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Environmental effects of genetically modified crops: differentiated risk assessment and management

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Abstract

A review of the literature shows that the environmental risks and benefits of genetically modified crops have varying degrees of certainty. For example, field studies have documented growing resistance to highly used pesticides. However, the risks of gene flow and deleterious effects on non-target organisms have not been evaluated at large field scales. Similarly, reduced pesticide use and toxicity have been estimated for some transgenic crops in some regions. Yet, the effects of herbicide-resistant crops on erosion, carbon loss and supplemental water use generally have not been evaluated. Recent assessments have concluded that inadequate monitoring and evaluation of the ecological risks are being conducted. Among other limitations, the US regulatory system must rely on the small science base to assess the biophysical risks of transgenic crops. The system evaluates the occurrence of a suite of hazards for all such crops and applies the standard science protocol of minimizing type-I error (i.e., rejecting the null hypothesis of no environmental risk, when in fact the null is true). However, genetically modified crops vary widely in their potential for environmental risks, some with minor and others with major possible ecological disruptions. We illustrate a differentiated risk-assessment process based on the 'novelty' of the genetically modified organism, as measured by the genetic distance from its source of variation. As 'novelty' increases, information about hazards and their probabilities generally diminishes and more precautionary risk-assessment standards would be invoked. Three different models are illustrated: (1) the current US approach that controls type-I error for crops that are close to conventionally bred crops; (2) a model for transgenic and similar crops that minimizes type-II error (i.e., accepting the null hypothesis when the alternative of significant ecological effect is true) at a moderate power of test standard, and (3) a model for the most novel and complex genetically modified crops that imposes a very high power of test standard. The discussion then develops parallel risk-management approaches that include economic costs for the first and second models. The paper concludes with a discussion of how a biosafety regulatory system that effectively distinguishes the relative risks of genetically modified organisms can stimulate public and private research into a new generation of biotechnology crops that reduce unwanted environmental risks and perhaps provide ecological benefits.

Keywords: environmental; risk; hazard; transgenic; genetically modified; precautionary; type-I error; type-II error

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Introduction

The growth in transgenic-crop plantings is the most rapid technology revolution in the recent history of United States (US) agriculture. Beginning from zero in 1996, data from the US Department of Agriculture (USDA) show farmers intend to plant approximately 80 percent of soybean acreage, 70 percent of cotton, and 38 percent of corn to transgenic varieties (NASS 2003). Barring a serious environmental or human-health problem linked to the crops, these plantings likely will grow and spread across ecosystems throughout the US over the next decade.

Given the rapid pace of adoption, perhaps it should not be surprising that knowledge of the environmental risks and benefits of the crops is immature. Independent appraisals have concluded that the science on the environmental risks of transgenic crops is small and incomplete (Ervin et al. 2001; Wolfenbarger and Phifer 2000). Estimates of the benefits also are crude, mostly aggregate changes in pesticide use. A root cause of the science deficiencies is inadequate monitoring of environmental effects at field or ecosystem scales (Ervin et al. 2001; National Research Council NRC 2002).

The central question addressed in this paper is how to make sound regulatory decisions about releasing transgenic crops under such information deficiencies. We suggest the development of risk assessment and management approaches that are tailored to the nature of the ecological risks posed by the genetically modified (GM) plant. Two reasons underpin the need for such a differentiated approach. First, the organisms inserted into transgenic crops vary and expose the environment to quite different hazards. The distance between the engineered organism and the source of the genetic variation may be a useful measure for assessing the novelty of the introduced genetic changes and risks (Nielsen 2003). A second related reason is the varying amount of information about the environmental risks and benefits of transgenic crops. For example, field studies have documented growing resistance to highly used pesticides. In contrast, the risks of gene flow and deleterious effects on non-target organisms mostly have not been evaluated at large field scales. Reduced pesticide use and toxicity have been estimated for some transgenic crops in some areas, albeit not in relation to ecological conditions. But, the effects of herbicide-resistant crops on yields, soil erosion, carbon loss and supplemental water use have not been measured or estimated.

We begin with an interpretative summary of the latest evidence on the environmental risks and benefits of transgenic crops in the US. After a brief review of the current US regulatory process and its limitations, we develop the framework for a differentiated risk-assessment approach. We close with a discussion of the implications of more effective regulation on private and public R&D for GM crops.

Environmental risks¹

Transgenic crops do not present new categories of environmental risk compared to conventional methods of crop improvement. “However, with the long-term trend toward increased capacity to introduce complex novel traits into the plants, the associated potential hazards, and risks, while not different in kind, may nonetheless be novel” (National Research Council NRC 2002, p. 63). The nature of the risks vary depending on the characteristics of the crop, the ecological system in which it is grown, the way it is managed, and the private and public rules governing its use. Three categories of hazard emerge from the interaction of these factors². Table 1 shows often-mentioned environmental concerns for herbicide-tolerant, virus-resistant and insect-resistant crops.

Table 1. Selected transgenic traits and environmental concerns

Genotype	Environmental concerns
Herbicide tolerance (HT)	<ul style="list-style-type: none"> • Increased weediness of wild relatives of crops through gene flow • Development of HT weed populations through avoidance and selection • Development of HT ‘volunteer’ crop populations • Negative impact on animal populations through reduction of food supplies
Insect resistance (IR)	<ul style="list-style-type: none"> • Increased weediness of wild relatives of crops through gene flow • Development of IR populations • Toxicity to non-target and beneficial insect and soil micro-organism populations
Virus resistance (VR)	<ul style="list-style-type: none"> • Increased weediness of wild relatives of crops through gene flow • Disease promotion among plant neighbours of VR crops through plant alteration • Development of more virulent and difficult to control viruses through virus alteration

Resistance evolution

Current commercial transgenic crops emphasize effective pest control via the increased use of certain pesticides, such as *Bt*. Crops bred to resist herbicides, viruses and insects have the potential to change agricultural practices dramatically. The lack of long-term studies poses a serious obstacle to performing an adequate assessment of the potential environmental effects. Nevertheless, some studies have assessed the impacts.

Herbicide-tolerant crops

The primary environmental concern from herbicide-tolerant (HT) crops is the development of weed populations that are resistant to particular herbicides. This resistance can occur from the flow of herbicide-resistant transgenes to wild relatives

or to other crops or from the development of feral populations of herbicide-resistant crops (National Research Council NRC 2002). Also, if farmers rely on only one or a few herbicides, weed populations can develop that can tolerate or ‘avoid’ certain herbicides, which enables them to out-compete weeds that do not manifest such tolerance. Weed scientists find the latter development likely. In fact, Owen (1997) reports that in Iowa “[c]ommon waterhemp (*Amaranthus rudis*) populations demonstrated delayed germination and have ‘avoided’ planned glyphosate applications. Velvetleaf (*Abutilon theophrasti*) demonstrates greater tolerance to glyphosate and farmers are reporting problems controlling this weed”. And VanGessel (2001) reports that horseweed (*Conyza canadensis*) has been found to be resistant to glyphosate through experiments conducted in a farmer’s field in Kent County, Delaware.

