and employment-intensive staples production, without further depleting non-renewable resources and causing environmental damage. In other words, how do we move towards sustainable agricultural practices that do not compromise the health and economic well-being of current and future generations? In order to think in terms of sustainable agriculture, factors responsible for soil, water and environmental deterioration must be identified and corrective measures taken.

Research on transgenic crops, as with conventional plant breeding and selection by farmers, aims selectively to alter, add or remove a character of choice in a plant, bearing in mind regional needs and opportunities. It offers the possibility of not only bringing in desirable characteristics from other varieties of the plant, but also of adding characteristics from other unrelated species. Thereafter the transgenic plant becomes a parent for use in traditional breeding. Modification of qualitative and quantitative characteristics, such as the composition of protein, starch, fats or vitamins by modification of metabolic pathways, has already been achieved in some species. Such modifications increase the nutritional status of the foods and may, in some characteristics, help to improve human health by addressing malnutrition and under-nutrition. GM technology has also shown its potential to address micro-nutrient deficiencies and thus reduce the national expenditure and resources required to implement current supplementation programs (Texas A&M University 1997). These nutritional improvements have rarely been achieved previously by traditional methods of plant breeding.

Transgenic plants with important traits such as pest and herbicide resistance are most necessary where no inherent resistance has been demonstrated within the local species. There is intense research on the development of resistance to viral, bacterial, and fungal diseases; modification of plant architecture (e.g., height) and development (e.g., early or late flowering or seed production); tolerance to abiotic stresses (e.g., salinity and drought); production of industrial chemicals (plant-based renewable resources); and the use of transgenic plant biomass for novel and sustainable sources of fuel. The benefits from transgenic plants under study include increased flexibility in crop management, decreased dependency on chemical insecticides and soil disturbance, enhanced yields, easier harvesting and higher proportions of the crop available for trading. For the consumer this should lead to decreased cost of food and higher nutritive value.

A large proportion of developing world agriculture is in the hands of small-scale farmers whose interests must be taken into account. Concerns regarding GM technology range from its potential impact on human health and the environment to concerns about private sector monopolies of the technology. It is essential that such concerns are addressed if we are to reap the potential benefits of this new technology.

We conclude that steps must be taken to meet the urgent need for sustainable practices in world agriculture if the demands of an expanding world population are to be met without destroying the environment or natural resource base. In particular, GM technology, coupled with important developments in other areas, should be used to increase the production of main food staples, improve the efficiency of production, reduce the environmental impact of agriculture, and provide access to food for small-scale farmers.

EXAMPLES OF GM TECHNOLOGY THAT WOULD BENEFIT WORLD AGRICULTURE

GM technology has been used to produce a variety of crop plants to date, primarily with "market-led" traits, some of which have become commercially successful. Developments resulting in commercially produced varieties in countries such as the United States and Canada have centered on increasing shelf life of fruits and vegetables, conferring resistance to insect pests or viruses, and producing tolerance to specific herbicides. While these traits have had benefits for farmers, it has been difficult for the consumers to see any benefit other than, in limited cases, a decreased price owing to reduced cost and increased ease of production (Nelson et al. 1999; Falck-Zepeda et al. 1999).

A possible exception is the development of GM technology that delays ripening of fruit and vegetables, thus allowing an increased length of storage. Farmers would benefit from this development by increased flexibility in production and harvest. Consumers would benefit by the availability of fruits and vegetables such as transgenic tomatoes modified to soften much more slowly than traditional varieties, resulting in improved shelf-life and decreased cost of production, higher quality and lower cost. It is possible that farmers in developing countries could benefit considerably from crops with delayed ripening or softening, as this may allow them much greater flexibility in distribution than they have at present. In many cases small-scale farmers suffer heavy losses due to excessive or uncontrolled ripening or softening of fruit or vegetables.

The real potential of GM technology to help address some of the most serious concerns of world agriculture has only recently begun to be explored. The following examples show how GM technology can be applied to some of the specific problems of agriculture, indicating the potential for benefits.

