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Considerations on the Use of Transgenic Crops for Insect Control

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ABSTRACT *The adoption of agricultural technologies, whether developed through biotechnology or other methods, depends on social, political, regulatory and biological parameters. This article first presents an example of a low-input, non-biotechnological method of pest control that, while seemingly reasonable to researchers and extension agents, was not adopted by farmers. It then analyses a method for insect management developed through biotechnology that is becoming widely adopted: transgenic plants expressing insecticidal proteins from the bacterium* Bacillus thuringiensis *(*Bt*). Globally increasing adoption of* Bt *plants, by small and large farmers in both low- and high- income countries requires explanation in terms of biological properties of cropping systems and insect populations, alternative control techniques and social policy considerations.*

I. Introduction

Increases in agricultural production depend on the development and adoption of new technologies; however, there is no simple set of guidelines that will help predict the adoption of a specific technology. Even those technologies that work well from a biological standpoint and seem 'reasonable' to outsiders may fail to be adopted. Some agricultural technologies that would seem especially attractive to resource-poor farmers are not; it is worth exploring one example before discussing a product of biotechnology that is becoming widely adopted.

II. Slug Control in Honduras

This example is a 'classic' in the field of pest management in resource-poor countries and is described in detail by Bentley and Andrews (1991), two individuals directly involved with the project. In 1983 an innovative program, *Manejo Integrado de Plagas en Honduras* (MIPH), was begun in Honduras to help farmers deal with pest problems. The MIPH program did not take a top-down approach for

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research-education, but team members and farmer collaborators experimented with old and new technologies in sub-plots of *campesinos'* fields, comparing the efficacy and cost of each technology. One of the first projects focused on controlling a particularly troublesome slug, *Sarasinula plebeia*. Slugs lay their eggs in the corn crop which precedes bean planting, but immature slugs do not cause severe injury to the fast-growing corn. However, as the corn dries down in the fall, slugs move to the newly planted beans, which are usually planted between the rows of the drying corn. Slugs eat bean leaves and can eliminate a whole field of beans overnight. Some growers had tried cutting the maize stalks at ground level early in the fall and stacking the maize upright in the field to help it dry, then planted the beans in open areas rather than between the rows of old corn. They noticed that slugs tended to congregate under the stacks of corn. This makes good biological sense since slugs need to avoid desiccation by avoiding sunlight and open areas. The MIPH personnel took this knowledge of slug biology and agronomic practices and developed the idea of a 'trash trap' for managing slugs. This technology involved making piles of corn stalks at regular distances in the field during the spring when slug populations were low and then turning them over regularly and killing the slugs with a sharp stick or machete.

As Bentley and Andrews (1991) noted, this technique was a promising technology because it used labour when it was abundant, required no purchased input and seemed a commonsense approach to solving a problem, and was certainly safer than continuing to apply the rather toxic pesticide mephosulfan to control slugs in the beans. However, the adoption rates were low because the MIPH personnel made assumptions about several issues, primarily labour. They assumed that this very labour-intensive technology would be welcomed by growers because of its low cost and availability of labour. They neglected to realise that walking through corn fields is difficult because the leaves cut the arms and face of the person and that in the spring, when this practice would be done, poor people are the hungriest and tend to conserve their energy. Furthermore, poor farmers would have to adopt a change in perspective by planning well in advance and working in the spring to control a pest that occurs in the fall. Perhaps the biggest mistake that MIPH made was its assumption that growers would increase their labour output, a reversal of the general trend in agriculture to decrease labour by adopting various technologies (for example, mechanisation). After the failure to adopt the trash trap technology, MIPH worked to develop a program of using smaller doses of a much less toxic pesticide to control the slugs, and this was adopted. While this might only be considered a 'half success' for the poor *campesinos*, it did reduce environmental and human health risks and provided reliable control for a difficult pest. This strategy, however, did remain dependent on a 'more modern' technology – one that would reduce labour. A central theme throughout the history of agricultural production has been to reduce labour, either through mechanisation or other technical advance.

