Applying the Precautionary Principle in Assessing Transgenic Corn Technologies in the U.S.

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A. Introduction and the Global Context

This summer nearly a quarter of U.S. corn acreage will be planted to a hybrid expressing *Bt* toxins for control of the European corn borer (ECB). *Bt*-transgenic corn technology for ECB control has been and remains the most controversial agricultural biotechnology reviewed and approved by the U.S. government. The review process has been driven by top-down policy-imperatives, industry pressure, and politics.

Approval of *Bt*-transgenic corn has already had global consequences. Millions of dollars in U.S. corn exports have been disrupted; ships have been and will continue to be turned away from ports. Food companies are struggling to either find GMO-free corn or a way to answer questions and complaints from customers. Internationally, mandatory labeling is just a matter of time and demand for tests to check for GMO content has given birth to a new cottage industry.

More shoes are bound to drop. An advisor to the Transatlantic Business Dialogue (TABD), a United States and European Union organization of chief executive officers originated, staffed and funded by the U.S. Commerce Department, wrote in 1996 that "its ultimate goal is a New Transatlantic Marketplace, and eventually a global system whereby a product is tested once and approved everywhere [*sic*]."[1]

One brave, new world. Whatever you may think of the TABD model of globalization, it is advocated at the highest levels of the U.S. government. In a 1998 speech to TABD, Vice President Al Gore, stated that "of the 129 recommendations TABD has made in the past three years, over 50 percent have been implemented into law. I wish we had that same level of success with Congress!"[2] As Vice President Gore works the business community this year for campaign support it is likely that many promises will be made for action in the new administration on at least some of the TABD's languishing priorities.[3]

The TABD assumes that "in the era of the transnational corporation and rapid global economic integration, the national-based regulatory regime is no longer rational or

[1] Paula Stern, "The Transatlantic Business Dialogue: A New Model for Trade Expansion and Regulatory Harmonization," speech to The Transatlantic Business Dialogue, 1996. http://www.tabd.org/index1.html
[2] "Vice President [Al] Gore speech to the Transatlantic Business Dialogue Charlotte Conference (Charlotte, North Carolina; November 6, 1998). http://www.tabd.org/index1.html
[3] We note in passing that the Clinton Administration has yet to implement a single recommendation from the Transatlantic Civil Society Dialogues.

efficient."[4] To realize its goal of "approved once, accepted everywhere", TABD has recommended and the U.S. government has implemented an initial Mutual Recognition Agreement (MRA) of "the functional equivalence of regulations and standards" for such products as marine engines and telecommunications equipment.[5] Under the aegis of NAFTA, the U.S. EPA is working with Canada and Mexico regulatory agencies to carry out, on a pilot- project basis, joint reviews of new pesticide active ingredients. The three nations are working toward harmonization of several pesticide data requirements, policies, and processes. Likewise, the EPA pesticide program is working with the European Union on harmonization and how review responsibilities can be shared.

The TABD hopes that an MRA for "biotechnology products" will be among the next group of MRAs established.[6] The Transatlantic Economic Partnership pilot project on biotechnology is working to prepare the way for an MRA. Several more public, private and public-private initiatives can be expected.

In its "Mid-Year 2000 Report", TABD erroneously hearkens to the Rio Declaration as the origin of the precautionary principle. The TABD "is increasingly worried that the principle, taken out of its original context and applied by governments at different levels, will cause serious barriers to transatlantic trade and lead to conflict product requirements."[7] The TABD is apparently comfortable with the precautionary principle as a guide for multilateral decision-making, but is much less comfortable when the principle is applied at national or sub-national levels of government. Implicit in this dichotomy is the high price the business community is willing to pay for harmonization.

Business community discomfort over the precautionary principle is driven, in large part, by concern over how government regulatory agencies might respond to uncertainty in deciding whether to approve biotechnologies. While the U.S. government is engaged in dialogue over the principle at multiple levels, there remains a huge gap between words and deeds. In a U.S. government paper on "Precaution in U.S. Food Safety Decisionmaking," presented to the recent OECD conference on biotechnology, the discussion of uncertainty in a 55 pp. paper is limited to a single mention of "an uncertainty factor to account for the suspectibility of sensitive subgroups; extrapolation from animal data to human applications".[8]

Furthermore, the authors of this paper state shortly afterward, "[w]hat also is obvious is the improbability that any simple principle or model could serve as a useful compass to decision making, in the face of uncertainty, for a wide variety of complex

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[4] Stern, ibid.
[5] "Transatlantic Business Dialogue 2000 Mid-Year Report," (Brussels, Belgium, May 23, 2000), 6. http://www.tabd.org/
[6] Stern, ibid.
[7] "Transatlantic Business Dialogue 2000 Mid-Year Report," 9.
[8] "Precaution in U.S. Food Safety Decisionmaking: Annex II to the United States National Food Safety System Paper," presented to the OECD conference "GM Food Safety: Facts, Uncertainties and Assessment: OECD Conference on the Scientific an Health Aspects of Genetically Modified Food," Edinburgh, United Kingdom, 28 February – 1 March 2000, p. 5.

issues."[9] Despite this apparent empiricism, the U.S. regulatory system for agricultural biotechnology is founded on the general principle of "substantial equivalence"[10] and "familiarity."[11]

The mantra is now familiar -- there is no difference between a new crop variety developed through classical plant breeding and one developed with the tools of modern biotechnology. This assertion is patently false for many reasons, some of which are obvious to most lay people. Still, many scientists continue to try to explain why it is natural and no different from classical plant breeding when a company moves a fish gene into a tomato. Our colleague Dr. Michael Hansen has done a thorough job explaining why there are indeed major differences.[12]

New science published since 1996 has eroded much of the rational and science-base underlying early *Bt*-corn approvals. EPA and USDA have tried to appear responsive to new science, but agency concern has clearly not reached a threshold sufficient to change policy or past decisions. History shows that agencies are not inclined to admit mistakes made, even when mistakes become apparent largely due to new evidence. Nor does the EPA have the support needed in the Congress or White House to deny extensions of *Bt*-corn conditional registrations, as their own regulations would seem to require, at least for those events that do not meet the now semi-official "high dose" criterion. (An "event" is a technique for expressing *Bt* endotoxins in corn plant tissues. Each event expresses a different *Bt* protein at different levels over time in different tissues. The "high-dose" criterion is a key component of resistance management plans; more details follow).