Pest Resistance

There is clearly a benefit to farmers if transgenic plants are developed that are resistant to a specific pest. For example, papaya-ringspot-virus-resistant papaya has been commercialized and grown in Hawaii since 1996 (Gonsalves 1998). There may also be a benefit to the environment if the use of pesticides is reduced. Transgenic crops containing insect-resistance genes from *Bacillus thuringiensis* have made it possible to reduce significantly the amount of insecticide applied on cotton in the United States. One analysis, for example, showed a reduction of 5 million acre-treatments (2 million hectare-treatments) or about 1 million kilograms of chemical insecticides in 1999 compared with 1998 (U.S. National Research Council 2000). However, populations of pests and disease-causing organisms adapt readily and become resistant to pesticides, and there is no reason to suppose that this will not occur equally rapidly with transgenic plants. In addition, pest biotypes are different in various regions. For instance, insect resistant crops developed for use in the United States and Canada may be resistant to pests that are of no concern in developing countries, and this is true both for transgenic plants and those developed by conventional breeding techniques. Even where the same genes for insect or herbicide resistance are useful in different regions, typically these genes will need to be introduced into locally adapted cultivars. There is need, therefore, for more research on transgenic plants that have been made resistant to local pests to assess their sustainability in the face of increased selection pressures for ever more virulent pests.

Improved Yield

One of the major technologies that led to the "Green Revolution" was the development of high-yielding semi-dwarf wheat varieties. The genes responsible for height reduction were the Japanese NORIN 10 genes introduced into Western wheats in the 1950s (Gibberellin-insensitive-dwarfing genes). These genes had two benefits: they produced a shorter, stronger plant that could respond to more fertilizer without collapsing, and they increased yield directly by reducing cell elongation in the vegetative plant parts, thereby allowing the plant to invest more in the reproductive plant parts that are eaten. These genes have recently been isolated and demonstrated to act in exactly the same way when used to transform other crop plant species (Peng et al. 1999). This dwarfing technique can now potentially be used to increase productivity in any crop plant where the economic yield is in the reproductive rather than the vegetative parts.

Tolerance to Biotic and Abiotic Stresses

The development of crops that have an inbuilt resistance to biotic and abiotic stress would help to stabilize annual production. For example, rice yellow mottle virus (RYMV) devastates rice in Africa by destroying the majority of the crop directly, with a secondary effect on any surviving plants that makes them more susceptible to fungal infections. As a result this virus has seriously threatened rice production in Africa. Conventional approaches to the control of RYMV using traditional breeding methods have failed to introduce resistance from wild species to cultivated rice. Researchers have used a novel technique that mimics "genetic immunization" by creating transgenic rice plants that are resistant to RYMV (Pinto et al. 1999). Resistant transgenic varieties are currently about to enter field trials to test the effectiveness of their resistance to RYMV. This could provide a solution to the threat of total crop failure in the Sub-Saharan African rice growing regions.

Numerous other examples could be given to illustrate the range of current scientific research, including transgenic plants modified to combat papaya ringspot virus (Souza 1999), blight resistant potatoes (Torres et al. 1999), and rice bacterial leaf blight (Zhai et al. 2000); or as an example of an abiotic stress, plants modified to overproduce citric acid in roots and provide better tolerance to aluminum in acid soils (de la Fuente et al. 1997). These examples have clear commercial potential but it will be imperative to maintain publicly funded research in GM technology if their full benefits are to be realized. For example, while GM technology provides access to new gene pools for sources of resistance, it needs to be established that these sources of resistance will be more stable than the traditional intra-species sources.

Use of Marginalized Land

A vast land-mass across the globe, both coastal as well as terrestrial, has been marginalized because of excessive salinity and alkalinity. A salt tolerance gene from mangroves (*Avicennia marina*) has been identified, cloned and transferred to other plants. The transgenic plants were found to be tolerant to higher concentrations of salt. The gutD gene from *Escherichia coli* has also been used to generate salt-tolerant transgenic maize plants (Liu et al. 1999). Such genes are a potential source for developing cropping systems for marginalized lands (M.S. Swaminathan, personal communication 2000).

Nutritional Benefits

Vitamin A deficiency causes half a million children to become partially or totally blind each year (Conway and Toennissen 1999). Traditional breeding methods have been unsuccessful in producing crops containing a high vitamin A concentration and most national authorities rely on expensive and complicated supplementation programs to address the problem. Researchers have introduced three new genes into rice—two from daffodils and one from a micro-organism. The transgenic rice exhibits an increased production of beta carotene as a precursor to vitamin A and the seed is yellow in color (Ye et al. 2000). Such yellow, or golden, rice may be a useful tool to help treat the problem of vitamin A deficiency in young children living in the tropics.