Are there technologies derived through biotech that could provide benefits to the poor and that they would adopt? What assumptions of promoters of a specific technology would encourage poor people to adopt or ignore a product of biotechnology? And what are the risks and benefits to the grower, his/her family, and to the environment of a particular technology? Each technology has its own set of risks and benefits; it would not be prudent to judge all products of biotechnology as being cut from the same fabric. What I will present are some discussion points about plants created through biotechnology to express proteins of a bacterium, *Bacillus thuringiensis*, that are toxic to some insect species. Though trade regulations, intellectual property and other issues influence adoption of products of biotechnology, I will confine my remarks to the biological and environmental impacts of a single technology, that of *Bt* plants.

III. *Bacillus thuringiensis* (*Bt*) and *Bt* plants

Bt is an endospore-forming bacterium in the genus *Bacillus* that produces endotoxins included in crystals formed during sporulation. The crystals of different strains of most *Bt*s contain varying combinations of insecticidal crystal proteins (ICPs), and different ICPs are toxic to different groups of insects. Insecticidal products containing subspecies of *Bt* were first commercialised in France in the late 1930s, and by 1995 there were 182 *Bt* products registered by the United States Environmental Protection Agency (EPA). Although *Bt* was promoted in Rachel Carson's *Silent Spring* (1962) as an alternative management practice to harsher insecticides, even in 1999 the total sales of *Bt* products constituted less than 2 per cent of the $US 8 billion spent globally for all insecticides (Shelton *et al.*, 2002). The reasons for the low adoption were several: compared to other available insecticides, *Bt* was less toxic to insects; *Bt* did not have good residual activity so had to be applied repeatedly; it would only work against selected groups of insects and thus had a very narrow spectrum of activity compared with most other products; it was relatively expensive compared to other products.

Bt, which had limited use as a foliar insecticide for the past five decades, became a major insecticide when genes that produce *Bt* insecticidal proteins were engineered into major crops. *Bt* was first introduced into tobacco plants in 1987 (Vaeck *et al.*, 1987). However, more effective plants incorporating synthetic genes modeled on those from *Bt*, but designed to be more compatible with plant expression, were introduced a few years later (Shelton *et al.*, 2002). Transgenic plants expressing insecticidal proteins from *Bt* were commercialised in 1996, and at least 16 companies were involved in developing *Bt* crops (Roush and Shelton, 1997). Of the $US 8 billion spent annually on all insecticides worldwide, it has been estimated that nearly $2.7 billion could be substituted with *Bt* biotechnology products (Krattiger, 1997). In 2004, *Bt* plants were commercially grown on 22.4 million ha worldwide (James, 2004). Insects targeted for control by *Bt* plants through the production of Cry1Ab, Cry1Ac, Cry 1F, and Cry 2Ab proteins (Cry9C registration expired and was not renewed) are primarily Lepidoptera such as the European corn borer and pink bollworm, major pests of corn (maize) and cotton, respectively. However, plants expressing Cry3Aa have been used on a limited scale for control of the Colorado potato beetle, *Leptinotarsa decemlineata*, and a newly registered product expressing Cry3Bb is being used against the rootworm complex in corn. All presently registered *Bt* crops express a single Cry protein, except for Bollgard II®, which expresses Cry1Ac and Cry2Ab. More than 100 *Bt* toxin genes have been cloned and sequenced, providing an array of proteins that can be expressed in plants (Frutos *et al.*, 1999). Additional *Bt* crops being developed are rice, canola/rapeseed, tobacco, tomato, apples, soybeans, sunflower and peanuts. Broccoli and cabbage have been transformed to express ICPs for control of the diamondback moth, *Plutella* *xylostella*, a major pest of crucifers worldwide. In the United States, 41 per cent of the cotton and 25 per cent of the field corn grown in 2003 used *Bt* plant technology (NASS, 2003), and in China about 50 per cent of the cotton crop is *Bt* (James, 2004).

