Biological considerations for a new approach to regulating genetically modified crops in the United States

by

Ashley McDonough

A PROJECT

submitted to

Oregon State University

University Honors College

in partial fulfillment of
the requirements for the degree of

Honors Bacclaureate of Science in Biology

Presented August 2, 2006
Commencement June 2007

AN ABSTRACT OF THE THESIS OF

Ashley McDonough for the degree of Honors Bacclaureate of Science in Biology presented on August 2, 2006. Title: Biological considerations for a new approach to regulating genetically modified crops in the United States.

Abstract approved:

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Steven Strauss

The debate over GM crops is one of the most controversial issues of recent decades. The debate has many dimensions, including environmental impacts, benefits and risks to human health, intellectual property rights, adequacy of biosafety regulations, and fundamental ethical acceptability. The potential benefits of GM crops are numerous, including improved nutritional value, decreased production costs, resistance to pests, and reduced pesticide use. However, there are also substantial and complex health, environmental, and social risks, including effects on gene flow and biodiversity, creation of new toxins or allergens in food, consolidation of seed companies, and restricted access to genetic information and methods. Current US regulations are imposed only on crops produced through recombinant DNA methods, though all of these risks apply to crops modified through conventional biotechnologies as well. I argue that this current regulatory system impedes progress by presenting large obstacles to even low risk GM crops with medical and economic benefits. I suggest that a better approach would be a tiered system that takes into account the specific biological properties of the modified traits, the biology of the crops in which they are produced, and the environments in which they are grown.

KEYWORDS: GMOs, agriculture, GM crops, biotechnology, regulations

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I understand that my project will become part of the permanent collection of Oregon State University, University Honors College. My signature below authorizes release of my project to any reader upon request.

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Ashley McDonough, author

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Introduction to the Issue of Genetically Modified Crops

Genetic engineering allows scientists to select genes from a variety of species, modify them, and insert these genes into another organism. This endows an organism not only with a new segment of DNA, but with a new trait, ability, or phenotype (Table 1). An additional benefit of this technology is that it is very precise compared to traditional breeding, enabling single genes to be specifically modified (Fernandez-Cornejo and Caswell 2006). This technology is often used for a variety of purposes, such as using bacteria to produce pharmaceutical products, or to aid in basic genetic research. Genetically engineered crops are subject to governmental regulation under three agencies: the Environmental Protection Agency (EPA), the United

Table 1. Selected Definitions

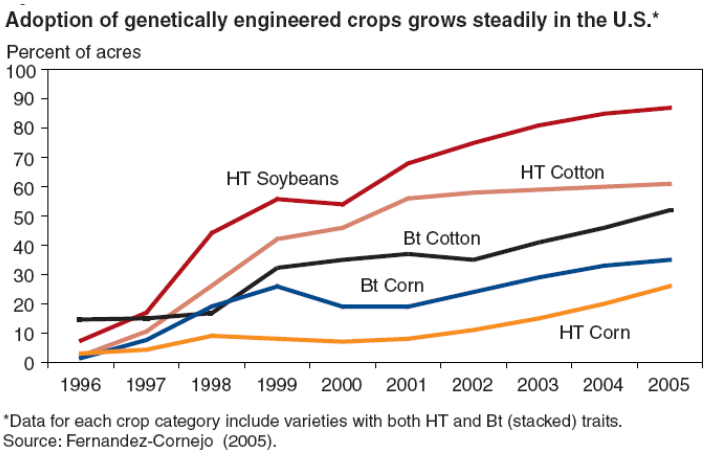
Genetic engineering[1]	The deliberate modification of the genetic material in an organism through recombinant DNA methods.
Genetically modified organism (GMO)[1]	An organism with genetic material that has been altered by genetic engineering.
Policy[2]	A set of principles to guide specific decisions.
Regulation[2]	A rule dealing with details or procedure.
Weediness[3]	The potential for undesired plants that become a nuisance in managed ecosystems such as agriculture, to successfully colonize an area.

Sources:
1 CSIRO. 2004. Glossary of Terms. <http://genetech.csiro.au>
2 Merriam-Webster Online. 2005. <www.Merriam-Webster.com>
3 AGBIOS. 2005. Weediness Potential. <http://www.agbios.com/cstudies.php?book=ESA&ev=MON810&chapter=Weediness&lang=>

States Department of Agriculture (USDA), and the Food and Drug Administration (FDA), depending on the crop and the type of modification.

Genetically modified (GM) crops are at the center of social and political debates. GM crops have become an important issue in the past decade in parallel with its rapid adoption by farmers in the United States (US) and several other countries (Figure 1, Fernandez-Cornejo and Caswell 2006). Between the years of 1999 and 2001, the total area of GM crops grown in the United States increased from 28.7 million hectares to 35.7 million hectares (Nap et al 2003). In terms of world-wide growth, the area of GM crops increased from 1.7 million hectares in 1996 to 81.0 million hectares in 2004 (Chapman and Burke 2006). However, in contrast to the increasing numbers of GM crops being grown in the United States, the number of permits for field tests issued by APHIS, a division of the USDA and one of the main regulating agencies, has decreased slightly (Figure 2). There appears to be little diversity in which kinds of crops are grown as well.