Iron fortification is required because cereal grains are deficient in essential micro-nutrients such as iron. Iron deficiency causes anemia in pregnant women and young children. About 400 million women of child-bearing age suffer as a result, and they are more prone to stillborn or underweight children and to mortality at childbirth. Anemia has been identified as a contributing factor in over 20% of maternal deaths (after giving birth) in Asia and Africa (Conway 1999). Transgenic rice with elevated levels of iron has been produced using genes involved in the production of an iron-binding protein and in the production of an enzyme that facilitates iron availability in the human diet (Goto et al. 1999; Lucca 1999). These plants contain 2-4 times the levels of iron normally found in non-transgenic rice, but the bioavailability of this iron will need to be ascertained by further study.

Reduced Environmental Impact

Water availability and efficient usage have become global issues. Soils subjected to extensive tillage (ploughing) for controlling weeds and preparing seed beds are prone to erosion, and there is a serious loss of water content. Low tillage systems have been used for many years in traditional communities. There is a need to develop crops that thrive under such conditions, including the introduction of resistance to root diseases currently controlled by tillage and to herbicides that can be used as a substitute for tillage (Cook 2000). Applications in more developed countries show that GM technology offers a useful tool for the introduction of root disease resistance for conditions of reduced tillage. However, a careful cost-benefit analysis would be needed to ensure that maximum advantage is achieved. Regional differences in agricultural systems and the potential impact of substituting a traditional crop with a new transgenic one would also need to be carefully evaluated.

Other Benefits of Transgenic Plants

First generation transgenic varieties have benefited many farmers in the form of reduced production costs, higher yields, or both. In many cases, they have also benefited the environment because of reduced pesticide usage or by providing the means to grow crops with less tillage. Insects are responsible for huge losses to crops in the field and to harvested products in transit or storage, but health concerns for consumers and for environmental impact have limited the registration of many promising chemical pesticides. Genes for pest resistance, carefully deployed in crops to avoid selecting for future pest resistance, provide alternative opportunities to reduce the use of chemical pesticides in many important crops. In addition, lowering the contamination of our food supply by pathogens that cause food safety problems (e.g., mycotoxins) would be beneficial to farmers and consumers alike.

Pharmaceuticals and Vaccines from Transgenic Plants

Vaccines are available for many of the diseases that cause widespread death or human discomfort in developing countries, but they are often expensive both to produce and use. The majority must be stored under conditions of refrigeration and administered by trained specialists, all of which adds to the expense. Even the cost of needles to administer vaccines is prohibitive in some countries. As a result the vaccines often do not reach those in most need. Researchers are currently investigating the potential for GM technology to produce vaccines and pharmaceuticals in plants. This could allow easier access, cheaper production, and an alternative way to generate income. Vaccines against infectious diseases of the gastro-intestinal tract have been produced in plants such as potato and bananas (Thanavala et al. 1995). Another appropriate target would be cereal grains. An anti-cancer antibody has recently been expressed in rice and wheat seeds that recognizes cells of lung, breast and colon cancer and hence could be useful in both diagnosis and therapy in the future (Stoger et al. 2000). Such technologies are at a very early stage in development and obvious concerns about human health and environmental safety during production must be investigated before such plants can be approved as specialty crops. Nevertheless, the development of transgenic plants to produce therapeutic agents has immense potential to help in solving problems of disease in developing countries.

About one-third of medicines used today are derived from plants, one of the most famous examples being aspirin (the acetylated form of a natural plant product, salicylic acid). It is believed that less that 10% of medicinal plants have been identified and characterized, and the potential exists to use GM technology in a way that increases yields of these medicinal substances once identified. For example, the valuable anti-cancer agents vinblastine and vincristine are the only approved drugs for treatment of Hodgkin's lymphoma. Both products are derived from the Madagascar periwinkle, which produces them in minute concentrations along with 80-100 very similar chemicals. The therapeutic compounds are therefore extremely expensive to produce. Currently, there is intensive research in progress to investigate the potential of GM technology to increase the yields of active compounds, or to allow their production in other plants that are easier to manage than the periwinkle (Leech et al. 1998).

We recommend that transgenic crop research and development should focus on plants that will (i) improve production stability; (ii) give nutritional benefits to the consumer; (iii) reduce the environmental impacts of intensive and

extensive agriculture; and (iv) increase the availability of pharmaceuticals and vaccines; while (v) developing protocols and regulations that ensure that transgenic crops designed for purposes other than food, such as pharmaceuticals, industrial chemicals, etc. do not spread or mix with either transgenic or non-transgenic food crops.