While this technology has been rapidly adopted by growers, there are debates about its biological sustainability, impact on the environment and potential use in helping farmers manage insect populations. Questions about biological sustainability largely focus on whether insects will rapidly develop resistance to the one or more *Bt* proteins expressed in plants. Questions about the effect of *Bt* plants on the environment usually focus on the potential for *Bt* genes to escape and flow into related plant species and interact with their insect communities, or on the likelihood of *Bt* plants to affect non-target organisms. Amalgamated into these more biological questions are sociological, regulatory and political debates about biotechnology per se and how emphasis on biotechnology may divert efforts away from other agricultural technologies that some consider more favorable from a biological, sociological or political perspective. A large knowledge base has been developed on many of the biological and economic questions, and the following sections provide some synthesis of that knowledge.

IV. Human Safety Aspects

Crops produced through conventional breeding and biotechnology share many of the same safety concerns, but more attention has been given to biotechnology crops. The principal food safety concerns for *Bt* plants are potential toxicity and allergenicity of the introduced proteins, potential changes in nutrient composition of the plants, and the safety of antibiotic resistance-marker-encoded proteins included in the transgenes (Chassy, 2002). A review of these issues is presented in a joint FAO/WHO publication (WHO, 2000). For commercialisation of *Bt* plants, data are required to ensure a reasonable certainty that proteins behave as would be expected of a dietary protein, are not structurally related to any known food allergen or protein toxin, and do not display any oral toxicity when administered at high doses (Shelton *et al.*, 2002). Acute oral toxicity is assessed through feeding studies with mice using a pure preparation of the plant-pesticide protein at doses of greater than 5000 mg/kg bodyweight. None of the *Bt* proteins registered as plant pesticides in the United States has shown any significant effect (WHO, 2000).

The potential allergenicity of a *Bt* protein is examined through in vitro-digestion assays, but further assessment is done by examining amino acid homology against a database of known allergens (WHO 2000). StarLink® corn, which produced Cry9C and was registered only for animal feed, was pulled from the market because of its potential as a human allergen, and because it was detected in processed products for humans. Later studies concluded that it had a low allergen probability (US EPA, 2001). Products produced from *Bt* crops are normally highly processed, which destroys proteins and DNA, and many of the *Bt* products are processed into oils which contain neither the proteins nor DNA. Furthermore, the long-term use of foliar *Bt* sprays without any documented cases of human health problems supported the safety of *Bt* plants.

Despite concerns about toxicity and allergenicity, there are beneficial ways in which *Bt* crops affect human health. The most common effect is the reduction in use of more toxic and persistent insecticides. The most dramatic reductions in insecticide use have occurred in cotton, the crop that receives the most insecticide of any crop worldwide. Estimates of the reduction of insecticides due to *Bt* cotton have varied from 5.4 fewer sprays per crop each season in Arizona (Carriere *et al.*, 2001) to 8.7 million (1998) and 15 million (1999) fewer sprays in total for all states (Carpenter, 2001; Carpenter and Gianessi, 2001). In Australia it has been estimated that *Bt* cotton led to a 43–57 per cent decline in foliar sprays, and in China similar reductions in sprays have been documented (Pray *et al.*, 2001; Wu and Guo, 2005). In a survey of 283 cotton farmers in China, Pray *et al.* (2001) reported that farmers using *Bt* cotton reported less pesticide poisonings than those growing conventional cotton.

Reduction in pesticide application is one positive health effect, but there are others. For example, common ear rot diseases of corn are associated with mycotoxins which are highly toxic to mammals and probably carcinogenic to humans (Munkvold and Desjardins, 1997). Use of *Bt* corn significantly lowers the incidence and severity of ear rots and their associated mycotoxins by eliminating insect feeding, a primary cause of ear rots (Munkvold *et al.*, 1999).