Virus-resistant crops

There is a relative dearth of research on the ecological risks associated with these crops. However, scientists have voiced several environmental concerns related to virus-resistant (VR) transgenic crops. First, these bio-engineered varieties may promote disease in neighbouring plants by altering such plants so they become hosts for particular viruses, when such plants were not previously susceptible to infection by the viruses of concern. Second, VR transgenic crops may alter the methods through which viruses are transmitted (Rissler and Mellon 1996; Royal Society 1998). These changes could result in the development of stronger viruses (Hails 2000; Rissler and Mellon 1996; Royal Society 1998). Scientists are also concerned that the genome in VR crops may recombine with the plant-virus genome (which is comprised of RNA in most/all plant viruses) during viral replication (Rissler and Mellon 1996; Royal Society 1998). Researchers believe that such recombination could lead to genetically unique viruses that may be difficult to control (Greene and Allison 1994). Third, the flow of VR transgenes may enhance the weediness of wild relatives of VR crops (see section Transfer of genes – gene flow on the next page). A National Research Council (NRC) assessment (2000) found that the USDA’s assumption that transgenic resistance to viruses engineered in cultivated squash will not result in enhanced weediness of wild squash through gene flow, needs verification through longer-term studies. The NRC study also concluded that the USDA’s assessment of the potential for virus-protective transgenes in cultivated squash to affect wild populations of squash “is not well supported by scientific studies”, especially for transgenic squash engineered to be resistant to several viruses instead of three or fewer (2000, p. 124). In a new report, the NRC (2002, p. 134) argued that the evidence collected to date is “scientifically inadequate” to support the conclusion of USDA’s Animal and Plant Health Inspection Service (APHIS) that gene flow from VR squash would not result in increased weediness of free-living *Cucurbita pepo*.

Insect-resistant crops

The innate ability of insect populations to adapt rapidly to pest-protection mechanisms poses a serious threat to the long-term efficacy of insect-resistant (IR) biotechnologies. Such adaptations can have environmental impacts. For example, adaptation by insect populations to a more environmentally benign pest-control technique, such as *Bt*, could result in the use of higher toxicity pesticides (National Research Council NRC 2000). The Canadian Expert Panel on the Future of Food Biotechnology (Royal Society of Canada 2001) finds that it is important to account for insect movement when devising resistance-management plans. Regional or

interregional-scale plans, rather than local, are needed if the insect of concern is highly mobile (Gould et al. 2002; Hails 2000). Field outbreaks of resistance to *Bt* crops have not yet been documented (Morin et al. 2003). The body of science to inform resistance management is limited to laboratory studies of specific insect pests (Ervin et al. 2001; Morin et al. 2003). Such studies show the potential for resistance to develop. Indeed, the NRC (2002, p. 76) finds that the evolution of “insect resistance to *Bt* crops is considered inevitable”. Similarly, Tabashnik and colleagues write that eventually insects will develop resistance to IR crops, and therefore, “...any particular transgenic crop is not a permanent solution to pest problems” (Tabashnik et al. 2001, p. 1). A recent laboratory study found that *resistant* populations of diamondback-moth larvae may be able to use a toxin derived from *Bt* “...as a supplementary food protein, and that this may account for the observed faster development rate of *Bt* resistant insects in the presence of the *Bt* toxin” (Sayyed, Cerda and Wright 2003).

One of the few field studies by Tabashnik and colleagues (2000; 2001) found that in 1997 approximately 3.2 percent of pink-bollworm larvae collected from Arizona *Bt* cotton fields exhibited resistance. This level was far above what was expected, raising fears that rapid resistance development would occur. However, data collected in 1998 and 1999 showed no increase in resistant populations of pink bollworm. Tabashnik and colleagues (2001) conclude that there might be high fitness costs for insects to develop resistance to *Bt*. In addition, Carrière and colleagues (2003, p. 1523) found that widespread and sustained use of *Bt* cotton can suppress regional pink-bollworm populations and thus, “...*Bt* cotton could reduce the need for pink bollworm control, thereby facilitating deployment of larger refuges and reducing the risk of resistance”. In addition, a recent greenhouse study found that stacking or pyramiding two unrelated *Bt* toxins in a plant can slow the rate of resistance development (Gould 2003; Zhaio et al. 2003).

The potential for insect resistance implies that integrating transgenic crops into a multiple tactic pest-management regime may prove to be a more effective long-term strategy. The exact path of the emergence of insect resistance is yet to be characterized. However, progress has been made on identifying resistant alleles in pests of certain crops, such as the pink bollworm in cotton (Morin et al. 2003). Therefore research is needed to better define the parameters of resistance development, as well as to design crops that minimize the opportunities for resistance to develop in the first place. This latter point on fostering precautionary technology development is discussed in the concluding section.

Transfer of genes – gene flow

There is little doubt in the scientific community that genes will move from crops into the wild (Hails 2000; National Research Council NRC 2000; Snow and Palma 1997). The relevant research questions are whether transgenes will thrive in the wild, and how they might convey a fitness advantage to wild plants that makes them more difficult to control in areas (Hails 2000; Keeler, Turner and Bolick 1996; National Research Council NRC 2000; Royal Society of Canada 2001; Snow and Palma 1997).

Generally, crops with wild relatives in close proximity to the areas where the crops are grown, pose higher risk for gene flow to wild relatives. US examples include sunflower (*Helianthus annuus L*) and oilseed rape (*Brassica napus*) (Hails 2000; Keeler, Turner and Bolick 1996; Snow and Palma 1997). Gene transfer could become a problem if the transferred genes do not have deleterious effects on the crop-wild hybrids, but instead confer an ecological advantage (Hails 2000; Royal Society of Canada 2001; Snow and Palma 1997). Gene flow from classically bred crops to wild

plants has been documented. Ellstrand (2001) finds that classically bred crop-to-wild gene flow has enhanced the 'weediness' of weeds for seven of the world's thirteen most important crops (e.g. Johnson grass (*Sorghum halepense*) from cultivated sorghum (*Sorghum bicolor*)).