In the midst of ongoing turmoil over what to do about *Bt*-corn for ECB control, the agency received in late 1999 an application from Monsanto for another major *Bt*-based transgenic corn technology – this time involving Cry3Bb proteins for control of corn rootworms, the "mother" of all corn insect pests. A second *Bt*-based technology for rootworm control, relying upon a different transformation event and *Bt* endotoxin, has

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9 Ibid., 6.

10 The assumption of substantial equivalence between genetic engineering and traditional plant breeding was repudiated by FDA scientists to their risk managers at least since 1991, as revealed in documents discovered through a Center for Food Safety lawsuit against FDA. For example, Linda Kahl, FDA Compliance officer wrote to her supervisor Jim Maryanski on January 8, 1992 to comment on the FDA "Statement of Policy: Foods from Genetically Modified Plants": "The processes of genetic engineering and traditional breeding are different, and according to technical experts in the agency lead to different risks. . . .the acknowledgment that the risks are different is lost in the attempt to hold to the doctrine that the product and not the process is regulated." In "The Litigation Against Unregulated, Unlabeled Genetically Engineered Foods: FDA Documents Released Through Discovery," THE CENTER FOR FOOD SAFETY (http://www.icta.org), 5.

11 E.g. Sally L. McCammon, "Regulating the Products of Biotechnology," US Department of Agriculture, *Economic Perspectives*, October 1999.

12 E.g. Michael Hansen, "Genetic Engineering Is Not An Extension of Conventional Plant Breeding: How Genetic Engineering Differs From Conventional Breeding, Hybridization, Wide Crosses and Horizontal Gene Transfer," Briefing Paper for Food and Drug Commissioner Hanney," www.biotech-info.net/wide_crosses.html

been advanced by Dow AgroSciences in conjunction with Pioneer; Novartis-Syngenta are expected to submit a third technology for review before the end of the year.

This paper highlights the "lessons learned" from the review and approval of *Bt*-corn for ECB control and applies these lessons to the assessment of pending applications for *Bt*-corn for rootworm control. Our focus is on how a precautionary approach to the review of ECB technology in the 1995-1998 period would have produced, in retrospect, a better set of decisions. It also would have advanced by years the science-base guiding current and future use of this technology. Insights into how a precautionary approach would have improved the ECB approval process and advanced science are applied to how EPA should conduct the review and decide to approve or deny applications for *Bt*-corn for rootworm control.

B. The Importance of *Bt* to Global and U.S. Agriculture

Before diving into the details of the U.S. regulatory review process, it is critical to establish clearly why the ongoing debate over *Bt*-transgenic technologies has been so spirited. (People familiar with the importance of *Bt* and the basics of corn insect pest management may wish to proceed directly to section D.).

Bt foliar insecticides are the backbone of Lepidopteran IPM systems on sustainable fruit and vegetable farms. Without them, reliance would dramatically increase on high-risk insecticides. The costs of organic production systems would rise markedly and their viability in some areas would be in jeopardy. This is why many NGOs and farmers are so focused on this set of biotechnologies and so adamant that the efficacy of *Bt* must be preserved. Plus, the importance of *Bt* foliar insecticides is clearly rising for farmers worldwide, especially fruit and vegetable growers as a result of the implementation of the 1996 U.S. law, the Food Quality Protection Act.

Reliance on *Bt* Foliar Insecticides

The critical importance of *Bt* foliar insecticides to conventional farmers is rarely stressed in public dialogue about the loss of *Bt*. The efficacy, stability and reliability of *Bt* products have greatly improved over the last decade. They offer the best fit for farmers moving toward prevention-based biointensive IPM systems, since foliar *Bt* sprays have few adverse impacts on non-target beneficial insects.

Resistance management on farms using *Bt* sprays is much easier and more likely to be successful. Compared to transgenic cultivars that express high levels of *Bt* continuously, foliar sprays exert far less and more short-lived selection pressure, even when farmers apply multiple applications in a season. Plus, the endotoxin in foliar sprays is more complex and much less likely to trigger resistance in contrast to the truncated version used in transformation events to produce *Bt*-producing plants.[13]

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[13] For an analysis of why the truncated forms of *Bt* endotoxins in transgenic plants are more likely to lead to resistance, see the excellent 1997 paper by Dr. Beatrix Tappeser of the Institute of Applied Ecology, accessible at <http://www.biotech-info.net/*Bt*_differences.pdf>.

Advances in fermentation and formulation technologies have brought the price of *Bt* sprays way down, often to less than $5.00 per treated acre (not counting application costs; *Bt* is typically added to a tank-mix of other pesticides or fertilizer). For these reasons, *Bt* insecticides are the mainstay of Lepidopteran control on many fruit and vegetable farms. For example, in 1998 some 95 percent of Florida bell pepper acreage was treated an average of 9.5 times with *Bt* sprays. In California, where pepper growers face much less insect pressure, one-quarter of the acreage was still treated an average 4.9 times. Almost half of Florida's strawberry acres were treated 10 times in 1998 and over three-quarters of the State's fresh market tomato acreage were treated an average of 5.2 times (NASS, 1999).

Reliance on *Bt* in tree fruit production is also rapidly increasing, a trend that will accelerate as the EPA restricts post-bloom uses of higher-risk organophosphate (OP) and carbamate insecticides. Innovative growers are now perfecting insect IPM programs combining pheromone-based mating disruption, *Bt* sprays, an application or two of an Insect Growth Regulator (IGR), and either spinosad or a lower-risk OP or carbamate when populations grow over thresholds.

To date in the U.S., the pesticide and biopesticide industry has focused investment on development and marketing of *Bt*-products for Lepidopteran control, although there are a few *Bt* products on the market for mosquito larval control and beetle pest management. These products use different *Bt* endotoxins, such as the *Bt.tenebrionis*, the endotoxin related to the one in *Bt*-potatoes and the Cry3Bb toxin in Monsanto's transgenic corn for rootworm control. There are hundreds of known *Bt* strains and probably hundreds more yet to be discovered (Martin, 1994).