Figure 1. Increase of GM crops

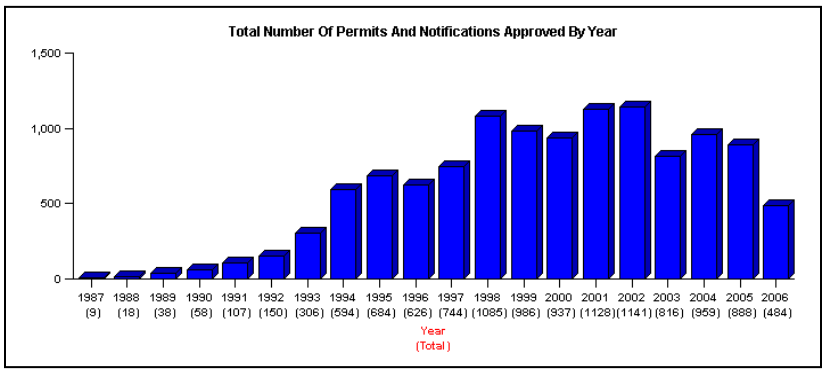


Reprinted from Fernandez-Cornejo & Caswell, USDA, 2006

A number of issues are entangled with the debate over the regulation and marketing of GM crops that touch upon economic, environmental, social, ethical, health, and safety concerns. In order to protect the health of both humans and the environment, regulations have been put in place (Madsen and Sandoe 2005). These regulations demand

a large amount of time and money for the testing and field trials of a genetically modified organism (GMO) prior to its deregulation (Potrykus 2005, Nap 2003). In some cases, this may demand large investments for a crop, between $20-30 million per product (Bradford et al 2005) that differs only very slightly from its traditionally farmed natural variety (Nap 2003). A better approach to evaluating the safety of GMOs would be to use a tiered approach that examines the biology of a newly created GM crop to determine how much testing is necessary to deem a crop safe for general agricultural use (Bradford et al 2005, Hancock 2003).

Figure 2. Number of permits and notifications issued for GM crops



Source: Information Systems for Biotechnology <http://www.isb.vt.edu/>

In this thesis the benefits and risks of GM crops will be discussed to provide background information on the debate and controversy surrounding the process of genetic engineering and the application of this technology to potential food sources. An outline of the current regulations will be provided, as well as propose guidelines for an alternative regulatory scheme as a means of reducing the regulation of low risk GM.

Perceived Risks of GMOs

Economics and International Trade

Many public and economic concerns regarding the deregulation and subsequent marketing of GM crops are important to the GMO issue. At the core of the public concerns is the concept of the consumer's right to be informed and make decisions. Repercussions of the public's right to choose have influenced governments to enact rules or legislation, imposing restrictions on crops and labeling. In the case of the European Union (EU), regulations have necessitated clear labeling and documentation in order to track genetically engineered products through shipments and across borders, which, it has been claimed, facilitates the public's ability to choose (Gray 2004). This type of legislation, coupled with market pressure from consumers and anti-GMO organizations such as Greenpeace, has effectively kept virtually all GMO foods out of the market in Europe. The testing and field trial requirements for deregulation in one country, for example the US, may not be the same as those in place in another country, such as nations of the EU, which may pose varying challenges to corporations who wish to market internationally (Nap 2003). For biotechnology companies who are seeking to expand the marketing base of their GM seeds and food products, these differing requirements create many costs and obstacles.

An example of the economic difficulties is the exportation of soybeans to Europe from the US in 1996. Included in the shipment were approximately 2% herbicide-resistant soybeans. At the time, approximately only 796 field trials had been conducted in

Europe. Uncertainty and lack of experience led to public concern and debate, which prompted action by the government. Regulations were tightened and a moratorium was issued on new approvals until regulations for GMOs had been revised and put into effect (Madsen and Sandoe 2005). In later years, the Cartagena Protocol on Biosafety was drafted by EU member nations and led to further restrictions on trade. The protocol advocates a precautionary approach towards viable GMOs, as described in the document as living modified organisms (LMOs) (UNEP 2002). The protocol outlines regulations for the transboundary movement of LMOs and is aimed at conserving biodiversity in member nations. This strict protocol on the handling and release also outlines a plan for liability in the event of the accidental release of a viable GMO into the environment, an act which is tantamount to serious pollution (UNEP 2002). The Cartagena Protocol must be taken into account by any corporation wishing to sell its seeds in a country that adheres to the protocol, as well as any farmers who wish to sell their products to such nations as it outlines approval guidelines and attributes liability.

The Ethics of Patenting Biological Material

The development of a GMO is a potentially lengthy process that necessitates a great deal of financial support. Product development takes an estimated four to eight years of scientific research and development while deregulation of a product takes an estimated additional five years. Such a process is described by Potrykus (2005) as being difficult to finance and one that provides no opportunities for scientific publication. To deregulate a product increases the amount of money a company must put into making its

product ready for the market, and also increases the time a company must wait to begin earning money back on its investment. Partly as a method of protecting these large investments, companies apply for patents on biological material or methods of processes engineering to ensure that no other individuals or companies may create a similar product that would compete on the market.

A primary ethical question that relates to this process is whether or not any one individual or corporation can own biological material. This ethical question is doubly raised as farmers may find patented genes unintentionally in their own, supposedly organic and non-modified, crops. Can such individuals sue for damages, since their agricultural products are no longer marketable in some cases, or must farmers pay the rightful owners of these genes? According to the Cartagena Protocol, which is in effect in Europe, the answer is that corporations are accountable for genetic pollution (UNEP 2002). In the US, proposed legislation along similar lines of accountability in Vermont ultimately failed (Legere 2005). Another major ethical issue concerns whether or not genes should be transferred from one species to another. This becomes particularly relevant in the issue of food safety, where concern exists when genes for cold resistance are taken from fish and inserted

Table 2

Estimated U.S. seed market shares for major field crops, 1997

Company	Corn	Soybean	Cotton
Pioneer Hi-Bred	42.0	19.0	
Monsanto[1]	14.0	19.0	11.0
Novartis	9.0	5.0	
Delta & Pine Land[2]			73.0
Dow Agrosciences/Mycogen	4.0	4.0	
California Planting Seed Distributors			6.0
All-Tex			2.0
Four largest total	69.0	47.0	92.0

[1]Monsanto acquired DeKalb in 1997 and Asgrow in 1998.
[2]The merger proposed between Monsanto and Delta & Pine Land in 1998 was called off in December 1999.
Source: Fernandez-Cornejo, 2004.