Snow and Palma (1997) argue that widespread cultivation of transgenic crops could exacerbate the problem of gene flow from cultivated to wild crops, enhancing the fitness of sexually compatible wild relatives. Traditional breeding typically results in the inclusion of deleterious alleles (i.e., alternative forms of a gene at a given site on the chromosome) linked to the desired beneficial genes. The inclusion of the deleterious genes decreases the likelihood that crop-to-wild outcrossing will result in enhanced weediness of the wild plants. In contrast, biotechnological methods enable solitary genes to be selected without including neutral or deleterious genes (Snow and Palma 1997; National Research Council NRC 2000, p. 85).

Scientists generally expect that herbicide-resistant transgenes will not result in increased weediness of wild relatives, as such genes tend to impose a cost, or are neutral, to wild relatives. Nonetheless, in situations where herbicides are typically used to control weedy plants, herbicide resistance could confer a competitive advantage to unwanted volunteer crops (Keeler, Turner and Bolick 1996). Indeed, the flow of herbicide-resistant transgenes has already become a problem regarding within-crop gene flow. Hall, Huffman and Topinka (2000) reported the presence in a Canadian farmer's field of volunteer oilseed rape resistant to three herbicides: glyphosate, imidazolinone, and glufosinate. The 'triple-resistant' oilseed rape developed from gene flow among three oilseed rape varieties designed to resist each of the herbicides, which were planted in close proximity to each other. The Canadian expert panel finds that "...herbicide-resistant volunteer canola plants are beginning to develop into a major weed problem in some parts of the Prairie Provinces of Canada" (Royal Society of Canada 2001, p. 122). They expressed special concern about the potential for 'stacked' resistance to multiple herbicides, which could force farmers to employ older herbicides that are often more environmentally harmful than newer classes (Royal Society of Canada 2001).

In general though, ecologists tend to be more concerned about potential fitness advantages of insect- and virus-resistant transgenes (Hails 2000). For example recent research has shown that the *Bt* gene for lepidopteran resistance can increase seed production in wild sunflowers (Snow 2002; Snow et al. 2003). Another study showed that crossing *Bt* oilseed rape with a wild relative (*Brassica rapa*) did not enhance the weediness of the resulting plant relative to unmodified *Brassica rapa* (Adam 2003). To understand the contrasting findings, more studies along with monitoring and testing are needed to detect potential ecological problems. However, actions by Pioneer Hi-Bred International and Dow AgroSciences to the Snow and colleagues (2003) study may impede such research. The firms blocked a follow-up study by denying access to the materials they controlled that were needed to conduct further investigation (Dalton 2002). The firms denied three requests to continue studying *Bt* sunflower using the scientists' research funding. Therefore, Snow and her colleagues are legally barred from continuing their investigations (personal e-mail communication, April 25, 2003).

Impacts on non-target animals and plants

While crops bred to resist pests may suffer less damage and lead farmers to use less insecticide, there is concern that the toxins these plants produce may harm non-target organisms, including animals and plants that are not pests (Royal Society 1998;

National Research Council NRC 2002). Laboratory research confirms that transgenic insecticidal crops can have negative impacts on potentially beneficial non-target organisms, including lacewings (Hilbeck et al. 1998a; Hilbeck et al. 1998b), ladybird beetles (Birch et al. 1997), monarch-butterfly larvae (Losey, Raynor and Carter 1999) and soil biota (Watrud and Seidler 1998).

Tabashnik (1994) asserts that reductions in pest populations due to transgenic crops may negatively affect available numbers of desirable natural predators. Similarly, the NRC finds that “Herbicide tolerant crops might cause indirect reductions on beneficial species that rely on food resources associated with the weeds killed by the herbicides” (National Research Council NRC 2002, p. 70). In this vein, Watkinson and colleagues (2000) modelled the potential impacts on skylarks (*Alauda arvensis*) from a reduction in seeds of a weed of sugar beet (primary food supply of skylarks) from the introduction of HR sugar beet. They found that the weed populations could be almost completely eradicated depending on the conditions surrounding adoption of such transgenic sugar beets, such as the management practices. Severe reductions in weed populations could significantly affect the skylark’s use of fields as a food source. Conversely, some bird populations may increase if farmers replace broad-spectrum synthetic herbicides, which have cut into the birds’ food supply, with transgenic crops (National Research Council NRC 2000, p. 80).

Recent farm trials in the UK confirm that enhanced weed-control efficacy from using herbicide-tolerant crops can reduce food supplies and lower the populations of non-target species such as bees, butterflies and seed-eating beetles. However the results varied considerably by the type of herbicide employed in the system. Additional findings from the data collected from these trials should be forthcoming and help to shed further light on these complex interactions (Andow 2003).

Other potential neutral and positive impacts on non-target species of transgenic crops have also been found. For example, research sponsored by the European Commission on the safety of genetically modified organisms (GMOs) found no negative impacts on honeybees from transformed oilseed-rape plants. Also, *Galanthus nivalis* agglutinin (GNA) lectin accumulation in aphids did not result in acute toxicity to ladybird beetles or prevent *Eulophus pennicornis* from successfully parasitizing tomato-moth larvae (Kessler and Economidis 2001; Pham-Delègue et al. 2000). A field study in Wisconsin found that populations of predators and parasites were higher in *Bt* potato fields than in conventional potato fields where conventional insecticides were used. Non-chemical or less-intensive chemical treatments were not evaluated (Hoy et al. 1998). This finding points to the need to evaluate the impacts of transgenic crops relative to conventional chemically intensive practices and alternative systems (Dale, Clarke and Fontes 2002; National Research Council NRC 2002).

Given that research results on potential impacts on non-target organisms point to negative, neutral and positive effects, generalizations may well be inappropriate as to the impact on non-target organisms, with each crop and region requiring specific research. For example, in a widely publicized laboratory study, Losey, Raynor and Carter (1999) found a 44% mortality rate in monarch-butterfly larvae fed on milkweed leaves dusted with *Bt* corn pollen. No mortality occurred in monarchs fed on leaves with non-*Bt* corn pollen. These laboratory finding on the toxicity of *Bt* corn to monarch butterflies generated significant controversy and prompted responses as to the applicability of the finding to field settings (Beringer 1999), follow-up research supporting the original findings (Hansen-Jesse and Obrycki 2000), and a risk-assessment study finding that monarchs are not at risk from *Bt* corn since “overall

exposure of monarch larvae to *Bt* pollen is low” (Sears et al. 2001). In its turn, the NRC panel asserted “In the upper Midwest, herbicide-tolerant soybeans might cause indirect reductions of monarch populations because their milkweed host plants are killed by the herbicides” (National Research Council NRC 2002, p. 71). Though many consider the debate over monarchs and *Bt* corn closed, there are still questions being raised about the effects of long-term and low-level exposure to *Bt* in corn pollen on monarch-larvae survival and fitness (Stanley-Horn et al. 2001).