V. Effects of *Bt* Crops on Non-Target Organisms

This is a far less contentious issue than when it first arose. The body of evidence, from published reports and interim reports, indicates that use of *Bt* crops, while managing the target pest, has conserved natural enemies of agricultural pests and non-target organisms far more effectively than any other technique. In those cases in which numbers of natural enemies have been reduced because of *Bt* plants, it has generally been attributed to a reduction in their hosts, that is, the insect pests for which *Bt* plants were grown. These reports have been summarised by the Environmental Protection Agency (EPA), the agency charged with regulating the use of *Bt* plants in the US. In addition to EPA's reports (US EPA, 2001), additional synthesis studies have been published by Snow and Palma (1997) and Carpenter *et al.* (2002). The most recent synthesis (O'Callaghan *et al.*, 2005) indicates that even with the extensive testing on non-target plant-feeding insects and beneficial species that has accompanied the long-term and wide-scale use of *Bt* plants, no reports have detected significant adverse effects. This report also states that *Bt* plants appear to have little impact on soil biota, such as earthworms, collembolans and general microflora. A forthcoming issue of the journal *Environmental Entomology* is devoted to studies on the effects of *Bt* plants on non-target organisms, and the articles contained therein confirm the previous findings.

Three examples, often invoked against *Bt* plants, are worth noting. The first is that of natural enemies being harmed by *Bt* corn pollen or by feeding on insects that have ingested *Bt* proteins from plants. The most widely publicised reports were those of Hilbeck *et al.* (1998a, b), who reported increased mortality and prolonged development when lacewing larvae were reared on pest caterpillars that had ingested corn leaves expressing Cry1Ab. Their experimental design did not permit a distinction between a direct effect of the *Bt* protein on the predator versus an indirect effect of consuming a sub-optimal diet consisting of sick or dying prey that had succumbed to the *Bt* protein; no firm conclusions could be reached. Even ignoring the considerations of the validity of the laboratory methods, the authors state that no conclusions can be drawn because it was not know how results from laboratory trials might translate to the field (Hilbeck *et al.*, 1998a) and that *Bt* transgenic plants are still more environmentally friendly than most, if not all, chemical insecticides (Hilbeck *et al.*, 1998b). Those who present the work by Hilbeck and her colleagues as evidence against *Bt* plants often ignore the authors' statements. In addition, further work in which the predator was directly fed Cry1Ab confirmed that lacewings were not harmed by this protein (Romeis *et al.*, 2004).

The second example is the highly publicised, preliminary laboratory study on the effect of *Bt* corn pollen on the monarch butterfly (Losey *et al.*, 1999). While this study has been strongly criticised for its poor methodology and interpretation (Hodgson, 1999; Shelton and Sears, 2001), it continues to circulate. A series of papers published from laboratory and field experiments over a two-year period concluded that the effect of *Bt* corn pollen on monarchs under present field conditions is 'negligible' (Sears *et al.*, 2001).

A third set of reports suggested that *Bt* exudates from the roots of 13 *Bt* corn hybrids could accumulate in the soil during plant growth as well as in crop residues (Saxena *et al.*, 1999). To assess the effects of Cry1Ab toxin released in the root and from biomass on soil organisms, they introduced earthworms into soil grown to *Bt* and non-*Bt* corn or amended with biomass of *Bt* or non-*Bt* corn. Although the protein was present in the casts and guts of worms in the *Bt* treatments, there were no significant differences in mortality or weight of the earthworms, nor in the total numbers of nematodes and culturable protozoa, bacteria (including actinomycetes), and fungi between rhizosphere soil of *Bt* and non-*Bt* corn or between soils amended with *Bt* or non-*Bt* biomass (Saxena and Stotzsky, 2001).

Considerable research has been done to assess changes in composition of natural enemy populations in *Bt* and non-*Bt* crops. Several studies have shown lower natural enemy populations in *Bt* crops, although this is attributed to reduced populations of the hosts they would have fed on because of the effectiveness of the *Bt* crops (Carpenter *et al.*, 2002; O'Callaghan *et al.*, 2005). It is generally recognised that natural enemy populations are more negatively impacted by use of alternative insecticide treatments. Although the data to date do not indicate striking problems with *Bt* proteins on non-target organisms, they point out the difficulty in working in a complex environment. Studies often focus on single organisms under specific environmental conditions and over an often-short period of time. Under these conditions the power to test for differences is relatively low, and longer-term and more complex studies are needed to ensure the integrity of important non-target organisms. The goal of such research is to ensure that the most environmentally benign technologies are used whenever possible.