Reprinted from Fernandez-Cornejo & Caswell, USDA, 2006

into tomato plants.

Closely linked to the ethical debate over intellectual property rights and the ownership of genetic material are a number of social issues that relate to corporate behavior and monopolies. The public appears to perceive the nearly total privatization of the biotechnology industry as a threat which does not have the public's best interests in mind (Gray 2004). This privatization is demonstrated by the fact that six biotechnology firms account for nearly 80% of all GM crop field trials since 1998, and these same corporations have controlled over 40% of all biotechnology patents issued in the US since 2002 (King and Schimmelpfennig 2005). As demonstrated in Table 2, the seed market shares of the four largest biotech companies in 1997 accounted for 69% of corn, 47% of soybeans, and 92% of cotton. These figures do little to assure the public that these few corporations are acting in the best interest of the public. Furthermore, the concentration of power and races between corporations to obtain patents leave the public wondering whether the patenting of certain technology may prevent further research (Lesser 2005). The public's view of corporate behavior can be best summed up by one ecologist's remark that: "It is interesting to speculate how different the public debate might be were the genes that have been used to transform crops in public ownership." (Gray 2004) Interestingly, pharmaceutical corporations indulge in similar practices of patenting chemical compounds and medications, creating monopolies on the market with apparently little public concern.

Power in the hands of a few is not the only social concern which plagues the debate over GM crops. Often such crops are heralded as a panacea for world hunger problems (Lucca et al 2001, Potrykus 2000, Sharma 2001). The rebuttal to this is that

biotechnology corporations must seek profit rather than focus on humanitarian results. Even the proponents of GM technology point out that private sector research is unlikely to give priority to such crops, given the lack of future profits, and farmers may have to purchase new seed each year (Sharma 2001). One must also consider whether or not the target group of poor third-world country farmers will receive the technology, or whether it will it remain out of their reach due to lack of funds. The creation of several enriched crops, containing increased levels of bioavailable Vitamin A and iron, by the public sector and made available to poor farmers for free, counter these arguments (Lucca et al 2001). As technology progresses and patents expire, biotechnology being seen as a tool to aide humanitarian efforts.

Biological Concerns

Perhaps the most discussed aspect of the GMO debate is that of environmental risks. Legislation and the process of deregulation attempt to prevent harmful, or potentially harmful, products from being released into the environment. On the scientific front, scientists debate the validity of risk assessments and discuss the problems inherent in such studies. For all the ethical and abstract questions that relate to genetic engineering, the issue of potential environmental harm provides several strong and concrete problems which must be addressed to satisfy both the scientific and legislative communities. Other issues, it can be said, remain largely subjective or are based on economic data rather than scientific research into the biology and science of the process.

The environmental concerns which relate to genetically modified plants can be condensed to a few main themes such as uncertainty, fear of genetic pollution, fear of a super-weed emerging in the environment, reduced biodiversity, and unforeseen side effects. Scientists agree that gene flow can, will, and does occur (Conner 2003, Hancock 2003, Sharma 2001), but there is no agreement as to the extent of detrimental effects it may have on ecosystems. Due to variation in genes, plant biology, and environment the results of different studies can differ greatly. Measuring the rates of gene flow alone in an agricultural setting is a difficult task to accomplish because of the complexity of ecosystems and agricultural settings (Lu and Snow 2005). Determining the ecological impacts of such gene flow is then even more difficult (Conner et al 2003). These difficulties and uncertainties inherent in such studies raise questions as to the validity and extent to which conclusions can be drawn based on short-term ecological studies.

For example, in a study of gene flow between herbicide resistant canola and wild-type relatives, pollen flow from the transgenic plants to the wild-type did occur but at very low amounts. The probability of actual gene flow between the GM and non-modified versions was measured as being less than $2\text{-}5 \times 10^{-5}$, but the study concluded that the exact risks of this gene flow were undetermined and speculative at best (Legere 2005). Another study of sunflowers determined that wild-type and GM sunflowers readily hybridized and a transgene could rapidly spread through wild populations of sunflowers. However, the scientists did not expect a more invasive or weedy sunflower as a result of this hybridization (Chapman and Burke 2006). Even well-executed ecological studies can lead to ambiguous risk assessments which provide no concrete conclusions, making decisions on GM crops difficult.

Another area of concern is non-target effects of transgenic plants. For example, a maize plant with *Bacillus thuringiensis.* toxins may cause unpredicted effects on the food chain of an area by removing a food source from the ecosystem or by poisoning unintended organisms. A good study of a transgenic plant in the environment seeks to take into account as many trophic levels in an ecosystem as possible, which can be a very daunting and difficult task. In a plant with engineered insect resistance scientists must account for the biology of the insect, the mechanism by which the insecticidal proteins are toxic, and the impact that removing large numbers of this insect from the environment may have on natural enemies (Sharma 2001). Non-target organisms may include predators that may accumulate toxins by eating affected insects and/or suffering from reduced reproductive success or high death rates due to indirect consumption of pesticidal proteins present in engineered crops. However, this concern for non-target effects due to GM crops fails to take into consideration similar risks that conventional agricultural practices, such as the addition of natural or synthetic pesticides, chemicals, and manures added to the soils may have on those same insect species and trophic levels. This complexity only adds to the confusion and questionable validity of risk assessments for specific GM crops and the difficulty in assessing the significant environmental risks of certain GMOs.