Insects and other animals are not the only organisms potentially affected by transgenic crops. The Canadian expert panel found the cultivation of transgenic crops could impact the diversity and abundance of soil microflora, however the impacts are “...minor relative to the natural variability...” (Royal Society of Canada 2001). They observed that transgenic manipulation aimed at modifying biogeochemical cycles should receive more scrutiny. The NRC (2002) largely concurs by arguing that no effects on soil organisms have been found to date, though it has been discovered that *Bt* toxin ‘leaks out’ of corn roots and can persist in the soil for months (Saxena and Stotzky 2000; Dale, Clarke and Fontes 2002).

Risk summary

In general, the environmental hazards associated with transgenic crops are potential risks. However, research results provide emerging parameters to evaluate the relative magnitude of the potential risk. For example, good evidence is emerging that the combination of natural promiscuity regarding gene flow among crop varieties and engineered herbicide resistance is a serious concern. Likewise, it is becoming clearer that HR crops will probably not create ‘superweeds’ through crop–wild flow of genes that enable plants to tolerate particular herbicides. Rather weed problems will be enhanced by the selection of resistant weed populations through increased use of herbicides tied to particular transgenic crops, such as glyphosate-resistant soybeans. Research efforts should concentrate on the latter potential risks.

Also of concern is the enhanced weediness of wild relatives of crops from the flow of genes enabling plants to resist insects and viruses. However, the research to evaluate the extent of these risks is incomplete. More study is needed to assess the potential for the widespread adoption by farmers of IR sunflower and VR squash to promote the development of wild plants with improved fitness relative to other wild plants. The improved fitness of particular plants in wild populations could alter plant and animal ecosystems. The controversy over the potential for *Bt* corn to harm monarch butterfly populations also illustrates the need to move beyond laboratory studies to comprehensive field scale when assessing the potential negative impact on susceptible but beneficial populations. That is, studies that account for the temporal and spatial interaction between the introduced technology and the organism of interest.

That field outbreaks of resistance to *Bt* crops have not yet been documented despite widespread adoption of such crops deserves more investigation. Potential questions include:

- Have the refugia plans prevented the development of such resistance?
- If so, can such plans be developed for herbicide-resistant technologies to delay the development of weed populations resistant to herbicides linked with HR crop varieties?

Environmental benefits

Reduced pesticide use and toxicity

Data to assess the effects of transgenic crops on pesticide use should capture the full range of climate, pest and economic conditions. The data should also be linked to environmental conditions to estimate changes in acute and chronic toxicity on ecological systems (Antle and Capalbo 1998). The impacts of changes in pesticide use for transgenic crops on the environment can be determined only by comparing the fate, transport and toxicity of the full array of compounds available to farmers, and how they are applied. The following estimates for three major US transgenic crops do not yet measure up to these standards.

Bt cotton

Results from farm surveys generally indicate that farmers who plant *Bt* cotton apply fewer insecticides than on conventional cotton (Carlson, Marra and Hubbell 1998; Hubbell, Marra and Carlson 2000; Economic Research Service USDA 1999a; 1999b; Fernandez-Cornejo and McBride 2002). USDA analysts recently estimated that *Bt* cotton plantings in 1997-98 reduced insecticide use by approximately 250,000 pounds of active ingredients (a.i.) (Fernandez-Cornejo and McBride 2002). Other studies have found that the reductions vary by area and year depending on pest pressures and other factors. For example, Carlson, Marra and Hubbell (1998) report that the average number of insecticide applications by farmers who adopted *Bt* cotton in 1996 was 3.29 on their traditional acres in the upper South, but only 2.58 in the lower South, a difference that likely reflects different insect conditions in the two regions. Farmers who plant *Bt* cotton likely use more conventional insecticides in the first place and can save more money than farmers who applied lower levels. The long-term effects of *Bt* cotton on insecticide use may require analyses of 10 years or more to cover the cycles of pest, climate and economic variations.

Herbicide-tolerant soybeans

The latest national analysis estimated that planting of HT soybeans in 1997-98 increased overall pesticide use by approximately 2.5 million pounds a.i. (Fernandez-Cornejo and McBride 2002). The increase was largely in the form of glyphosate, which is anywhere from 3 to 16 times less toxic than the herbicides it has replaced and 1.6 to 1.9 times less likely to persist in the environment (Heimlich et al. 2000). Whether and how long these shifts in herbicide composition on soybeans will persist depend on how fast the resistance problems discussed above unfold. If glyphosate becomes ineffective, farmers will use other herbicides to control weeds that develop resistance to it, and the environmental implications depend on the substitute compound, location and other conditioning factors.

Herbicide-tolerant corn

Over 1997-98, US farmers who planted HT corn were estimated to decrease their herbicide use by approximately 5 million pounds a.i. (Fernandez-Cornejo and McBride 2002).

Net effect

The overall effect for the three crops was a net reduction of approximately 3 million pounds of pesticide a.i. in 1997-98. This is characterized as "...a small but statistically significant effect..." (Fernandez-Cornejo and McBride 2002, p. 36). Since

nearly 80% of the reduction in pesticide treatments is attributed to switching to glyphosate, the overall toxicity quotient decreased by more than the simple volume reduction. Since 1997-98, the adoption of transgenic crops has spread and the decrease in pesticide volume and toxicity likely has increased as well, but likely still remains a small percentage of overall pesticide use.

Reduced tillage, erosion, carbon loss and water savings

Several other potential environmental benefits of transgenic crops have been hypothesized. For example, manufacturers and advocates of transgenic crops have asserted that HT varieties will increase use of conservation tillage. However, the USDA analysis could not support this hypothesis, concluding that farmers already using conservation tillage were more likely to adopt HT crops (Fernandez-Cornejo and McBride 2002). Evidence on the other potential environmental benefits has been nil.

The current environmental regulatory process

The US Environmental Protection Agency (EPA) and USDA's Animal, Plant, and Health Inspection Service (APHIS) share responsibility for assessing the environmental risks of transgenic crops before their release for testing and commercialization. EPA evaluates plant-incorporated protectants, such as *Bt* in cotton and corn, and regulates them in the same way it regulates conventional chemical pesticides. The APHIS evaluation, depending upon the particular plant line, covers a broad range of potential environmental effects: (1) the potential for creating plant-pest risk; (2) disease and pest susceptibilities; (3) the expression of gene products, new enzymes or changes to plant metabolism; (4) weediness, and impact on sexually compatible plants; (5) agricultural or cultivation practices; (6) effects on non-target organisms, including humans; (7) effects on other agricultural products, and (8) the potential for gene transfer to other types of organisms (McCammon 2001).