TRANSGENIC PLANTS AND HUMAN HEALTH AND SAFETY

Through classical plant breeding techniques, present day cultivated crops have become significantly different from their wild counterparts. Many of these crops were originally less productive and at times unsuitable for human consumption. Over the years traditional plant breeding and selection of these crops have resulted in plants that are more productive and nutritious. The advent of GM technology has allowed further development. To date, over 30 million hectares of transgenic crops have been grown and no human health problems associated specifically with the ingestion of transgenic crops or their products have been identified. However numerous potential concerns have been raised since the development of GM technology in the early 1970s. Such concerns have focused on the potential for allergic reactions to food products, the possible introduction or increase in production of toxic compounds as a result of the GM technology, and the use of antibiotic resistance as markers in the transformation process.

Every effort should be made to avoid the introduction of known allergens into food crops. Information concerning potential allergens and natural plant toxins should be made available to researchers, industry, regulators, and the general public. In order to facilitate this effort, public databases should be developed which facilitate access of all interested parties to data.

Traditional plant breeding methods include wide crosses with closely related wild species and may involve a long process of crossing back to the commercial parent to remove undesirable genes. A feature of GM technology is that it involves the introduction of one or, at most, a few well-defined genes—rather than the introduction of whole genomes or parts of chromosomes as in traditional plant breeding. This makes toxicity testing for transgenic plants more straightforward than it is for conventionally produced plants with new traits, because it is much clearer what the new features are in the modified plant. On the other hand, GM technology can introduce genes from diverse organisms, some of which have little history in the food supply.

Decisions regarding safety should be based on the nature of the product, rather than on the method by which it was modified. It is important to bear in mind that many of the crop plants we use contain natural toxins and allergens. The potential for human toxicity or allergenicity should be kept under scrutiny for any novel proteins produced in plants with the potential to become part of food or feed. Health hazards from food, and how to reduce them, are an issue in all countries, quite apart from any concerns about GM technology.

Since the advent of GM technology, researchers have used antibiotic resistance genes as selective markers for the process of genetic modification. The concern has been raised that the widespread use of such genes in plants could increase the antibiotic resistance of human pathogens. Kanamycin, one of the most commonly used resistance markers for plant transformation, is still used for the treatment of the following human infections: bone, respiratory tract, skin, soft-tissue, and abdominal infections, complicated urinary tract infections, endocarditis, septicemia, and enterococcal infections.

Scientists now have the means to remove these marker genes before a crop plant is developed for commercial use (Zubko et al. 2000). Developers should continue to move rapidly to remove all such markers from transgenic plants and to utilize alternative markers for the selection of new varieties. No definitive evidence exists that these antibiotic resistance genes cause harm to humans, but because of public concerns, all those involved in the development of transgenic plants should move quickly to eliminate these markers.

Ultimately, no credible evidence from scientists or regulatory institutions will influence popular public opinion unless there is public confidence in the institutions and mechanisms that regulate such products.

We recommend that: (i) public health regulatory systems need to be put in place in every country to identify and monitor any potential adverse human health effects of transgenic plants, as for any other new variety. Such systems must remain fully adaptable to rapid advances in scientific knowledge. The possibility of long-term adverse effects should be kept in view when setting up such systems. This will require coordinated efforts between nations the sharing of experience and the standardization of some types of risk assessments specifically related to human health; (ii) information should be made available to the public concerning how their food supply is regulated and its safety ensured.

TRANSGENIC PLANTS AND THE ENVIRONMENT

Modern agriculture is intrinsically destructive of the environment. It is particularly destructive of biological diversity, notably when practiced in a very resource-inefficient way, or when it applies technologies that are not adapted to environmental features (soils, slopes, climatic regions) of a particular area. This is true of both small-scale and large-scale agriculture. The widespread application of conventional agricultural technologies such as herbicides, pesticides, fertilizers and tillage has resulted in severe environmental damage in many parts of the world. Thus the environmental risks of new GM technologies need to be considered in the light of the risks of continuing to use conventional technologies and other commonly used farming techniques.

Some agricultural practices in parts of the developing world maintain biological diversity. This is achieved by simultaneously cultivating several varieties of a crop and mixing them with other secondary crops, thus maintaining a highly diverse community of plants (Toledo et al. 1995; Nations and Nigh 1981; Whitmore and Turner 1992).

Most of the environmental concerns about GM technology in plants have derived from the possibility of gene flow to close relatives of the transgenic plant, the possible undesirable effects of the exotic genes or traits (e.g., insect resistance or herbicide tolerance), and the possible effect on non-target organisms.