There is great fear that a transgene, such as one which conveys herbicide resistance, will be transferred to a wild relative and, due to the presence of GM varieties with resistance to other herbicides and additional crossing events, breed a new species of super-weed that has resistance to multiple herbicides. In a worst case scenario, this super-weed will choke out its agriculturally profitable and nutritious counterpart on farmlands,

thereby causing great losses on the part of farmers and potentially result in a food shortage. Thus a major question in the development and early testing stages is whether or not a novel trait may or may not increase the fitness of a plant should it escape from agricultural fields. In the case of some modifications, such as domesticating traits like dwarfed varieties, a modified plant may exhibit a decreased fertility outside of the agricultural zone, effectively reducing the risk of gene flow (Conner et al 2003).

Another major concern of ecologists and the public is the threat that transgenic plants pose to biodiversity, particularly genetic biodiversity. Large expanses of monocultures are generally considered to have a low biodiversity at the genetic and species levels. In theory, fields of closely related and/or genetically identical plants increase the vulnerability of a crop and apply selective pressures on potential predators to adapt in order to better capitalize on this homogenous food source (Sharma 2001). Since monocultures are generally the norm for conventional, non-modified crops, there is further debate over whether or not the genetic homogeneity of transgenic crops is a greater threat to biodiversity than traditional agricultural production is (Conner et al 2003). Nonetheless, a lack of genetic variability and reduced biodiversity due to monocultures and transgenic crops are factors which should be taken into account for any agricultural system, whether it consists of GM crops or non-modified crops.

Another threat to biodiversity is posed by increased efficiency of weed control in fields of herbicide resistant crops. More effective control could lead to lower food availability within the ecosystem (Wolfenbarger and Phifer 2000). Evidence of increased weed control negatively impacting farmland biodiversity by reduction of weeds was demonstrated in the United Kingdom. In a study of farmlands, it was demonstrated that

weed biomass was greatly decreased in fields of some GM crops that contained herbicide resistance. Such effects were seen as negative environmental impacts, since farmlands are major reserves of biodiversity and bird habitat in the United Kingdom. Thus, without sufficient reserves to preserve biodiversity, increased weed control may, in some cases, be a negative rather than positive side effect of GM crops. However, the study also noted that modern farming practices were of concern and might have contributed to declines in farmland biodiversity, leaving the impact of GM crops on biodiversity issue open for debate (Freckleton et al 2003).

Food Safety

There is concern that *B.t.* toxins, or other genes which convey pest resistance, will create a toxic or allergenic response in humans (Sharma 2001). When genetic crossing between a transgenic plant and a non-modified strain occurs there is also some worry that the novel genetic material will disturb the entire genome, creating unknown and potentially dangerous side-effects (Mann 2002). Consumers also worry about the possibility for transgenic DNA to be toxic or easily integrated into their own genomes (SOT 2002).

No matter which method is chosen to produce a new crop, it is difficult to achieve complete safety. Even conventional foods consumed in small quantities, such as peanuts, can pose a great risk to individuals who are allergic. A complete analysis of food can be difficult, as many complex compounds are being consumed and individuals vary in their responses. It is, however, widely agreed that current GM crops intended for human

consumption pose no greater risk to human health than do their non-modified counterparts. Similar health and environmental risks exist for plants created using conventional breeding methods such as crossing with wild-relatives, mutagenesis, and irradiation. These conventional methods may introduce unexpected consequences and mutations, increase the concentration of toxins in a plant, and create other disturbances in the plant genome. However, there is surprisingly little debate about plant modifications created using these methods, which are less exact than genetic engineering. Conventional methods are, by contrast, completely free from government regulation (Bradford et al 2005). Nutritionally enhanced crops may, in fact, provide a safe and healthy alternative to conventional crops and are viewed favorably by both the American Dietetic Association (ADA) and Society of Toxicology (SOT) (ADA 2006, SOT 2002). Research data has shown no adverse health affects arising from the consumption of GM food (SOT 2002).

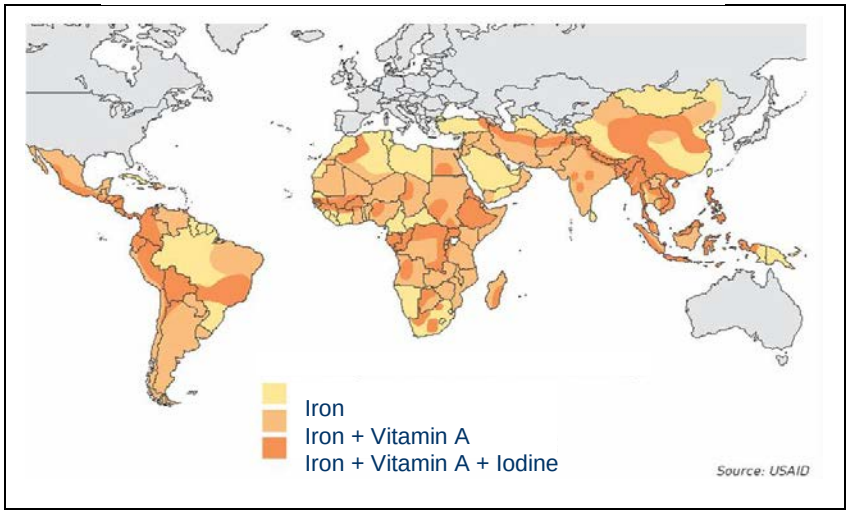
Benefits of GMOs

Humanitarian Efforts

Considering the many potential risks and social issues that surround GMOs, there must be several benefits that make it worthwhile to continue producing and deregulating GM crops. These include increased crop yields, higher protein content, improved nutritional value (e.g. increased vitamin content), tolerance to abiotic stress and adverse conditions (e.g. increased tolerance to salinity), disease resistance, herbicide resistance, and insect resistance (Ervin 2003, Lu 2005, Sharma 2001).