Each agency conducts a risk analysis of the biophysical effects of the crop. We discuss the more comprehensive APHIS process here. The risk analysis includes three stages – hazard identification (as covered in the previous section Environmental risks), risk assessment and risk management. The risk assessment stage is the focus of this section. One or more of several techniques may be used to perform the assessment: (a) epidemiological analysis; (b) theoretical models; (c) experimental studies; (d) expert judgments, and (e) expert regulatory judgments. APHIS generally uses expert regulatory judgment, a less rigorous technique than (a), (b) or (c) according to the NRC (2002, p. 60).

APHIS uses a two-part model in which a transgenic plant is divided into (1) the unmodified crop and (2) the transgene and its product (National Research Council NRC 2002, p. 90). The theoretical reasoning behind this choice is that the transgene is a small genetic change that is likely to have only a small phenotypic effect. Invoking that principle accepts the simple linear model of 'precise' single gene modifications that do not significantly alter other plant processes. Experts have reservations about this rationale: "...unanticipated changes can be induced by expression of a novel gene, and their phenotypic consequences need to be assessed empirically across time and environments" (Royal Society of Canada 2001, p. 185). The NRC panel also noted the assumption that single gene changes have small ecological effects is not always true (National Research Council NRC 2002, p. 91).

The APHIS risk-assessment process evaluates the risk of the unmodified crop separate from the risks of the transgene and its products. The test for biophysical risk basically attempts to control the type-I error, α , of rejecting the null hypothesis that the transgene has *no* effect on the environment when in fact the null is true³. Minimizing the frequency of type I-error (a ‘false positive’) by requiring a high level of certainty, most often 95%, is the dominant approach used for hypothesis testing in science. It is also considered to be a conservative approach in detecting an ecological effect, because it is difficult to construct studies with sufficient power to reject the null hypothesis under $\alpha = 0.05$. This is especially true for studies dealing with environmental issues where natural variation, both in space and time, is typically great (Buhl-Mortensen 1996; National Research Council NRC 2000). The effect of this high variation is to spread out the distribution of the random variable for testing the null hypothesis and increase the range of values for which the sample test statistic is interpreted as not rejecting the null hypothesis.

The NRC panel (2002), noting several limitations of the two-part model, recommended more evaluation of ‘fault-tree’ and ‘event-tree’ risk analyses that systematically search for potential ecological risks. These and other techniques place more emphasis on understanding and controlling type-II error, β , the error of failing to reject the null hypothesis when it is in fact false, i.e., a ‘false negative’ when the transgene actually causes an ecological hazard. Lemons, Shrader-Frechette and Cranor (1997) argue that scientists and decision-makers should be more willing to minimize type-II errors (and accept higher risk of committing type-I errors) because of the pervasiveness of scientific uncertainty in complex ecological processes. They explain that the normal argument to minimize type-I error when adding new scientific knowledge does not apply equally to environmental regulatory decisions. Type-I error with a 95% confidence level is appropriate for evaluating new scientific results in order to prevent or minimize the inclusion of “speculative knowledge to our body of [scientific] knowledge” (Lemons, Shrader-Frechette and Cranor 1997, p. 228). However, knowledge generation to support environmental regulatory decisions is different in kind as it is based on finding whether negative environmental or health outcomes are likely, or unlikely, to occur, and not generating new scientific results per se (Lemons, Shrader-Frechette and Cranor 1997, p. 224-230). Buhl-Mortensen (1996) also notes that since ecosystem models, with a few exceptions, have low predictive power, it is prudent to control for type-II error when evaluating the potential ecological impacts of industrial processes or technologies. In a similar vein, Jasanoff concludes that the current US system has “...biased the assessment exercise away from large, holistic questions...” (Jasanoff 2000, p. 279), instead focusing on relatively precise genetic manipulations. Part of the reason for the bias may be the lack of post-market monitoring and testing of biotechnology crops to provide adequate data for examining the larger ecological questions (National Research Council NRC 2002; Taylor and Tick 2003).

Figure 1 illustrates the differences in risk-assessment tests under control of type-I versus type-II errors. Assume for purposes of illustration that the horizontal axis measures the difference in seed production by wild relatives containing a transgene compared to seed production in wild plants without the transgene. The hypothetical distributions measure the probability density of various values. The distributions centred over $\mu = 0$ and $\mu = SD_a$ are the null and alternative population distributions. If a value of SD^* is observed from the sample test, the APHIS risk assessment would fail to reject the null hypothesis of no significant gene flow, because SD^* lies to the left of the critical test statistic for a one tailed test, assuming $\alpha = 0.05$ (and $\beta = 0.20$).

However, under a criterion to minimize type-II error by setting β at 0.10 (i.e., the power of the test = 0.90), the alternative hypothesis of a positive effect on seed production in wild relatives would fail to be rejected. Note also that if the natural processes and the assumed distribution become more variable or flatter, the range under which the alternative hypothesis is not rejected would expand. That is, the probability of a ‘false negative’ increases, *ceteris paribus*.