As with the development of any new technology, a careful approach is warranted before development of a commercial product.

It must be shown that the potential impact of a transgenic plant has been carefully analyzed and that if it is not neutral or innocuous, it is preferable to the impact of the conventional agricultural technologies that it is designed to replace (Campbell and Cooke 1993; May 1999; Toledo et al. 1995).

Given the limited use of transgenic plants worldwide and the relatively constrained geographic and ecological conditions of their release, concrete information about their actual effects on the environment and on biological diversity is still very sparse. As a consequence there is no consensus as to the seriousness, or even the existence, of any potential environmental harm from GM technology. There is therefore a need for a thorough risk assessment of likely consequences at an early stage in the development of all transgenic plant varieties, as well as for a monitoring system to evaluate these risks in subsequent field tests and releases.

Risk assessments need base line information, including the biology of the species, its ecology and the identification of related species, the new traits resulting from GM technology, and relevant ecological data about the site(s) in which the transgenic plant is intended to be released. This information can be very difficult to obtain in highly diverse environments. Centers of origin or diversity of cultivated plants should receive careful consideration because there will be many wild relatives to which the new traits could be transferred (Ellstrand et al. 1999; Mikkelsen et al. 1996; Scheffler et al. 1993; Van Raamsdonk and Schouten 1997). For special environments, transgenic plants can be developed using technologies that minimise the possibilities of gene flow via pollen and its effects on wild relatives, through the use of male sterility methods or maternal inheritance resulting from chloroplast transformation (Daniell 1999; Daniell et al. 1998; Scott and Wilkinson 1999).

Studies of gene transfer from conventional and transgenic plants to wild relatives and other plants in the ecosystem have so far concentrated on species of economic importance such as wheat, oilseed rape and barley. A virtual absence of data, particularly for species like maize, imposes the need to carefully and continuously monitor any possible effects of novel transgenic plants in the field (Hokanson et al. 1997; Daniell et al. 1998). In addition there is a continued need for research on the rates of gene transfer from traditional crops to indigenous species (Ellstrand et al. 1999).

When monitoring a small-scale pilot release of a transgenic crop the following issues should be considered in addition to any concerns specific to a particular local environment:

(a) Does the existence of a transgenic plant with resistance for a particular pest or disease exacerbate the emergence of new resistant pests or diseases, and is this problem worse than that with the traditional alternative? (Riddick and Barbosa 1998; Hillbeck et al. 1998; Birch et al. 1999).

(b) If traits (e.g., salt tolerance, disease resistance, etc.) are transferred to wild varieties, is there an expansion in the niche of these species that may result in the suppression of biological diversity in the surrounding areas?

(c) Would the widespread adoption of stress-tolerant plants promote a considerable increase in the use of land where formerly agriculture could not be practiced in a way that destroys valuable natural ecosystems?

The risk assessments performed should be standardized for plants new to an environment. Most nations already have procedures for the approval and local release of new varieties of crop plants. Although these assessments are based primarily on the agronomic performance of the new variety compared with existing varieties, this approval process could serve as the beginning or model for a more formal risk assessment process to investigate the potential environmental impact of the new varieties, including those with transgenes.

Historically, both poverty and structural change in rural areas have resulted in severe environmental deterioration. The adoption of modern biotechnology should not accelerate this deterioration. It should instead be used in a way that reduces poverty and its deleterious effects on the environment.

We recommend that: (i) coordinated efforts be undertaken to investigate the potential environmental effects, both positive and negative, of transgenic plant technologies in their specific applications; (ii) all environmental effects should be assessed against the background of effects from conventional agricultural practices currently in use in places for which the transgenic crop has been developed or grown; and (iii) *in situ* and *ex situ* conservation of genetic resources for agriculture should be promoted that will guarantee the widespread availability of both conventional and transgenic varieties as germplasm for future plant breeding.

FUNDS FOR RESEARCH ON TRANSGENIC CROPS - THE BALANCE BETWEEN PUBLIC AND PRIVATE SECTOR

The public sector and charitable foundations funded the national and international crop research in the post-war period that led to doubling or tripling crop yields in large parts of Asia and Latin America, along with gains in employment and nutrition in the developing world. The dwarf wheat and rice plants and other high-yielding varieties which were at the center of this "Green Revolution" met the needs of millions of poor farmers and consumers.