VI. Gene Flow in *Bt* Crops

Gene flow and delaying resistance to *Bt* plants are probably the most important and contested issues involving *Bt* plants. Gene flow is common; nearly all important crops grown worldwide are capable of hybridising with wild relatives and have done so for centuries (Ellstrand *et al.*, 1999). However, there has been increased attention to this phenomenon because of biotechnology. The presently used *Bt* crops do not employ methods of controlling the flow and expression of *Bt* genes in subsequent generations. Genes move between plants, but what are the potential consequences of the genes when outside the biotech crop? With the presently available *Bt* crops, there are two mechanisms by which transgenes can move between plant species: dispersal in viable pollen or dissemination in seed. Gene flow through pollen depends on the distance between the donor and recipient plant, the amount of pollen produced and its longevity, the method of dispersal (wind, insects, or other animals), and climatic conditions. Gene flow through seed can occur with seed left in the field, dispersed during transportation or by human intention or by animals. In the case of the presently available *Bt* plants grown in the US (corn and cotton), studies have concluded there is not a reasonable possibility of passing their traits to wild relatives because of differences in chromosome number, phenology, and habitat (US EPA, 2001). The only exception is cotton in Florida and Hawaii, where feral populations of other *Gossypium* species exist. EPA has prohibited or restricted the use of cotton in these areas. However, depending upon the crop and distance involved, such *Bt* transgenes can flow into and pollinate cultivated sister crops, and this has become a hotly debated topic, especially with corn. Corn pollen loses its viability in a few hours and does not generally travel far out of the field because of its weight. However, *Bt* corn can pollinate nearby non-*Bt* corn, albeit at a very low level. This remains a contentious issue especially with organic growers whose standards do not allow the presence of *Bt* corn. Molecular methods for containing gene flow are becoming available (Daniell, 2002), but they will have to be tailored to each crop system. In the meantime if *Bt* and non-*Bt* crops are to be grown in the same area, other tactics such as border crops or reasonable isolation distances will have to be invoked.

VII. Insect Resistance to *Bt* Crops

A frequently mentioned argument against putting *Bt* genes into plants is that insects will soon develop resistance and render this natural product useless. This argument has many sides and requires a bit more scrutiny. First, there are dozens of *Bt* insecticidal proteins, many with different binding sites; if resistance to one does occur, the insect may still be susceptible to others. In this way, *Bt* is unlike most other types of insecticides in which resistance to one member of a class of insecticides generally renders all other insecticides in that class useless. Additionally, if resistance does eventually occur, one should consider the accumulated environmental benefits of *Bt* plants prior to the evolution of resistance.

Still, careful stewardship of *Bt* plants is required. *Bt* is an insecticide and there are hundreds of strains of insect species that have developed resistance to one or more conventional synthetic insecticides, organic insecticides, naturally occurring pathogens, and even to cultural practices like crop rotation. Two species of insects have developed resistance to a *Bt* protein when it was applied as a foliar spray under commercial conditions, and this is further evidence of the need for caution. However, despite the widespread use of *Bt* plants since 1996, there have not been any increases in the frequency of resistance caused by exposure to *Bt* crops in the field (Tabashnik *et al.*, 2003). Likewise, monitoring of field populations in regions with high adoption of *Bt* crops has not yet detected increases in resistance frequency. Monitoring efforts include those for the European corn borer, *Ostrinia nubilalis*, in the US; the pink bollworm, *Pectinophora gossypiella*, in Arizona; *Helicoverpa armigera* in northern China; and *Helicoverpa zea* (Boddie) in North Carolina.