One of the key benefits is that these modifications could be used as a tool to combat hunger in developing countries. Of particular interest is the rice plant (*Oryza sativa*), which is a major food source for millions in developing countries. By modifying the nutritional value of the rice plant it may be possible to reduce malnutrition and the incidence of disability and death due to vitamin deficiencies. In the case of Golden Rice, scientists have modified rice so that it contains a pathway that produces provitamin A in the mature rice grain (Potrykus 2000).

Figure 3. Nutritional deficiencies across the world



According to the strain's developer, Potrykus (2000), enriching the main food source of millions could prevent at least 65,700 deaths due to vitamin A deficiency in six years time.

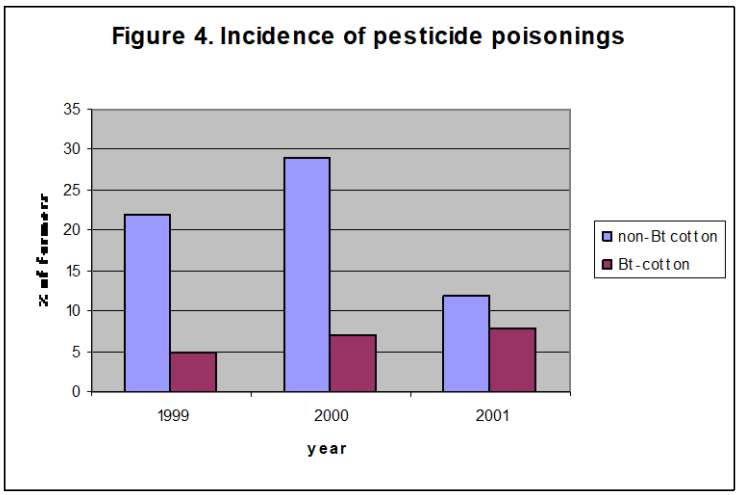
Other nutritional deficiencies of zinc, iron, and essential amino acids are of great concern in developing countries (Figure 3), affecting nearly two billion people worldwide (Pinstrup-Andersen 2000). In addition to nutrient deficiencies, more than 800 million people are food insecure (Pinstrup-Andersen 2000). For a number of nutrient deficiencies there are currently varieties of crops in development that provide nutritional assistance (Lucca et al 2001). The goal is to modify existing strains of crops to contain better nutrition and thus help ameliorate malnutrition and food insecurity in developing nations.

The effect of a single trait can be powerful. In the instance of a non-transgenic crop, traditional wheat breeding using a dwarfing gene enabled the creation of a high-yielding variety of wheat. This wheat not only had an increased yield, but it was bred to be resistant to fungus and contain certain other specific traits. The effect of modifications enabled yields to be increased from 0.75 to 8 tons per hectare (Mann 1997). The effects of plant breeding were promising enough that the same techniques were applied to other countries (Mann 1997). This is a model for how GM traits could be utilized to produce similar results.

Preservation and Conservation

While the opponents of GM crops see transgenic plants as posing a threat to the environment by way of genetic pollution, others see GM crops as providing a method of preserving the environment. While nutritional modifications to plants are possible, the more traditional uses of biotechnology are to impart crops with pest and disease resistance. While using traditional farming methods it is necessary to prevent loss of the crop by spraying to minimize pest damage, a method which requires both money and labor. However, spraying with chemical pesticides leaves residues on food and may also produce adverse non-target effects (Sharma 2001). Chemical pesticides may also contaminate the environment and the groundwater that humans depend on (Sharma 2001). The utilization of GM crops with insect resistance could reduce the further deposition of harmful chemicals into the environment. Tangible results have already been observed in the US where the deployment of insect-resistant crops led to a reduction of 1 million kg of pesticides from 1998 to 1999 (Sharma 2001). Similar results were observed in China where *B.t.* cotton reduced the use of pesticides by an average of 49.9 kg per hectare and reduced farming costs by approximately $762 per hectare per season (Huang et al. 2002). It was also reported that due to reduced costs for production of cotton and pesticide use, the cost to produce a kilogram of cotton dropped 28% following the deployment of *B.t.* cotton in China (Huang et al. 2002). Additionally, an 80% drop in the amount of toxic pesticides and chemicals used was noted, which resulted in fewer poisonings and an improvement in farmer health (Figure 6, Huang et al. 2002). To a farmer in a developing country who lacks financial resources transgenic crops with insect resistance may save a great deal of money and minimize crop losses, thereby increasing crop output and profit.

Low agricultural productivity is considered one of the major causes of poverty in developing nations (Sharma 2001). Genetic manipulation via conventional means has already created numerous strains of crops which have, in some way, been improved or optimized so that the crop yield is much higher than un-domesticated strains of plants. As discussed above, in some cases this is accomplished by creating dwarfed plants so that plants allocate less energy to plant height and more energy to seed production. In other varieties the plant's structure has been altered to more efficiently harvest light (Nap 2003). Plants which have been modified to perform under harsh abiotic conditions may increase the productivity of marginal environments. Likewise, plants resistant to diseases, fungi, and pests may have reduced mortality and increased harvest yield. These effects could lead to more efficient water usage and result in less land being converted to agriculture in order to feed growing populations (Sharma 2001). Rapidly growing demands for water have led to the concern that supplies of fresh water are becoming a scarce commodity, particularly in developing countries where little control is placed on inputs into freshwater systems (Mann 1997). There is particular concern that water may become a limiting factor in agriculture, which could place further strain on already impoverished nations struggling to produce enough



Source: Pray et al., 2002. Plant J. 31:423-430

food (Pinstrup-Andersen 2000). An increase in crop productivity could also result in fewer wild lands being settled and cultivated for agricultural purposes, resulting in conservation rather than a reduction of biodiversity. Similarly, the modification of crops to withstand abiotic stressors, such as high salinity, drought, or temperature extremes, could result in more efficient use being made of marginal landscapes (Sharma 2001). More efficient land use could also result in water conservation, less tillage, reduced carbon loss from soils, and reduced erosion (Ervin 2003, Fernandez-Cornejo and Caswell 2006).