The balance of funding for this kind of research has shifted significantly during the past decade from the public to the private sector, and there has been a corresponding reduction in national, non-commercial agricultural research capacity that needs to be reversed. Substantial public-sector agricultural research still exists, however, notably in North America, Australia, Europe, China, India, Brazil, and in the Consultative Group for International Agricultural Research (CGIAR) system. The CGIAR system comprises 16 international research centers with interests that include wheat and maize (Mexico), rice (Philippines), potatoes (Peru), and millet and sorghum (India), but the financial support for the CGIAR has been declining in real terms. Whereas fundamental research is still being carried out in the public sector, the strategic application, in sharp contrast to the "Green Revolution," takes place largely in the private sector where much of the intellectual property is controlled.

In these circumstances, research priorities are driven by market forces (e.g., price signals). Companies produce products whose costs are recoverable in the marketplace. There are also goods that benefit society as a whole rather than individuals and whose costs cannot be recovered in the marketplace (so-called public goods). Public sector funding is needed for such public-good work (Stiglitz 1993). A classic example of a public good would be an improved plant that can be propagated by farmers with little deterioration, as with self-pollinated (e.g., wheat and rice), or vegetatively propagated (e.g., potatoes) crops. If such crop improvement research were left to normal markets for private provision, then it would be systematically under-supplied. This is a typical feature.

The main reason why aid donors and foundations support international agricultural research is to ensure that public-good research of relevance to small-scale farmers and to complex tropical and subtropical environments is undertaken. If such research were wholly private, even in a perfectly functioning market, the demands of rich consumers for innovation in their own interests would overwhelm the price signals from poor consumers and small-scale farmers.

Given the limited resources so far available to them for research, the non-commercial (public and charitable foundation) sectors have achieved more than could have been expected (e.g., beta-carotene-enhanced rice and rice resistant to the yellow mottle virus).

We recommend that: (i) governments should fully recognize that there will always be public interest/goods research requiring public investment even in the market-driven economy; it is imperative that public funding of research in this area is maintained at least at its present level in both CGIAR and national research institutions; (ii) governments, international organizations and aid agencies should acknowledge that plant genomics research is a legitimate and important object for public funding, and that the results of such research should be placed in the public domain;

(iii) innovative and vigorous forms of public-private collaboration are urgently required if the benefits of GM technologies are to be brought to all the world's people; (iv) incentives are needed to encourage commercial research companies to share with the public sector more of their capacity for innovation; and (v) care should be taken so that research is not inhibited by over-protective intellectual property regimes.

CAPACITY BUILDING

The development of a strong capability in the plant sciences is an absolute priority for all national research programs. This is necessary because only local plant breeding can address local agricultural environments and only local initiatives can appreciate cultural preferences. It is very likely that genes and gene functions will, as our understanding grows, be increasingly transferable between crops and between agricultural environments. However, in order for these genes to be incorporated into adapted, tested, safe and effective varieties, a sustained local research capacity will be necessary. This is equally true whether the genes are transferred by GM technology or by conventional breeding.

The international research centers (those under CGIAR sponsorship) and national research programs must use partnerships with advanced research institutions to increase their efforts to extend the new GM technologies to crops such as bananas, plantains, beans, sorghum, wheat, maize, cassava and potatoes, which are important resources for many countries. These centers should also take a lead in developing alliances with advanced and strategic research institutions, both public and private, in order to ensure the transfer of the appropriate technologies. In addition, the new communications technologies should be vigorously supported to facilitate the free exchange of knowledge and best practices among the world's agricultural research and farming communities.

If world agriculture, and developing countries in particular, are to benefit from the many potential advantages of GM technology, it will be important to promote capacity building in risk management. In order to be effective, the following objectives must be included:

(a) Build sufficient scientific and technical human resources in each country to enable it to assess the relative benefits and the risks of GM technology;

(b) Strengthen local and global infrastructure;

(c) Monitor and evaluate the short-, mid- and long-term effects of transgenic plants and share data between all relevant countries;

(d) Develop simple techniques to readily and reliably distinguish non-transgenic and transgenic plants where necessary.

We recommend that: (i) national governments ensure that endogenous capacities are built up to facilitate the implementation of biosafety guidelines or regulations; (ii) the safe development, transfer and application of biotechnology require that nations develop and/or strengthen policies, facilities, information systems, and training in biotechnology (including risk-assessment, risk-management and biosafety procedures); (iii) nations involved in the development, use, release or production of transgenic plants should have the means to assess and manage the potential risks and the benefits; (iv) as considered in the recently agreed UN Cartagena Protocol on Biosafety, an overarching body should maintain and disseminate a public database that includes all newly released varieties and their performance in different environments.