Recent discoveries and advances in formulation technology applicable to new *Bt* products, coupled with recent discovery of generic *Bt*-synergists, have stimulated new interest in the marketing of a broader array of *Bt*-based products controlling a greater range of insects than currently possible. Indeed, if just one percent of the resources invested in *Bt*-transgenic had instead been invested in producing improved *Bt* foliar insecticides, there would in all likelihood be dozens of new, improved products on the market. This investment may still come in time, heightening the importance of contemporary efforts to avoid creating a pool of *Bt*-resistant genes in a number of target insect pests.

Why Reliance on *Bt* is Rising

Broad-spectrum organophosphate and carbamate insecticides bear the major burden worldwide in managing most insect pests. Most insecticides in these families of chemistry pose high risks to applicators, farmers and their families, rural communities, many non-target organisms, and to consumers via residues in food and drinking water.[14]

[14] For extensive data on OP risks and impacts, see the many recent risk assessments of OPs completed by the EPA in response to the FQPA. The schedule for OP reviews and decisions, and risk assessment documents are accessible at <http://www.epa.gov/pesticides/op/status.htm>.

OPs also undermine IPM by routinely triggering secondary pest problems. For these reasons, many farmers are glad to see them go.

Regulatory action by the U.S. EPA, driven by the Food Quality Protection Act (FQPA), is likely to accelerate this process in most parts of the world. As EPA completes OP risk assessments, it is revoking many hundreds of tolerances and will lower dozens more.[15] In August 1999, several uses of methyl parathion and azinphos methyl were banned or restricted. Just last week the Agency announced restrictions on key fruit and vegetable uses of chlorpyrifos. Many more similar actions on other OPs will be announced in the next 12 months.

The chlorpyrifos decision to dramatically reduce tolerances covering major kids food uses – apples, grapes, and tomatoes – sets a key precedent.[16] It now appears that EPA will reduce higher-risk OP tolerances covering fruit and vegetable uses to or near the limit of detection, between 0.005 and 0.02 ppm for most OPs. The only uses that will remain on product labels are early year applications or dormant sprays – use patterns not likely to leave detectable residues in food, the key focus of the FQPA.

Since U.S. residue tolerance levels govern access to the U.S. market, they become *de facto* tolerance levels in all countries hoping to export fresh or processed fruit or vegetables to the U.S. Accordingly, *Bt* use in the South American fruit industry, for example, will rapidly increase. Ditto, *Bt* use across the sizable and growing Mexican and Central American vegetable industries. We doubt this is the kind of harmonization the agribusiness members of the Transatlantic Business Dialogue have been hoping for.

C. *Bt*-Transgenic Technology for Corn Insect Pest Management

The first wave of *Bt*-transgenic technology targeted management of the European corn borer. Regulatory applications were submitted in the 1994-1997 period. Significant commercial use started in crop year 1996, expanded rapidly in crop years 1997-1999, and is projected to decline some 25 percent this year (crop year 2000). Adoption has peaked because of grower-concern about marketing constraints and evidence that the extra cost of *Bt*-corn seed cuts into profit margins more frequently than not. Purdue University researchers are the latest to publish a sobering (for farmers) assessment of the costs and returns associated with *Bt*-corn for ECB control (Hyde et al., 2000; accessible at http://www.biotech-info.net/*Bt*corn_adoption.html).

The second wave of *Bt*-corn technology is under regulatory review and targets the corn rootworm complex of insects. Across the U.S., the corn rootworm complex is the most damaging and prevalent insect pest. Rootworms are both more likely to cause

[15] For a detailed update on recent EPA actions under the FQPA, see the Consumers Union FQPA website. The status of tolerance actions as of August 1999 is reviewed at <http://www.ecologic-ipm.com/CUTRT.html>; high-risk food-pesticide-country of origin combinations are reviewed at <http://www.ecologic-ipm.com/findings_CU.html#reports>).

[16] The chlorpyrifos apple tolerance will be lowered 150-fold, the grape tolerance, 100-fold. Both will be set next year at 0.01 ppm, just above the limit of detection. These tolerances will largely eliminate residues from these key foods.

serious economic losses and are easier to control with insecticides applied at planting. It is for this reason that experts expect farmers to adopt *Bt*-transgenics for rootworm control faster and more broadly than hybrids engineered to resist ECB damage. And thus the pressure on EPA is immense, as are the stakes for farmers, biotech companies, and the country as a whole.[17]

There have yet to be any large-scale field tests of the proposed rootworm technologies and hence major gaps persist in the science-base needed for a thorough review, especially of resistance management plans and non-target ecological effects. Full commercial approval will probably not occur for at least two years and is by no means a sure thing, especially if the EPA chooses to proceed more cautiously and incrementally.

Dealing with ECB Damage

The European corn borer (ECB) is an episodic pest that can cause modest to moderate economic losses in one or two years out of every five. Most farmers do not treat fields for this pest. Infestations are markedly more serious in limited geographic regions in the southwestern Corn Belt, where up to three generations of the insect can plague high-yield, irrigated corn typically grown in large monocultures.

Throughout its range, the insect is not amendable to management using Integrated Pest Management (IPM) and is hard to control using insecticides. For these reasons, since 1990 about one-tenth of corn acreage has been sprayed for ECB control. Only about one-third the corn acres treated with insecticides have targeted the ECB. In terms of corn insecticide pounds applied, ECB acre-treatments have accounted for no more than one-quarter of the total.

The portion of acreage planted to *Bt*-hybrids and/or sprayed with insecticide is highest in the southwest. The percent of corn treated for ECB and rootworm control is estimated in Table 1 based on recent USDA chemical use data. (Table appears at the end of this paper).

Applications to the U.S. Environmental Protection Agency (EPA) for approval of various *Bt* corn events for ECB control – from Monsanto, Novartis, and AgrEvo – moved through EPA review beginning in 1994. First, very limited annual Experimental Use Permits (EUPs) were approved, sanctioning a few thousand acres of plantings. In subsequent years, conditional registrations were granted allowing unlimited acres to be sown. Major regulatory milestones include –

- The first *Bt*-corn technology approved was Mycogen's Cry1Ab technology in 1995.