The economic benefits of GM crops are likewise tangible and closely tied with their environmental and health benefits. By reducing the amount of chemicals introduced into the environment by pesticides and by improving health through fortified grains, several healthcare issues will have been addressed. An increase in health will lead to a better quality of life in developing countries and also reduce labor losses as a result of health problems. Pest and disease resistance will reduce the money that farmers must spend to maintain their crops, helping to enable subsistence farmers towards financial stability (Lu 2005). By ensuring a consistent supply of food that is resistant to many environmental hazards, the problem of food insecurity may be relieved to some degree by incorporating GM crops into sustainable agriculture and population growth systems, which will enable poverty-stricken nations to begin recovering (Sharma 2001).

Current Regulations

In the United States regulation of crop products is based primarily on the characteristics of the product under review, though the trigger for regulation is the process of genetic engineering. The basic philosophy behind the approach in the US is one of substantial equivalence and familiarity, or how similar the GM plant is compared to its traditional non-modified version. Factors which are considered when a plant is evaluated for risks are the plant biology, the novel trait, and the agricultural practices and environment into which it will be introduced. A newly designed transgenic plant with a novel trait must be similar or better than the non-modified strain in that it poses no new environmental risks. Additionally, toxicology reports must indicate that no toxic compounds are produced by the transgene, other than those which naturally occur in that same crop (Nap 2003).

GM crops are regulated at nearly all levels of their development and testing. Local Institutional Biosafety Committees (IBCs) oversee that conditions and safety procedures set by the National Institutes of Health (NIH) are adhered to. The next level of regulation is the USDA Animal and Plant Health Inspection Service (APHIS), which must determine whether or not a GM crop is likely to have a negative impact on the environment in field trials and releases (Bryne et al 2002). For crops that are considered low-risk, a notification must be issued to APHIS 30 days prior to planting, though for higher risk crops, such as weeds or traits that are considered risky, a permit must be applied for at least 120 days prior to the intended planting date (USDA APHIS). At this stage a number of criteria must be met in order for field testing to proceed: the genetic material must be stable in the plant genome, the new crop must be non-pathogenic to

humans and animals, and there must be a low potential for weediness (Byrne et al 2002, USDA APHIS).

The next step in the process of developing GM crops is to seek deregulation for the crop. In order for this to occur, APHIS must be petitioned for non-regulated status. A great deal of data must be provided on the effects of the transgene on the crop's biology and environmental risks. Such petitions are granted only after years of field trials (Byrne et al 2002). According to APHIS, Biotechnology Regulatory Services (BRS) has 180 days to approve the petition, although it may take longer. If BRS finds that the GM crop is unlikely to pose a greater risk than the unmodified strain from which it was created, the petition may be granted (USDA APHIS).

However, APHIS is not the sole regulatory body to which scientists must petition for deregulation and permission to plant their crops. Both the EPA and FDA have the authority to regulate a crop, depending on its properties and uses. Pest resistant crops fall under the regulation of both the EPA and APHIS since they contain plant pesticides. Toxicology reports must indicate that the crop is non-toxic to humans, and if it is toxic then threshold levels must be determined. Additionally, the EPA is concerned with environmental aspects of the introduction of this crop and its pesticides into an ecosystem. The FDA oversees the food safety aspect of GM crops and can require removal of a food from the market based on the inclusion of possible allergens or altered substances (Byrne et al 2002).

In contrast to the US, the regulatory process in the European Union is based on a precautionary approach that regards genetic engineering as a new process for which existing legislation is not adequate (Nap 2003). In the US, the products of genetic

engineering are regulated under existing regulations (Byrne et al 2002). Legislation and regulations are based on the process in which a GMO is created. Information for approval of a GM crop in the EU is more extensive than in the US, mainly in respect to monitoring and traceability. The procedures and reports needed for deregulation in the EU make commercial release of any GM crop lengthy and an unappealing endeavor for many corporations (Nap 2003), particularly when approval may take up to ten years in some cases (Madsen and Sandoe 2005). While it may be appealing and conceivable, due to relaxed constraints, for a corporation to produce and market a crop in the US, the precautionary approach of the EU makes the marketing and deployment of many crops wholly unappealing due to the amount of time and money that must be invested in the process of deregulation. The risk must also be taken that approval will not be granted at all.

Other nations take different approaches to modified crops. For instance, in Canada not only are transgenic crops subject to monitoring and regulation, but so are phenotypically novel crops which have been produced using traditional plant breeding methods (Nap 2003). On the other end of the regulatory spectrum is China, whose government funds programs on a large scale to develop transgenic crops for commercial use (Jia and Peng 2002). The decision to fund such programs was based on the need for technology that did not depend on foreign nations to provide seed and genes, as well as to allow Chinese scientists to focus on crops of national importance and maximum benefit to local farmers (Huang et al. 2002).