INTELLECTUAL PROPERTY

Current industrial biotechnology is primarily oriented to the needs of large-scale commercial agriculture, rather than to those of the subsistence farmer. Most developing countries lack the financial resources and are limited in the scientific infrastructure needed to develop their own biotechnology programs for the crops that are important to feed their people. The long-term decline of public agricultural research, the increasing privatization of GM technologies, and the growing emphasis on the crops and priorities of the industrialized nations do not bode well for feeding the increasing populations of the developing world. As noted previously, without changed incentives for sharing access to GM technologies, the world is unlikely to direct much of its research for improved nutrition and employment-based access to staples for the poor.

The application of modern genomics research techniques to plant species promises an explosion of new knowledge and information that may lead to important new advances in agricultural production and the quality, quantity and variety of food products. Actual realization of these advances will depend to a significant extent on both publicly and privately funded research and on the development efforts of commercial companies supported by private investment. As in other areas of biotechnology, intellectual property rights are likely to play an important role in securing economic returns for the intellectual and financial investments that make the research and developments possible. An important consideration regarding such intellectual property rights in inventions and discoveries resulting from genomic research and from other applications of biotechnology is that overly broad intellectual property rights should not be granted. To grant such rights would stifle further research and development. Intellectual property rights should be narrowly tailored to be commensurate with the actual scope of new inventions and discoveries so as not to impede continuing research, innovation and development.

For the above reasons, it is important to consider the impact of intellectual property rights on developing countries. To benefit the growing populations of the developing world, new plant varieties will have to be developed through a variety of sources, including: (i) farmers who select plants that succeed best in their particular locality for the retention of seed for future use or sale; (ii) public or *pro bono* research institutions financed out of taxes or charitable grants that provide improved varieties to appropriate users free or at cost; and (iii) for-profit companies interested in creating new products and markets that develop new varieties financed through profits from seed sales. As instruments of public policy, intellectual property regimes should facilitate the maximum possible innovation in development of beneficial new crop varieties through individual, public and corporate sources, as well as promote research collaboration.

Special attention should be paid to international conventions that may affect innovation in agriculture. These conventions include Trade Related Intellectual Property (TRIPs), patent law, plant variety protection and the Convention on Biological Diversity. To be effective, these conventions should be consistent with each other so as to reduce any distortions in the promotion of innovation by farmers, public research institutions, and for-profit corporations. At present, it appears that many less developed countries are reluctant to join in international intellectual property agreements on plants because they believe that such agreements will create a system that strongly favors the corporate sector—while simultaneously hampering the public and private sector efforts that support their own citizens. In fact, many of the intellectual property rights that exist today in industrialized nations apply to the tools used in research and development to produce new transgenic plant varieties. If the rights to these tools are strongly and universally enforced—and not extensively licensed or provided *pro bono* in the developing world—then the potential applications of GM technologies described previously are unlikely to benefit the less developed nations of the world for a long time (i.e., until after the restrictions conveyed by these rights have expired).

Private companies today can obtain plant varieties free of charge from farmers and from non-commercial institutions such as the CGIAR, add one or more proprietary traits, and then release seed with a variety of forms of legal or technical protection against copying, farm retention, or farm-to-farm transmission. Thus, a market-based system exists, based in part on non-reimbursed contributions from farmers and institutions such as the CGIAR. This heavily concentrates advances in research within companies whose legitimate search for profit naturally fails to focus their research on poverty and long-term sustainability issues. Transgenic plants have intensified the dilemma because a high level of skill and infrastructure is needed to develop them. Moreover, broad patents have been granted to companies that secure their competitiveness in the market place. To help compensate, public-sector research by farmers, the CGIAR, and by national agricultural research systems needs to be strengthened and provided with increased resources and attention—both from governments and from the world's agricultural scientists. In addition, intellectual property rights should be obtained by these public-sector institutions for their discoveries so that these rights can be used in negotiations with the private sector to produce increased public benefit.

Intensive agriculture requires the use of certified seed (i.e., seed free of pathogens, pests, and weeds) and growers purchase new seed every year as an established practice. Most growers plant hybrid varieties of maize (corn) and other crops that are more uniform and vigorous than ordinary varieties because of heterosis (hybrid vigor) and these advantages are lost when second generation seed is used. In addition, some growers are under contract with food processors who demand specific quality standards that require new seed to be purchased annually. However, for some crops (e.g., soybeans) many growers save seed to plant in subsequent years (seed re-use) until reduced yields induce them to buy new seed.