While this lack of resistance to *Bt* plants has surprised some, others have not been so surprised since development and deployment of *Bt* plants has been accompanied by a more thoughtful developmental process and regulation than conventional insecticides (Bates *et al.*, 2005). First, expression of Cry proteins in plants has certain advantages compared to foliar sprays of the same Cry proteins. Expression levels of *Bt* proteins in plants can be maintained at higher levels than if *Bt* is sprayed, thus ensuring that insects are not exposed to sub-lethal doses that would exacerbate resistance development. Another factor delaying resistance to *Bt* crops is the EPA-mandated requirement for refuges of non-*Bt* host plants. These refuges enable survival of susceptible pests that can mate with individuals that are resistant. Since known resistance mechanisms to *Bt* are recessive, this essentially dilutes out resistance genes while maintaining control with the *Bt* plants. From a biological standpoint, it also appears that other factors contribute to the lack of resistance development: low initial resistance allele frequencies, costs associated with resistance that reduce fitness of resistant individuals relative to susceptible individuals on non-*Bt* hosts, and disadvantages suffered by resistant individuals on *Bt* hosts relative to their performance on non-*Bt* hosts (‘incomplete resistance’).

As we refine resistance management strategies for the currently available *Bt* crops, it is imperative that other strategies for managing overall resistance to *Bt* be developed and implemented in the near future (Shelton *et al.*, 2000). Controlling *Bt* expression in plants for particular periods of time (for example, through an inducible promoter) or in particular plant parts (for example, through tissue-specific promoters) may allow larger refuges for susceptible alleles both within the field and within a region while at the same time minimising crop loss (Bates *et al.*, 2005). Other options are already available. Theoretical models and laboratory studies suggest that pyramiding two dissimilar toxin genes in the same plant has the potential to delay the onset of resistance much more effectively than two different single toxin plants released spatially or temporally, and may require smaller refuges (Zhao *et al.*, 2003). One such plant, Bollgard II® cotton, has just been released. Other non-*Bt* genes may also aid in managing resistance to *Bt* crops. Currently the most promising ones being evaluated in transgenic plants include vegetative insecticidal proteins (Yu *et al.*, 1997) and various genes from other insects, animals, plants and bacteria that act as inhibitors of insect digestive enzymes, for example, protease inhibitors, alpha amylase inhibitors and cholesterol oxidase.

VIII. Conclusions

From this entomologist’s viewpoint, the introduction of *Bt* plants has allowed a rather minor and relatively ineffective biological insecticidal protein – long used on organic crops as a foliar spray – to become a major insecticide. *Bt* plants were deployed with the expectation that the environmental and human health risks would be lower than with current or alternative technologies and that the benefits would be greater. Based on the data to date, these expectations seem valid.

The development and implementation of engineered insecticidal plants is currently in its infancy, and the only available technology is that of *Bt*-transgenic plants. The most rapid adoption of *Bt* plants has been in the US, China and Australia, but the technology is likely to spread. At present (2005), only *Bt* corn and cotton are grown commercially, and both are low on the radar screen as crops for human consumption (although cotton seed oil and corn oil are consumed by humans). Perhaps the real test will be when the world's main crop (rice) is produced as a *Bt* crop. Recently published results of field trials of *Bt* rice in China have brought it one step closer to approval and demonstrated a 9 per cent yield increase and reduced use of insecticides (Zi, 2005). Chinese farmers generally have less than 0.1 ha of arable land and have low incomes. So, perhaps it is best to ask if *Bt* plants will help them. Will *Bt* rice provide them with economic and environmental benefits?

Environmental and human health damage due to some insecticides has been substantial; *Bt* plants on current evidence allow some pests to be controlled in a safer manner. One of the criticisms of *Bt* plants is that they are a continuation of the same old paradigm for controlling insects, that *Bt* crops perpetuate the 'pesticide treadmill'. Yet it seems that there is no single long-term sustainable practice to manage insect populations; rather, a combination of practices is needed; *Bt* plants can form a part. As the slug-control case indicates, growers want a strategy that is easily implemented. The rapid increase in area devoted to *Bt* plants indicates that the technology is appealing to growers. In resource-poor areas where growers often do not have ready access to sprayers or biological control agents, incorporation of *Bt* plants into their overall management system can pay substantial benefits. To the extent that any technology, including *Bt* plants, can enable safer production practices, there is a strong case for its adoption in low-income and high-income countries.

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