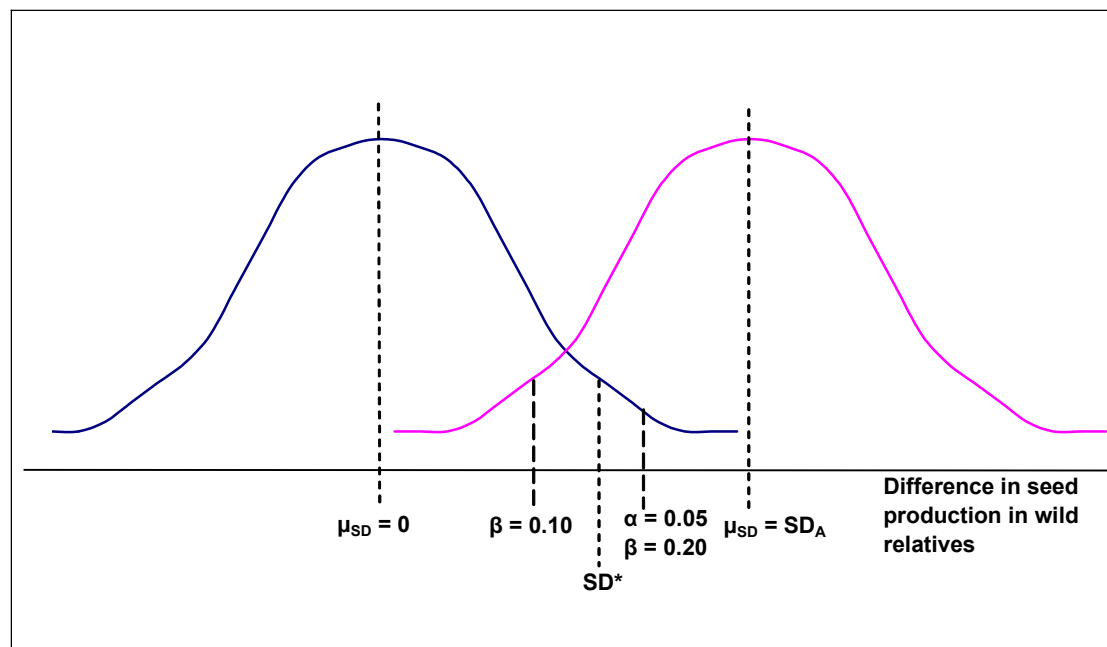


Figure 1. Differences in statistical tests to control type-I and type-II errors

The NRC analysis repeatedly emphasized that “For purposes of decision support, risks must be assessed according to the organism, trait and environment” (National Research Council NRC 2002, p. 63). The review of potential environmental risks also suggests information deficiencies could be added to this list. The recognition that GM crops vary in their potential for environmental risk invites consideration of a risk-assessment process that uses different methods and different standards of proof for different types of genetic modification.

A differentiated risk-assessment process

A differentiated risk-assessment process captures the novelty of the ecological hazard(s) from the GM crop and the information quality about the potential hazards and their occurrences. Different models might cover a range, from controlling type-I error for GM crops using high-quality information that shows little potential ecological risk to a very high standard of avoiding type-II errors for crops judged to pose serious potential ecological disruptions with little scientific evidence to assess the nature of the risk(s).

To differentiate the risk assessment, a robust method for characterizing the nature of the ecological risks of GM crops is needed. However, scientific or regulatory consensus on such a robust method does not exist. To facilitate our analysis, we adopt an approach suggested by Nielsen (2003), who argues for conceptual diversification in discussing and regulating genetically engineered organisms. She claims the current process-based categorization is imprecise and does not adequately convey the sources,

extent and novelty of the genetically modified organism. For example, GM crops with simple nucleotide changes are unlikely to generate serious ecological concerns beyond those of their traditional counterparts. In contrast, species-foreign genes, synthetic genes and some other changes in GM crops deviate substantially from what classical selective-based breeding has achieved. The latter organisms have genetic compositions that do not reflect evolutionary processes occurring under natural conditions. She cites *Bt* corn, derived by genetic engineering of several unrelated DNA segments, as an example of an organism that cannot be replicated by natural processes within the same time scale. Thus, the ‘genetic distance’ between the engineered organism and the source of the new genetic variation could serve as a functional criterion for determining the type of risk assessment conducted.

This approach dovetails with earlier arguments by Snow and Palma (1997) and the NRC (2000, p. 85), which imply that the differences between classical breeding approaches and transgenic methods can justify differences in risk assessment. However, historically the NRC (2002) has emphasized regulating the products of genetic manipulation over the processes (Snow 2003). Snow (2003) argues that focusing on the phenotype over the process used to engineer it into a plant is appropriate “...given that many GEOs [genetically engineered organisms] have truly new characteristics relative to what can be created by conventional breeding”. Therefore, as very novel traits are engineered into crops, regulating such traits in essence means regulating the process by which the traits were engineered. Classical approaches to breeding could never result in the production of crops with such truly novel traits.

We argue that as novel processes are developed, it could be in the public interest to consider the process in regulating the organism, in addition to the trait or phenotype expressed in the plant. For example, it may be appropriate to treat differently, two plants with the same engineered phenotype that was produced through different engineering processes. And that, as the ‘genetic distance’ (Nielsen 2003) from conventional techniques increases, the regulatory regime becomes increasingly precautionary in its approach and conceptualization.

It is important to note that we are not asserting that classical breeding inherently produces safer products and that deviations from this approach produce more dangerous products. Rather our argument is subtler. We believe that our long experience and familiarity with classical breeding techniques makes it reasonable to assume that as ecological or other problems potentially develop, we are more likely to recognize such problems and take corrective measures. It follows that our relatively brief experience with transgenic and other recently developed techniques and the scant science base makes it more likely that if a biosafety problem develops with these new crops, we may not recognize the problem as quickly because our ability to discern potential problems is primarily based on our experience with traditional breeding techniques. We believe our rationale and approach are consistent with the finding of the NRC stated at the beginning of section Environmental risks that “...the associated potential hazards, and risks [of transgenic crops], while not different in kind, may nonetheless be novel” (National Research Council NRC 2002, p. 63).

Nielsen (2003) proposes five genetic-distance categories that vary from low to high: (1) intragenic (within genome); (2) famigenic (species in the same family); (3) lineagenic (species in the same lineage); (4) transgenic (unrelated species), and (5) xenogenic (laboratory-designed genes). We combine categories 1 and 2 and categories 3 and 4 along with category 5 to develop three risk models based on increasing genetic distance⁴.

1. Intragenic and famigenic – These two categories of genetic modification respectively include those from directed mutations or recombinations including those arising in classical, selection-based breeding, and from the taxonomic family, including those arising from applying cellular techniques in classical breeding. The risk-assessment process for these cases could reasonably presume no substantial ecological risks from releasing the crops beyond those from conventional breeding. Thus, it would include a straightforward review of evidence submitted by the applying entity and application of the ‘probability rule’ criterion for all relevant effects reviewed by APHIS (Mooney and Klein 1999). A test of the null hypothesis of no significant effect would be conducted to control type-I error, i.e., failing to accept the null when it is in fact true, at the standard 0.05 level of significance.

2. Linegenic and transgenic – These two categories include organisms that contain genetic variability *beyond that* possible with conventional breeding. Linegenic includes species in the same lineage and the recombination of genetic material beyond what can be achieved by classical breeding methods. Transgenic covers those plants that contain DNA from unrelated organisms, and include most of the GM plants commercialized today. For these plants, the test shifts the framing hypothesis to one that assumes a significant environmental effect because of the increased novelty of the crop and less information. The standard of proof would be set at a specified power of test, for example 0.90 or $\beta = 0.10$. The decision of setting the standard of proof moves beyond science into the realm of public input and political decisions because the standard reflects society’s general preference for avoiding such risks, i.e., the degree of precaution (Van den Belt 2003).

3. Xenogenic – This category includes laboratory-designed genes for which no naturally evolved genetic counterpart can be found or expected, e.g., synthetic genes and novel combinations of protein domains. This class is the furthest of the three from natural genetic variability, and therefore poses the greatest potential for ecological hazard and risk. For the hazards that can be characterized with objective or subjective probability distributions, the bar for approval to release would be highest for such plant organisms. Since the genetic distance from classically bred crops is greatest for this category, a higher standard of proof would be applied to control type-II error than for category 2, for example $\beta = 0.05$.