[17] For extensive information on *Bt*-corn for rootworm control, see the special section of Ag BioTech InfoNet at <http://www.biotech-info.net/rootworm.html>. The January 2000 paper by Univ. of Illinois corn IPM specialist Dr. Michael Gray entitled "Prescriptive Use of Transgenic Hybrids for Corn Rootworms: An Ominous Cloud on the Horizon?" is especially insightful; go to <http://www.biotech-info.net/mgray.pdf>.

- Novartis Cry1Ab technology was also approved in 1995.
- Monsanto's YieldGuard corn with Cry1Ab proteins was approved in 1996.
- DeKalb gained approval of the first Cry1Ac event in 1997, and was subsequently purchased by Monsanto.
- AgrEvo won approval of its Starlink technology based on Cry9c endotoxins in 1998.

Government Action and Inaction Widens the Debate

As the controversy over *Bt*-corn deepened and gained public attention, the EPA and USDA scrambled to find acceptable ways to continue annual approvals of conditional registrations without appearing unconcerned about the loss of *Bt*-based pest management tools or adverse impacts on Monarchs. This has proved a largely futile exercise since people recognize that EPA actions are what really matter and thus far no previously approved *Bt*-technology has been taken off the market.

In fairness to EPA, once on the market in the U.S., the agency faces a very difficult, strict legal standard before it can cancel a registration. Plus, the government has gone on record strongly in support of biotechnology in general, and specifically, *Bt*-transgenic crops in its ongoing dialogue with Europe over grain export trade flows, as well as in the debate over the biosafety protocol. Given how far out on the *Bt*-limb the U.S. government is, it will take a boatload of compelling data showing adverse impacts before the EPA will change its tune on *Bt*-transgenics.

As Europe and international organizations backed away from acceptance of GMO foods, citing scientific uncertainties and evidence of potential risks, the U.S. tried to "hold the line." The government dug in its heels and argued to anyone who would listen that early approvals were "science-based" and that the evidence in support of the safety of GMOs was growing ever-stronger, when in fact a fair reading of the literature and regulatory docket supports neither conclusion.[18]

***Bt* Corn for Rootworm Control**

Monsanto applied for the first Experimental Use Permit (EUP) on Cry3Bb transgenic corn in June 1999. The EUP application was published in the Federal Register on December 8, 1999 and covered three transformation vectors. The EUP sought approval to plant about 1,600 acres each of three Cry3Bb transformed corn varieties in 27 states and Puerto Rico. If approved, the EUP would sanction a maximum planting of about 4,800 acres – as far as we know, the first field-scale trials with this technology.

Two weeks later on December 22, 1999, the EPA published a second Federal Register notice announcing receipt of an August 19, 1999 application from Monsanto for

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[18] For an extensive review of recent scientific findings reinforcing old and/or raising new concerns about GMO foods, see the electronically enhanced AAAS symposium paper "Who Controls and Who will Benefit from Plant Genomics?" (Benbrook, 2000), accessible at <http://www.biotech-info.net/AAASgen.html>.

the same technology – this time seeking full registration under Section 3 of the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA).

The timing was remarkable. In most cases EUP field trials are carried out over two to four years prior to a company seeking a full registration of a new transgenic crop. The purpose of EUPs is to collect detailed data on expression levels, environmental impacts, and performance under field conditions in order to satisfy registration requirements more convincingly. But Monsanto felt ready to go directly to market, in effect moving from greenhouse-scale research to unlimited field use in one year.

Some of the major deficiencies in the EUP application were described in comments submitted to the agency January 7, 2000.[19] More detailed comments were submitted on March 20, 2000 on the full registration application, and focus on ecological impacts and costs and benefits.[20]

D. A Precautionary Approach in Assessing *Bt*-Corn Costs and Benefits

1. Need for *Bt*-Corn Technology

Despite a recent behavioral change in western corn rootworms, crop rotations have been and remain the backbone of corn IPM systems. Typically, less than 10 percent of the acres planted to corn following soybeans or another crop require an insecticide treatment (Gray, 2000). The vast majority of these acres would not benefit from the planting of Cry3Bb corn. Rotations also help reduce ECB populations, but are not as reliable as in the case with rootworms.

According to University of Illinois corn IPM specialist Mike Gray, "Economic infestation levels of corn rootworm larvae do not occur in most cornfields. This knowledge supports the use of established scouting techniques for adult corn rootworms in late summer and the use of transgenic hybrids for corn rootworms the subsequent spring in only those fields that exceeded economic thresholds." (Gray, 2000).

Gray argues for the use of transgenic insecticidal corn varieties for corn rootworm only through "prescriptive use." Core components of such an approach governing *Bt*-corn plantings would include scouting and adherence to thresholds, crop rotations, proper placement and management of refuges, and adherence to resistance management plan provisions.

Gray and other land grant university entomologists believe that the risk of resistance emerging to *Bt*-toxins is great enough to justify the costs of developing and implementing a prescription use program. Steps likely to maximize and sustain the

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[19] The comments were prepared by the Institute for Agriculture and Trade Policy (IATP), the Science and Environmental Health Network (SEHN), and the Consumer Policy Institute/Consumers Union (CPI/CU) and can be accessed on the Internet at <http://www.biotech-info.net/Corn_EUP.pdf>.

[20] Comments submitted on behalf of Environmental Defense, IATP, SEHN, CPI/CU, and are accessible at http://www.biotech-info.net/Cry3Bb.pdf.

benefits of *Bt*-corn to growers are not compatible with the goal of maximizing sales and market share for the manufacturer.

The episodic nature of ECB infestations and the effectiveness of rotations in reducing corn rootworm populations raise the question of need for these technologies. In both cases, years of university research have shown that a high percentage of the acres actually treated by farmers with insecticides for these pests have been prophylactic and unnecessary. So prior to approval, EPA would have been well advised to consider where, and under what circumstances there was need sufficient to justify the costs associated with the use of *Bt*-transgenic technologies. In general, the ability to define when and where the technology would more assuredly delivery benefits would reduce potential plantings, improve the chances that RMPs would work, and provide a logic and basis for incremental approvals. It would also create incentives for the industry to support increased public funding for university scientists.