Support for a tiered approach

The techniques of genetic engineering have the potential to quickly and precisely change crops by introducing new genetic material into the genomes of plants which allows some of the limitations of plant breeding to be overcome (Lu and Snow 2005). This potential is demonstrably immense, ranging from increased nutritional value to allowing farmers make more efficient use of land (Sharma 2001). The process of regulation for GM crops appears to have been made based on the scientific community's uncertainty as to what information would be needed and relevant in years to come (Pinstrup-Andersen 2000). However, there comes a point when regulations must be updated in the face of new information. Although there are potential risks associated with genetically modified crops, there is also a wealth of information and years of experience on genetics and plant breeding that enables classifications of safety to be made based on biological criteria.

The process of deregulation as outlined in a presentation by Potrykus (2005) illustrates the reality of regulatory procedures. Golden Rice was first created in 1999 after years of product development, but due to field testing and regulatory procedures it may not be deregulated and on the market until sometime between 2007 and 2009 at the earliest. As part of the regulatory process and applications, a crop undergoes exposure evaluation, protein production and equivalence testing, molecular characterization, expression profiling, phenotype analysis, compositional analysis, and an environmental risk assessment. All this data can take years to produce and then reproduce in many regions and countries. In addition to the deregulation process being lengthy, it is also

financially costly which may impede the development of crops which could be useful tools in combating malnutrition and starvation in third world countries (Bradford et al 2005).

A number of criteria must exist in order for gene flow to occur between agricultural crops and wild-type relatives. First, relatives must exist that can interbreed with the genetically modified plant (Hancock 2003). Flowering times must be synchronous to some degree, in order that pollen from one crop may fertilize plant species outside the agricultural system (Legere 2005). In addition to this crucial requirement, hybrid offspring of GM and wild-type relatives of the crop must also be viable, that is, the seeds must be able to survive and mature into fertile plants to pass along the transgenes and promote the spread of the novel gene into wild populations (Chapman and Burke 2006). Numerous studies have concluded that the environmental risks of many kinds of GM crops are low despite the occurrence of gene flow and pollen drift (Jia and Peng 2002, Legere 2005). Furthermore, other studies have noted that transgenic crops do not persist longer than non-modified strains, which alleviates worries that all GM crops may become more invasive and persistent in the environment (Chapman and Burke 2006).

Another biological consideration is the fitness of the GMO compared to the wild-type or non-modified strain when the two escape from an agricultural setting. Some traits may be engineered into crops which have neutral or beneficial effects while that plant is in the agricultural environment. However, if the transgenic plant spreads into the wild or a hybrid is produced that contains this trait, the effect is detrimental to the plant's survival and it may not survive to reproduce and spread the transgene. In order to prevent the

proliferation of transgenes and hybrids a strategy may be employed in which a detrimental gene is paired with a beneficial one, preventing such plants and hybrids from being able to sufficiently compete with wild-type relatives and thus reducing the spread of genetically modified material (Chapman and Burke 2006). Most traits associated with domesticated crops, the results of years of plant breeding, are similarly deleterious to crops when they are introduced into the wild (Hancock 2003). If it is unlikely that non-modified domestic crops would escape into the environment and proliferate, if a GM crop is similar or lower in fitness than its non-modified counterpart there is no increased risk of invasiveness.

Based on considerations such as the presence of wild relatives, flowering times, and the nature of certain traits, the possibility exists to develop a new framework for the testing and approval of genetically modified crops based on biological criteria. This more individualized approach would take into account: 1) whether or not the potential existed for spread of the transgene to even occur based on whether or not compatible relatives are even present in the environment. If such relatives did exist, the biology would have to be examined to assess the risk and probability of gene flow occurring. Considerations would be flowering time as well as the nature of the trait. 2) If the trait would prove detrimental in the wild, then it would be of less regulatory concern than a trait that conferred an observable advantage in the wild. Admittedly, such an evaluation would need to be repeated for each introduction of the crop into a new region. However, even this necessity would still streamline the process and reduce the amount of time and money necessary to deregulate GM crops.

Proposals for new deregulation schemes

The difficulty in choosing which biological criteria to base the decision to deregulate on comes from disagreements in opinions as to what is important. A regulatory scheme by Hancock (2003) ranks both crops and the novel trait. Crops are ranked on a scale of S-1 to S-6 (Table 3), where S-1 crops have no compatible relatives present in the ecosystem, S-3 crops have no wild relatives but possess weediness traits, and S-6 crops have compatible wild relatives and/or many weediness traits. In addition to ranking crops by invasiveness and presence of wild relatives, Hancock's proposal also considers the trait that has been introduced (Table 4). Traits are ranked T-A through T-E, where T-A means the trait is neutral, T-B means the trait is detrimental in the native environment, and a rating of T-E suggests that the trait could be advantageous to the plant in its native environment.

Table 3. Risk categories based on biological characteristics of crop

Category (S)	Characteristics	Examples	Gene flow risk
1	Few to no weedy traits	Cotton, potato, soybean, tomato	No compatible relative(s) present
2	Intermediate number of weedy traits, low risk of escape	Peanuts, beans	
3	Many weedy traits, risk of escape and persistance	Barley, wheat	
4	Few to no weedy traits, low risk of escape	Maize, tobacco	Compatible relative(s) present
5	Intermediate number of weedy traits, moderate risk of escape	Strawberry, blueberry, carrot	
6	Many weedy traits, easily escapes and persists	Oats, rapeseed, rice, sunflower	

Source: Hancock, J. F. Bioscience 53: 512 - 519

Table 4. Risk categories by trait

Category (T)	Impact of Trait on Fitness (when in native habitat)	Example
A	Neutral	Marker genes (herbicide tolerance)
B	Detrimental	Altered fiber quality, altered fruit ripening, male sterility
C	Variable (Table 5) on invasiveness of crop	Herbicide resistance
D	Variable, depending on level of biological control	Viral, fungal, and pest resistance
E	Potentially advantageous	Cold, drought, metal tolerances

Source: Hancock, J. F. Bioscience 53: 512 - 519

The next step in Hancock's proposal is to merge the two ranking schemes to sort out which plants need experimentation beyond field trials and those for which further experimentation and documentation may be necessary (Table 5). For example, any crop,

regardless of its S-rank, possessing a T-A trait would need no further testing beyond initial field trials due to the trait being neutral. Such a trait would not affect an already invasive plant, so the consequences of releasing such a plant into the agricultural system are small or even beneficial. The types of trials needed for the deregulation of other combinations would be more field testing in order to determine if the crop is invasive or a threat to the biological diversity of neighboring populations of wild relatives.