To implement this risk-assessment framework for GM crops, a group of experts with sufficient breadth across ecological and other relevant sciences would be assembled. The composition and independence of the groups is critical if reliable risk assessments are to be completed. To counter criticisms that the expert panels used by USDA inappropriately favour releases, both government and university scientists would be involved and each would face sanctions if their contributions were subsequently determined to be biased, e.g., a bonding mechanism for liability. Due to the scant knowledge that exists for many GM crops, especially new transgenic varieties, the groups would at first conduct case-by-case assessments. However, over time with the accumulation of more systematic knowledge on the potential environmental risks due to the search for type-II errors, the assessments likely would shift to broader categories and become more routine and cost-efficient over time.

Differentiated risk management

The final stage of risk analysis is the management decision taken, including commercial release and regulatory measures that may accompany the releases, such as refugia requirements and post-commercialization monitoring and testing. The

differentiation of the risk-management process parallels that taken for risk assessment in that increasing degrees of precaution are imposed on more novel organisms. However, risk-management decisions would involve weighing environmental and economic considerations for the organisms that do not pose potential catastrophic and irreversible hazards. The answers to six questions in Table 2 summarize the differences for the APHIS-like process, a risk–benefit evaluation, and the precautionary approach for the three risk-management categories.

Table 2. Comparison of APHIS, risk–benefit and precautionary risk management

Questions	APHIS-like approach	Risk–benefit approach	Precautionary approach
1. What is the framing hypothesis?	No significant environmental hazard (the null hypothesis).	Significant environmental effect (alternative hypothesis)	Significant environmental effect (alternative hypothesis)
2. What rule is used to test the hypothesis?	Probability of rejecting null hypothesis when it is true (type-I error) is less than critical value, e.g., $\alpha = 0.05$	Power of test to correctly reject null hypothesis, (1 - type-II error) is high, e.g., 0.90.	Power of test to correctly reject null hypothesis, (1 - type-II error) is very high, e.g., 0.95.
3. What party is responsible for the burden of proof?	US Government	Shared between the US Government and entity introducing crop	Entity introducing the transgenic crop (as certified by independent party)
4. What costs are considered?	Lost production, environmental and health benefits from not releasing the crop	Lost production, environmental and health benefits from not releasing the crop	Potential ecological risks from releasing the organism outweigh economic considerations
5. What is the general rule for making release decisions?	Permit release if test to minimize type-I error at standard $\alpha = 0.05$ level indicates no significant ecological risk, or if net benefits exceed the ecological risks/costs.	Permit release if test to minimize type-II error at high power level does not indicate significant ecological risk, or if net benefits exceed the ecological risks/costs.	Permit release if test to minimize type-II error at very high power level is passed, but avoid irreversible risks until information is available to assure adequate ecological safety.
6. Will compensation be provided to negatively affected parties?	Collect some of the net benefits to compensate ‘losers’ or remediate damages	Collect some of the net benefits to compensate ‘losers’ or remediate damages	Not applicable

There is a substantial body of science on the potential environmental effects of intragenic and famigenic GMOs or products from similar techniques. Therefore, the evaluation would be the least precautionary by controlling type-I error using the standard 95% confidence level. If no significant effects were detected, the organism would be approved for release. However, if evidence is found to support the

hypothesis of a significant ecological risk, the crop would not be rejected automatically for release, but passed through a risk–benefit test. The estimated value of the ecological damages would be compared to the potential net benefits of releasing the crop, including production, human health and any positive environmental effects, such as pesticide toxicity reductions. Note the production benefits must incorporate the relevant social value of added production due to lowering the supply curve, which for the US and EU countries may be negative if excess supplies are creating deadweight losses. The decision to release is made by a comparison of the estimated ecological risks/costs against the potential social benefits. Non-market valuation methods would be applied to those ecological effects for which reliable monetary values could be estimated. It is doubtful that all effects could be reliably monetized. Thus, expert scientific and policy judgments would be necessary to compare order-of-magnitude effects and implement the decision rule.

If the estimated benefits outweigh the potential costs, then release would be permitted. To turn the cost–benefit decision rule into a real rather than potential Pareto improvement, a portion of the net benefits would be used to compensate for associated losses, such as contamination from genetic drift. The burden of proof lies with the government using information provided by the applying entity for this least precautionary category. Because novel risks are unlikely and good quality information about the ecological risks is likely available for these familiar crops, this risk assessment based on minimizing type-I error will result in more commercialization decisions than the following models. However, APHIS currently uses this probability rule to approve the field testing of approximately 99% of most transgenic crops, which would fall into the next model in our differentiated approach.

For linegenic and transgenic organisms, more stringent tests for ecological risk would be applied. Because of our relative lack of experience with these crops, they conceivably could introduce serious ecological risks. An independent scientific panel would first screen the crops for potentially serious irreversible impacts, and any such organisms would move to the precautionary risk-assessment process (model 3) with higher standards for release. For the remaining crops in this category, the framing hypothesis that the crop causes significant ecological risks would be tested to control type-II error by specifying a minimum power of the test, e.g., 90 percent ($\beta = 0.10$)⁵. Adequate ecological risk information is a prime requirement to frame and test the alternative hypotheses. However, this task presents a conundrum. Small-scale field trials before commercialization can detect order-of-magnitude differences in ecological effects, but low-probability and low-magnitude effects likely will escape detection (National Research Council NRC 2002). Evidence collected from large-scale field trials would be required. Thus, the test may have to be conducted in progressive stages of field experiments, followed by limited releases to gather sufficient data to assess all potential ecological impacts. This process would address a weakness in current ecological monitoring of GM crops (National Research Council NRC 2000, p. 19). The USDA and the entity proposing release would share responsibility in gathering the ecological risk data under scientifically certified protocols. The entity requesting permission to release could conduct the tests if the experimental design and measurement were independently certified. Alternatively, the tests may be conducted by an independent certifying body.

If the test indicates the crop does not cause significant ecological risk, its release would be permitted. Further monitoring of crops that pose unknown long-term effects would be conducted, such as cases of uncertain resistance development. Just as for intragenic and famigenic crops, if evidence is found to support the hypothesis of a

significant ecological hazard, the estimated production, environmental and health benefits of the linegenic or transgenic crop would be compared to its estimated ecological damages to decide upon release. Expert and diverse scientific panels would be used to evaluate the ecological effects and their impacts because of less familiarity with these organisms than with the first category. In cases where the science and evidence are not robust, the regulating authority may choose to permit release, but require periodic review with new monitoring data to improve the analysis of risks and renew or revoke commercialization. As for the first model, some of the net benefits would be used to compensate for associated losses, such as transgenic contamination of organic fields from genetic drift.