A fully precautionary approach by the EPA to the first approvals of ECB corn events would have restricted use to those parts of the Corn Belt where ECB pressure was routinely high. In these areas, a significant portion of the corn acres is treated each year with insecticides for ECB control. Adoption of *Bt*-corn in such areas would have led to real reductions in insecticide use and associated risks.

In approving limited use, the EPA should also have specified in some detail the terms and conditions it might accept in approving wider planting in subsequent years. For example, it would have been logical for the EPA to require registrants to explore new ECB scouting techniques to make it possible to identify with greater precision acres at risk in the next season. More in-depth monitoring of ECB movement, mating and over-wintering behavior across crops and as a function of crop rotations would also have provided useful information.

This is an example of how a precautionary approach can stimulate needed research and advance scientific understanding. Work done by registrants to justify approvals in the rest of the Corn Belt would provide the information needed to improve the targeting of use elsewhere. By requiring farmers planting *Bt*-corn in the southwestern corn regions to also experiment with resistance management strategies, the industry and agency would have generated better information and some field experience prior to facing the decision whether to allow the technology to be adopted across the Corn belt.

Likewise, the agency, USDA, and Congress should have assured that public sector researchers had access to adequate resources in the early years of adoption to carry out careful field-scale research. Key topics should have included *Bt*-toxin expression levels in various tissues and over time, ecological impacts, moth mating behavior and movement, and the impacts on soil microbial communities. Data obtained would have provided a needed check on information submitted by registrants. It could also serve as an early warning system, catching possible impacts on Monarchs, a problem that did not surface until three years after the first commercial planting.

If and as confidence was gained in the ECB technology, use could be allowed to spread to other areas incrementally, as long as farmers had a realistic basis to expect that ECB damage would warrant use of the technology. Broader use would be contingent on three factors – ability to target acres where the threat of damage justified use; adherence to a proven, effective resistance management plan; and, a solid basis to project minimal adverse ecological impacts.

In the case of Cry3Bb corn for rootworm control, a similar set of questions should be confronted before approval is granted. Why and where is crop rotation not a viable alternative to transgenic corn? How might Cry3Bb corn fit into an area-wide approach to suppression of corn rootworm populations? How might it's use be rotated with soil insecticides and other tactics? How might Cry3Bb be used strategically in concert with other control measures to suppress populations across wide areas to levels where other, less costly and risky practices would suffice, at least in most years?

As in the case with *Bt*-corn for ECB control, the likelihood of resistance to Cry3Bb varieties is a function of the percent of corn acres in an area being planted to transgenic varieties. Accordingly, EPA should explore with registrants some ways to limit the portion of a given farm that is planted to Cry3Bb and other *Bt*-corn, while also maximizing the diversity of corn rootworm IPM strategies.

2. Expression Levels

Application of the precautionary principle in the assessment of a chemical or genetic technology rests upon reasonably accurate exposure estimates, just as risk assessment relies on good estimates of exposure. In the case of *Bt*-transgenic corn, levels of *Bt* proteins in various plant tissues must be known over time for a variety of purposes. Levels must be measured in roots, leaves, stalks, silks, pollen, grain and crop residues. Variation in levels must be known over time. These data are necessary in order to –

- Project efficacy and reliability across a range of soil types and cropping systems.
- Assess whether the high-dose criterion[21] has been met, a key component of resistance management plans.
- Determine the potential for soil microbial community impacts or impacts on soil insects, worms, etc.
- Analyze impacts to non-target beneficials including, of course, insects in the same family as the target insect and important general predators.
- Estimate dose levels in animal feeds and human foods through grain, silage, roughage and stalks and impacts on animal digestive systems.

In retrospect, information on expression levels was clearly inadequate in the early applications for *Bt* corn varieties targeting the ECB. Some of the transformation events

[21] Resistance management plans for *Bt* crops rest on the high-dose/refugia strategy. Plants are engineered to express a high level of toxin in plant tissues such that there is a very high probability that 99 percent or more of the exposed insects will be killed. The few insects that develop tolerance for the *Bt* toxins will then, it is hoped, breed with susceptible moths in the refuge, producing susceptible off-spring.

had been on the market for three years by the time a judgement was made that they did not meet the high-dose criterion. Likewise, there had been inadequate attention to expression levels in pollen, the key variable in assessing risk to Monarchs. Until Stotzky's work (Saxena, et al., 1999), there was almost no attention to *Bt* protein fate in the soil through root exudates and the break down of tissues in the soil. By 1997, EPA had funded a team in Oregon to begin work on the soil health impacts of *Bt*-transgenics. Several interesting findings have already emerged, as well as a healthy appreciation for the complexity and difficulty of the science.[22]

Now that the importance of understanding expression levels has been made clear, it will be interesting and important to assess the degree to which new *Bt*-corn for rootworm applications contain this information. The Cry3Bb application from Monsanto is profoundly deficient in this area. In the 1998 test season, Monsanto notes a shortage of Cry3Bb transformed seed and also that some of the seed was of poor quality. Trials were carried out in seven locations. According to Monsanto's technical report (MRID # 449043-02), "Approximately fifty to seventy-five seeds were planted per plot of each event at each location," producing a stand count of between 11 and 37 plants per plot."

Thus, prior to submitting to EPA a full registration application, Monsanto scientists had about 300 corn plants to work with in assessing protein expression levels across the two main transformation events covered in the application. Such limited sampling provides a very sparse basis to estimate variability in expression levels across tissues as a function of agronomic systems, soil type, pest pressure and climatic variables.

Some of the most critical measurements of expression levels were done ***on only two plants*** (see the test for Cry3Bb1 and NPTII protein levels in roots and forage in Table 2, page 21). Recall, this *Bt*-corn must express and/or exude *Bt* toxins in the soil in order to work; the crux of resistance management will happen below ground. As a result there can be no serious assessment of the technology without good data on root and root exudate expression levels.