Another proposal recommends that GMOs be broken into three risk classes based on biologic and scientific criteria (Bradford et al 2005). Low risk crops are considered those with novel traits that are functionally equivalent to those obtained through conventional breeding methods and which impart no new biochemical functions. Additionally, such crops may possess domesticating genes, which reduce their fitness outside of the agricultural setting. Moderate risk crops are classified as containing novel products, such as pharmaceutical and industrial proteins, which have low to no human and environmental toxicity. High risk plants are those where there is reason to believe, based on scientific evidence and considerations, that there is the potential for harm to be caused to the environment or humans. An example of a high risk crop and trait combination

Table 5. Crops safe for release according to Hancock's proposal

Crop Category (S)	Trait Category (T)	Examples
1	A, B, C, D, E	Herbicide-resistant cotton
2	A, B, C, D	Disease-resistant potatoes
3	A, B	Wheat with male sterility
4	A, C	Herbicide-resistant maize
5	A, B, C	Delayed fruit ripening in strawberries/blueberries
6	A, B	Marker genes in rice

Source: Hancock, J. F. Bioscience 53: 512 - 519

would be a highly toxic compound, such as a scorpion toxin, produced in a transgenic plant.

Existing Tiered Approaches

APHIS has already put into effect new regulations and standards for the testing of industrial and pharmaceutical compounds in plants, recognizing that certain plants may pose a greater risk than others (USDA). In order to test plants containing such compounds a permit from APHIS must be obtained. Once obtained, rigorous standards of isolation and biological confinement must be followed. The guidelines for pharmaceutical plants are far more stringent than for other GM crops. For example, the distance between a field of pharmaceutical plants and other compatible crops must be at least a mile, and detailed procedures on seed handling and storage of the crops must be presented to APHIS. Although this is a step in recognizing that certain plants may need greater controls and more testing, it does not stratify other agricultural GMOs according to crop and trait as Hancock's plan does.

As an additional step towards a tiered approach, the FDA recognizes foods produced by the process of genetic engineering as falling under existing regulation. However, this is broken down as well. If the GM food contains genetic material from a nonfood source, it would be considered a food additive and require a full safety evaluation, which includes data on significantly altered proteins, its composition, allergenic proteins, and reports on the levels of known toxins. For GM foods that are derived entirely from food sources, the principle of substantial equivalence is generally

applied in regards to the composition and levels of nutrients and toxins (ADA 2006). This means that the GM food would be considered safe if the levels of its nutrients and other known compounds fall within the range of acceptable variation for that species and related varieties.

Concluding Remarks

Uncertainty is inherent in many aspects of environmental testing and control, particularly in regards to agriculture. The exact effects of agriculture on the environment are not entirely understood, although large expanses of monocultures and the introduction fertilizers and pesticides have obvious negative effects when compared to natural environments (Ervin 2003, Hancock 2003, Huang et. al. 2002). It becomes difficult then

to determine whether or not the introduction of a novel gene, previously foreign and not included in the genome of a plant, poses a greater risk to human health and the environment than conventional crops and agricultural processes. However, a great deal of this uncertainty has been reduced as a result of more than a decade of research and experience with commercialized GM crops, the use of which has become. On this basis, several scientists and research societies have concluded that there is no evidence that existing GM crops are more likely to be harmful to human health than conventional crops, nor are they more likely to pose an ecological threat (ADA 2006, Huang et. al. 2002, Madsen and Sandoe 2005, SOT 2002).

Current governmental regulations require that GM crops are tested and characterized to identify potential problems that its release would trigger. However, years of data have indicated that there are few significant and new risks associated with current GM crops (Madsen and Sandoe 2005). Though designed to protect against some risks, these regulations appear to also greatly impede the progress of science and humanitarian efforts, delaying the deployment of agricultural products that have demonstrated positive benefits in the form of increased nutritional content and reduced cost of production (Huang et al 2002, Sharma 2001, Potyrkus 2005). The possibility exists to streamline regulatory processes based on the biological characteristics of a crop and the ecosystem into which it will be grown. Furthermore, current regulations may encourage the public to negatively view biotechnology by perpetuating the excessive patenting of biological material which leaves only large multinational corporations capable of affording the production costs of a new GM crop.

The applications of genetic engineering have great potential to address various issues in agriculture, ranging from the need for more efficient water and land usage, to the need to reduce chemical inputs into the environment, to helping developing nations in a more a cost-efficient method production of food that addresses nutritional deficiencies (Mann 1997, Sharma 2001). The numerous benefits of GM crops are tangible and demonstrable in the form of economic and health benefits, while the environmental risks of GM crops lie in gene flow and unproven worst case scenarios of new highly invasive crops creating an ecological disaster. Intensive study has indicated that the food safety of GM crops is likely to be comparable or even better than many conventionally bred crops. There is need for control and regulation in agricultural crops, however the current regulations are stifling and have become outdated in light of recent data and information about agriculture and the effects of the process of genetic modification.

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