The final model applies to transgenic crops judged to hold the potential to cause serious irreversible ecological effects and to xenogenic crops. As for linegenic and transgenic crops, the framing hypothesis is for significant environmental effects and type-II error is controlled. However, the standard for approving release of these crops is extremely high. For example, the required power level could be increased over model 2 to 95% ($\beta = 0.05$). The entity applying for release must prove beyond scientific doubt that the organism is safe. Expert scientific panels with representation from all relevant ecological sciences would be used to implement the model and make decisions concerning release. The potential social benefits would not be considered until minimum levels of safety are assured for all ecological hazards.

It is important to note that a well-designed environmental regulatory process does more than minimize the potential for unwanted environmental hazards from new technologies. If implemented properly, environmental regulations can provide incentives and disincentives to influence the research and technology development process beneficially. Under the differentiated risk-assessment framework, imposing higher regulatory costs on organisms that potentially pose higher ecological risks stimulates research and development of GM varieties with traits that provide production benefits with acceptable environmental risk and perhaps ecological benefit. To realize this outcome, a new set of bio-engineered traits would be developed and inserted into important agronomic crops: traits that are less likely, for example, to result in resistant insect populations or harm non-target organisms. Increased and targeted involvement of the public-sector agricultural research and regulatory branches also is necessary to achieve these types of outcomes (Ervin et al. 2003).

In addition, the proposed framework may shift resources toward engineering processes that have less genetic distance from conventional techniques, at least in the short to medium term. However, it would not forestall innovation and even commercialization of crops developed through novel techniques. Rather, consistent with a precautionary approach, our proposed framework brings with it additional safeguards for engineering techniques and their products about which we are less familiar and have had less experience as consumers, regulators and scientists.

Conclusions

There is a substantial need for increased public research funding on the environmental effects of transgenic crops and for research of a different character. It is natural to ask why more public research is needed when private research on transgenic crops has increased so dramatically. Under current US biosafety regulatory policies, private industries have scant incentive to invest in the research to understand the environmental impacts of transgenic crops, especially the ecosystem effects

beyond the farm boundary. Most environmental risks stem from missing markets; there are few or no market incentives for reducing the environmental risks of transgenic crops. Thus, private research to control the full range of negatively affected environmental services will not be triggered by current market and regulatory signals (Batie and Ervin 2001).

Evidence in support of this argument is provided by the recent decision by Pioneer Hi-Bred and Dow AgroEvo to deny access to the proprietary materials required by independent scientists to conduct biosafety analysis of *Bt* sunflower (Dalton 2002). A decision made even more problematic by the fact that it was made after the firms initially co-operated with Snow and colleagues. Permission to access the material was withdrawn only after the scientists' preliminary findings indicated potential biosafety risks from *Bt* sunflower (Snow 2002; Snow et al. 2003).

Likewise, it is unrealistic to assume that most private firms will develop transgenic crops that provide ecological benefits and minimize potential risks in line with social preferences. The development of such crops would suffer from the same missing-markets dilemma since the environmental benefits would not merely accrue to the farmer that purchased the transgenic seed. Rather, other farmers, the general public, and even future generations would enjoy the benefits from such crops. For example, a vehicle for addressing many of the identified potential risks from insect-pest-resistant crops is to develop crops that are pest-damage-tolerant rather than toxic to the pest, as are *Bt* crops (Hubbell and Welsh 1998; Pedigo 2002). The difference between tolerance of damage and resistance to pests is fundamental. Tolerance does not rely on toxicity to kill pests and therefore does not negatively impact non-target organisms or promote resistance development (Welsh et al. 2002). Pedigo (2002) finds that certain crops display tolerance to pest damage. This characteristic has been used commercially with great success for decades with no public controversy. For example, cucumbers with stable tolerance to *Cucumber mosaic virus* have dominated the industry since the 1960s. Genetic modification could be used to amplify these types of properties in several other important crops (Pedigo 2002). The publicness of the environmental benefits potentially derived from such crops dampens private-sector enthusiasm to develop and commercialize them⁶.

However, if regulatory polices effectively control type-II error for transgenic crops, the private sector would receive signals and incentives to assess environmental risks more fully and to develop crops that cause less risk while providing production, health and other potential market benefits. If, for example, governments assigned liability for the deleterious environmental effects to the biotechnology company, perhaps through the posting of a significant bond upon commercialization, more private R&D resources would likely be devoted to controlling adverse effects either through risk-assessment research or developing technologies such as damage-tolerant crops. In essence, this approach forces firms to take into account the shadow price of environmental risks when making decisions about attempting to commercialize a transgenic technology or investing in the development of crops with particular sets of characteristics or traits.

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¹ Risk is used here to convey the combination of the probability of occurrence of some environmental hazard and the harm associated with that hazard (National Research Council NRC 2002, p. 54). This section updates a similar review in a forthcoming article in *Agriculture, Ecosystems and Environment* (Ervin et al. 2003). For more complete discussions of the risks, readers may consult Ervin et al. 2001, Wolfenbarger and Phifer 2000, National Research Council NRC 2002, and Royal Society of Canada 2001.

² The National Research Council (2002) defines four categories of hazards: (1) resistance evolution; (2) movement of genes; (3) whole plants; and (4) non-target effects. Categories (2) and (3) are combined here.

³ We assume for ease of exposition that the environmental hazards can be described by reliable probability distributions to illustrate the differences in the tests. For some hazards, probability distributions cannot be estimated, either objectively or subjectively, i.e., true uncertainty exists. For those cases, nonparametric analytical techniques must be used. For still other hazards, the outcome space is undefined, i.e., surprises may occur, and game-theory techniques can be used (Bishop and Scott 1999).

⁴ Because transgenic crops vary considerably in traits and biological makeup, a disaggregated taxonomy of transgenic crops would improve the analytical power of the differentiated assessment.

⁵ Knudsen and Scandizzo (2001) offer a similar approach by reversing the null hypothesis from one of no significant effect to one of presuming a significant effect.

⁶ Some new products follow this approach, but they are clearly the exception rather than the rule. The biopesticide *Messenger* is an interesting example of this approach to technology development. *Messenger* is a biopesticide that acts as a non-hormone growth regulator for a wide variety of plants. The active ingredient is the naturally occurring Harpin bacterial protein. Applying *Messenger* topically, as a spray, essentially signals plants to activate their natural plant defenses against a variety of diseases and boosts plant development and growth. The primary mode of action is not toxicity to the invading pathogen, but rather entrapment or the creation of a physical barrier to the movement of the pathogen through localized cell death (see EDEN Bioscience Corporation 2002a, 2002b; Wei et al. 1992).