Data from two samples of Cry3Bb expression in roots is obviously far from adequate, yet less than a month after this technical report was completed, Monsanto submitted its application for full, unrestricted registration. In the August 19, 1999 cover letter transmitting the package, Monsanto wrote:

> "Please note that approval of this registration by May, 2000 would reduce the need for additional submissions and reviews for year 2000 field trials."

In addition to expression levels in various tissues, recent findings in Germany documenting gene flow in the wild from rapeseed pollen via the digestive system of bees heightens the importance of better information on the environmental fate of *Bt* toxins as they move through the environment. Likewise, there is evidence that gene flow can and

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[22] See, for example, Donegan, K. K., and R. Seidler. "Effects of transgenic plants on soil and plant microorganisms," *Recent Res. Devel. Microbiology*, Volume 3: 415-424. 1999.

does occur in soil bacterium,[23] the guts of earthworms[24] and nematodes. Indeed it would be shocking if such gene flow did not occur given the high level of microbial activity in these environments and the degree of genetic exchange among bacteria that reside there (Ho, M.W., et al., 1999; Tappeser, B., et al., 1998).

A precautionary approach to the review and approval of *Bt*-corn hybrids for rootworm control would require a reasonably robust baseline of data on expression levels and environment fate prior to any approvals beyond the EUP stage. It is hard to imagine how the industry can develop this data in less than three to five years.

Literally dozens of new expression, exposure, and environmental fate scenarios will have to be analyzed. Methods do not even exist for most, and hence the EPA is in no position to impose a specific set of study protocols on applicants. So how to proceed?

<u>Confronting Uncertainty</u> One basic principle should be that the scope of commercial adoption should be constrained by the degree of uncertainty that remains in critical aspects of the risk assessment. The more irreversible potential impacts, the more conservative EPA should be prior to moving ahead with wider plantings.

Tough decisions and complex policy issues cannot be avoided. For example, we do not believe that industry can, will or should shoulder the full burden for developing and applying the risk assessment methods and risk management framework needed to explore and resolve these new areas of concern. To advance the science most rapidly and efficiently, public researchers must be heavily involved with the work and they must have solid independent funding and not be held hostage professionally if they dare publish a finding perceived as not supportive of a new biotechnology.

The need for public funding to produce answers to key questions raises a new set of issues. Whether the public money invested in biotechnology risk assessment is new or re-directed from current activities, it is fair to ask if this is the best use for it? This is a question that can be answered only through a political process. But lets suppose that the prospect of getting soil insecticides out of Midwestern agriculture does warrant some degree of public funding –

- Research priorities – who and how will they be set?
- Who owns and controls the data generated and how will intellectual property rights be divided?
- If the justification for the public funding is an incremental decrease in corn soil insecticide use for rootworm control, how will progress be monitored and judged relative to the goals set forth? What happens if there is no decrease in soil insecticide use after all? (Note that *Bt*-corn for ECB control has not reduced insecticide use targeted at this pest).
- How will resistance management and liability issues be factored into the equation?

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[23] See (Sorensen, et al.), (Gebhard and Smalla, 1998 and 1999) and (Smith, et al., 1999).
[24] See (Clegg, et al.).

As an aside, workshop participants might be interested in our personal views on these issues of need and the role of public funding in making it possible for *Bt* corn technology to be commercialized. Thirty years from now, we can envision some sectors of the public concluding that the commercialization of *Bt*-corn for rootworm control has been a net plus for Midwestern agriculture, given a full accounting of costs and benefits, and of course assuming resistance is, in fact, adequately managed. But we can not imagine a scenario where the same conclusion would be reached with respect to ECB *Bt*-corn.

This leads to another interesting question – why did industry forge ahead with *Bt*-corn for ECB control when the really important target was corn rootworms? What would it have taken to reverse the polarity of the product development process, so that the billions of public and private resources invested thus far in *Bt*-corn for ECB control could have been redirected to novel strategies for rootworm control, including *Bt*-corn?

This question brings up another key issue in the debate over the precautionary principle. In recent years, industry opportunities to develop, market and profit from applications of agricultural biotechnology has driven the agenda and funding priorities in both the private and public sectors. The agenda is not driven by the needs of farmers, society, nor the interests of global consumers or demands of the global marketplace. At what point should society reserve the right to not invest its funds in answering hard-core risk questions about an agricultural biotechnology, in effect stalling and maybe stopping commercialization? How might, or should this happen?

3. Mammalian Risks

Do *Bt*-transgenic crops pose a food safety risk? Regulatory approvals of Cry3A *Bt*-potatoes, Cry1Ab *Bt*-corns, and indeed all *Bt*-transgenic cultivars have or will rest upon a finding, or assertion, of "substantial equivalence" to the unengineered forms of *Bt* in sprayable insecticide formulations. In the end, the assumption of “substantial equivalence” may prove to be the most damaging and indefensible component of U.S. regulatory treatment of these technologies to date.

From a scientific perspective in the case of transgenic corn, the judgement of “substantial equivalence” requires a “Mostly Yes” answer to three basic questions –

- Are the protein toxins in *Bt*-transgenic plants essentially identical to the protein toxins in otherwise similar sprayable *Bt*’s? (That is, is the Cry3Bb toxin in *Bt* corn essentially the same as *Bt.tenebrionis* that is in sprayable *Bt* products and which has at least been tested to a modest degree in mammalian systems?).
- Are the exposure pathways, levels, and duration about the same?
- Are there any impurities, degradation products, or genetic components that might lead to different interactions with environments outside the plant, such as soil microbial communities, aquatic ecosystems, the digestive systems of pigs, people or bees?

It would take many, many pages to cite all the evidence that supports a clear "No!" in response to EACH ONE OF THESE QUESTIONS.

The Monsanto patent application underlying the Cry3Bb technology settles the first issue in a convincing way.[25] It explains in detail how and why they truncated the natural *Bt.tenebrionis* protein to make it easier to express in plants. They show that very small differences in this truncated form of the endotoxin makes an enormous difference in its expression and toxicity.