Saving seed is often not an optimal practice for reasons related to the contamination of seed with pests and pathogens. In developing countries, government programs often attempt to provide clean seed at affordable prices. However, in many instances, small growers cannot afford to purchase new seed every year, and they wish to maintain their long-standing practice of saving some of the seed from one year's crop in order to plant next year's crop. Historically, fertility and reproduction of grain crops in Africa, Asia and parts of the Americas have acquired a deep spiritual significance. Seeds are exchanged freely and are given away to travelers from far away lands. In any case, it is clear that growers in developing counties feel strongly that it is their right to decide whether to use their own seed or purchase fresh certified seed (Nuffield Council on Bioethics 1999). The general public would seem to be very much on the side of the growers on this issue.

To ensure financial return for their investments, many biotechnology seed companies have sought to prevent the use of second-generation seed produced from transgenic crops. For example, growers who purchase transgenic plant seeds are often required to sign contracts that specifically prohibit the saving and replanting of second-generation seed.

Over the long term, the most significant form of intellectual property protection for seeds may prove to be technological. A specific example of this that has been the source of much controversy is a patent application for an invention whereby traits in transgenic plants would be expressed only if a certain chemical activator was applied to seeds or plant (genetic use restriction technology, GURT) (Oliver et al. 1995). This technology involves the use of a chemical treatment of seeds or plants that either inhibits or activates specific genes involved in germination. One technology would involve a complex three-gene system whereby one gene produces a protein that interferes with proper plant embryo development, thus preventing seed germination. The expression of this gene is allowed by applying tetracycline (or other chemicals) which prevents a recombinase gene from being repressed by an induced protein. Once the recombinase is expressed after tetracycline application, a blocking sequence placed between a transiently active promoter and the killer gene is removed, thus allowing the expression of the protein lethal to the plant embryo. The seed sold to farmers would be pre-treated with either tetracycline or other chemicals (copper, steroids, etc.).

Most experts agree that there are considerable technical problems yet to be solved and that GURT will not be available for commercialization for several years. The possible commercialization of GURT technology for controlling the use of transgenic plant seeds has generated considerable public debate, being referred to as "terminator technology." On the one hand, growers, especially in developing countries, maintain their right to retain and plant second-generation seeds. On the other, the seed companies seek to obtain a return on investment so that they can continue to invest in new technologies. Both parties, as well as the general public, have an important stake in these issues. There is a clear need for a resolution that serves the wider public interest.

In an alternative GURT, the transgenic traits would be expressed only if a certain chemical activator was applied to seeds or plants. In this case, farmers would retain the ability to save their own seed, yet lack access to the added traits in the absence of payment for chemical activators.

GURTs potentially have beneficial applications for consumers, growers, and the environment that should not be overlooked in debates over intellectual property rights. For example, GURTs could be used to prevent transgenes from spreading to closely related wild plants by preventing germination of any crossbred seeds. Furthermore, this technology could potentially eliminate the problems of "volunteer" plants that appear from seed left in the field after harvest. Volunteer plants must be eliminated before the next crop is planted because they are hosts for pests and pathogens and can nullify the benefits of crop rotation. As with any growth regulator applied to crops, there are possible environmental or human health issues associated with the use of chemical activators (i.e., tetracycline, copper, steroids) and these would need to be addressed. Other concerns regarding the use of GURT are economic, related to the intellectual property rights and the monopoly of production of transgenic plants by particular companies.

It is critical that the potential benefits of GM technology become available to developing countries. To this end, we recommend that: (i) where appropriate, farmers must be allowed to save seed for future use (re-use seed) if they wish to do so; publicly funded research should investigate the value and limitations of re-using seed and the results of this research should be made freely available to interested parties; (ii) broad intellectual property claims, or claims on DNA sequences without a true invention being made, should not be granted because they stifle research and development; (iii) possible inconsistencies among international conventions, such as those that pertain to patent rights and the Convention on Biological Diversity, should be identified and clarified; (iv) research institutions should establish partnerships among industrialized and developing countries so that the benefits of GM research, applications and licensing will become much more widely available; and (v) an international advisory committee should be created to assess the interests of private companies and developing countries in the generation and use of transgenic plants to benefit the poor—not only to help resolve the intellectual property issues involved, but also to identify areas of common interest and opportunity between private sector and public sector institutions.

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