In terms of evidence on the safety of the unengineered endotoxin, Monsanto refers to data previously submitted on a foliar *Bt* spray called Raven (registered and tested by Ecogen), which contains the full, untruncated *Bt.tenebrionis* endotoxin. In the full registration application, Monsanto states that –

> "…two Cry3Bb proteins described in this registration request share 99.2% and 99.1% amino acid sequence identity with the Cry3Bb1, the holotype Cry3Bb protein present in Raven."

While seemingly reassuring, Monsanto's patent application covering the underlying technology also states that, in the case of Cry1 proteins, the "deletion of only 4 amino (pMON5448) acids resulted in a complete loss of activity" against Lepidopteran insects.

In the summary of the registration application, Monsanto states that the safety of corn containing Cry3Bb proteins to mammals rests on --

- Multiple studies showing very high NOELS ("No Observable Effect Levels") in acute feeding studies with a variety of Cry proteins in a number of species.
- Similarity of Cry3Bb proteins to other Cry proteins and *Bt* insecticides, especially the Ecogen product Raven, which contains a mixture of two Cry3 proteins and Cry1Ac.
- A 40-year history of safe use of *Bt* insecticides and Cry proteins.

There are indeed very wide margins of safety in terms of acute poisoning when mammals ingest Cry proteins, including in all probability Cry3Bb proteins. Acute toxicity should be investigated through dermal, inhalation and dietary routes of exposure. Except perhaps among people highly exposed occupationally, acute toxicity is not the human health or livestock endpoint of concern.

On the second point, little is known about the degree of similarity or differences between Cry3Bb proteins and other Cry proteins in terms of allergenicity, digestive system impacts, gene silencing, and the likelihood and nature of gene flow. Even less is known about differences across the Cry3Bb proteins associated with different transformation events.

[25] See (Fischhoff, 1998).

Finally, the American population has not been extensively exposed to any Cry proteins over 40 years – sprayable *Bt*s simply do not leave residues on food, except in rare circumstances (picking a ripe tomato from a greenhouse within a day of treatment and eating it unwashed). The only other possible route of significant dietary exposure since 1997 would be transgenic potatoes containing Cry3A proteins (New Leaf potatoes). But since New Leaf varieties have performed poorly in the field, they have never accounted for more than a few percent of national potato acreage.

A number of veterinarians and animal health specialists, including U.S. Food and Drug Administration scientists, have pointed to the profound differences in exposure levels when assessing potential impacts of *Bt*-transgenic crops on livestock. The basis of their concern is that corn makes up such a high percentage of the diet for many animals during much of their developmental period. Plus, these animals are typically housed in confinement systems, subjected to intense stress and disease pressure, and treated daily with a mix of antibiotics. Under such circumstances, the likelihood of gene flow from transformed corn to bacteria in the digestive systems of animals would seem impossible to dismiss. Indeed, Dutch scientists have now shown that transgenic DNA can be picked up by bacteria in the digestive system of rats and that it can translocate through cells in the stomach wall, entering blood and organs (Schubbert, R. et al., 1997).

Now that this long-feared example of gene flow has been demonstrated, a precautionary approach dictates that much more work be done on its significance prior to moving on with the planting of a large portion of U.S. corn to another *Bt*-based technology. This will require the development of new techniques to track gene flow and the fate of *Bt* toxins in animal digestive and vascular systems. In large part, the public sector should be responsible for developing, validating and applying these new research tools. But since the U.S. government has yet to back away from its "substantial equivalence" risk management framework, little new funding has been committed to GMO risk assessment and research. European scientists and institutions, on the other hand, have carried out a wide range of sophisticated studies. Recent findings have undermined key assertions by the industry and biotech defenders, and may soon lend considerable legitimacy to questions regarding human health impacts.

4. Resistance Management

From 1995 through 1998, the design and adequacy of resistance management plans (RMPs) was the primary bone of contention with *Bt*-corn for ECB control. Because of concerns over resistance, each year the terms of EPA-approved conditional registrations have become more encompassing, explicit, and restrictive. The portion of the crop set aside for refugia – a core element in all RMPs -- has evolved from a friendly suggestion of 5 percent to a requirement for 40 percent in areas where *Bt* corn and *Bt* cotton overlap.[26]

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[26] Higher refugia requirements were imposed in such areas because the ECB moves readily between these crops.

By 1996, several prominent U.S. consumer and environmental groups had called upon EPA to impose a moratorium on *Bt*-transgenic approvals and plantings, largely based on experience suggesting that despite RMPs, resistance was only a matter of time.[27] Industry statements had also acknowledged that resistance was likely, but might be delayed for 10 years. Such assurances did little to quell concerns.

Why has the controversy grown over the last five years? As noted earlier, conventional foliar insecticides containing *Bt* are as important to agriculture – organic and conventional farmers alike – as antibiotics are to doctors treating human infectious diseases. If and when the efficacy of foliar *Bt* sprays are undermined by resistance, the biotechnology industry will probably face the first truly "big league" class action lawsuit of the biotech era. There will be hundreds of millions dollars, if not billions in play.

EPA began in 1996 to make explicit in its conditional registrations that the registrants must develop and assure grower-adherence to effective, "science-based" resistance management plan. Most conditional registrations were approved for one- or two-year periods and several have already been renewed once. All are in need of extensions in the next 24 months if *Bt*-corn for ECB control is going to stay on the market beyond crop year 2002.

Future approvals are in doubt because of the erosion in confidence in RMPs. Opponents of future use and approvals will surely cite the May 1999 paper on the genetics of inheritance of the *Bt*-resistance trait by Huang et all in *Science*. This paper undermined one of the major assumptions behind high-dose plus refugia RMPs and no one has come up with an alternative pillar on which to rest the projected efficacy of today's RMPs.[28]

In a March 2000 paper in *Nature Biotechnology*, Shelton and colleagues showed that sprayed refuges were much less likely to work, calling into question another aspect of *Bt*-corn RMPs.[29] In our judgement, there is now no way the EPA can claim that the conditions it had set forth in conditional registrations have been met. The absence of proven RMPs is the strongest legal argument in favor of denial of the pending applications for extensions of the current ECB *Bt*-corn approvals.[30]

So what are the next steps on the RMP front for both *Bt*-corn technologies?

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[27] See the 1996 Consumers Union report *Pest Management at the Crossroads* (Benbrook, C. et al., 1996) and the 1998 Union of Concerned Scientists report *Now or Never: Serious New Plans to Save a Natural Pest Control*, Edited by Margaret Mellon and Jane Rissler.

[28] The Huang et all paper is accessible at <http://www.biotech-info.net/inheritance_resistance.pdf.

[29] This important paper and further commentary on the efficacy of refuges is accessible at http://www.biotech-info.net/field_refuges.html.

[30] For details on this argument and further documentation, see Benbrook's comments at the June 1999 USDA-EPA workshop on *Bt*-resistance management, accessible at <http://www.biotech-info.net/ECB.pdf>. A summary of the workshop presentations is at <http://www.biotech-info.net/meeting_report.html>.

The first and most important missing policy ingredient is a clear, unambiguous statement by EPA regarding the goal of a RMP. After all, how can the adequacy of RMPs be evaluated without a clear statement of their goal?

EPA has yet to firmly state that a RMP must ***prevent*** resistance rather than just delay it. Today's monitoring efforts will be adequate to document the emergence of resistance within a year or two of its first appearance in the field, but are clearly and unequivocally not adequate to prevent it from occurring. In comments to the June 1999 USDA-EPA *Bt*-resistance management workshop in Chicago, Benbrook offered one formulation of a goal for RMPs, referred to in that meeting as "Insect Resistance Management," or IRM.[31]

> "Before extending the conditional registrations for ***any*** *Bt*-corn variety, the EPA should be able to conclude, based on credible data and expert opinion that –
>
> > **The monitoring component in an IRM plan is sufficiently sensitive to identify the early stages of the emergence of resistance. A monitoring plan is "sufficiently sensitive" if it will identify increases in the frequency of either fully or partial resistant alleles in time to implement remedial actions that will prevent the emergence of stable resistance in pest populations. Hence, the projected time period between recognition of the first signs of resistance and the evolution of stable resistance is a critical evaluation criterion and important scientific question.**
> >
> > **Until more is known about corn insect pest movement, the genetic basis, and temporal dynamics of resistant gene flow within and across populations, the Agency must be conservative in its judgements and the requirements it imposes, just as it is when approving tolerances in the face of scientific uncertainty. In the instance of *Bt*-transgenic crops, the EPA should insist upon a few extra years for the monitoring plan to confirm the first stages of resistance and for the industry to put in place remedial actions sufficient to stop resistance before it becomes a stable part of some pest population."**

To assess a RMP, scientists must understand the genetics of resistance, as well as insect movement and mating behavior within and across fields and refuges. The genetics of resistance is necessary information to project the time between the first signs of resistance in a field population and the emergence of stable resistance. The industry is not required to submit such information and the few public sector scientists qualified to elucidate these mechanisms have had difficulty securing support for their work.

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[31] The full statement is accessible at <http://biotech-info.net/*Bt*_corn_resist_mgmt.html>, along with other presentations made at the workshop and a summary report.

Likewise, scientists do not understand how quickly resistance might spread through a population and across populations, nor how stable and hence reversible it might be. The National Corn Growers-industry RMP calls for remedial actions in regions where a resistant phenotype is found. No one knows, however, how effective the proposed remedial actions might be and whether it will be possible to accurately track their impact.

In light of these gaps in knowledge, a precautionary approach would require conservative assumptions in the absence of credible evidence from fieldwork. A cautious, incremental approach will be especially needed if the goal of public policy is to prevent resistance. If the EPA accepts resistance as an inevitable outcome, then the agency has no reason to demand or analyze information on the genetics of resistance. It matters relatively little if resistance emerges in 3 or 13 years, although the companies would much prefer a longer period to recoup their investments.

5. New Issues Emerge

Publication of the May 1999 Losey et all paper in *Nature* on potential impacts on Monarch butterflies struck a nerve worldwide and triggered a flurry of activity assessing the impacts of *Bt*-corn pollen on butterflies.[32] For months the U.S. government had responded vigorously to risk concerns about GMOs by pointing to the exhaustive risk assessments it had carried out on all approved transgenic crop varieties.

The Losey paper led many people to question the extent to which EPA had considered the potential adverse impacts of *Bt*-pollen on non-target Lepidopteran insects – species known to be susceptible to transgenic Cry 1Ab *Bt*-plants and pollen. It took little effort in reviewing the EPA docket to determine that the agency had hardly considered such impacts. Interest in and reaction to the Losey paper was driven in no small part by the revelation that the U.S. review and approval process was much more narrow and shallow than had been advertised.

After months of rancorous discussion, including well-orchestrated personal and professional attacks on the scientists who published the work, the EPA convened a Scientific Advisory Panel (SAP) meeting in December 1999. The panel was asked to review EPA non-target organism testing requirements applicable to *Bt* crops. To no one's surprise, the panel found the requirements inadequate and urged the agency to substantially expand the scope and quality of the studies it relies upon.[33]

Two critical issues remain in dealing with non-target impacts. First, what is the goal or standard for acceptability of a *Bt*-corn technology with respect to impacts on non-target species, whether a beneficial insect like lacewings or highly valued species like the Monarch? Possible answers range from "No Observable Impact" – a standard that seems

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[32] To view the Losey paper and for extensive reaction to it and more recent research, go to <http://www.biotech-info.net/butterflies_*Bt*corn.html>).

[33] The final report of the SAP panel is accessible at http://www.epa.gov/scipoly/sap/1999/december/report.pdf.

roughly consistent with expectations in Europe – to "No Impact Worse Than Conventional Insecticides," the standard favored by the U.S. biotechnology industry. The FIFRA statute sets the actual standard the U.S. EPA must apply – in short, EPA approves new technology if it determines that no risk thresholds are exceeded. The agency conducts a full risk-benefit assessment only in cases of technology already on the market when a risk threshold has been exceeded and the need for and nature of risk mitigation measures, including possibly a ban on further use, is under consideration.

Adhering to any of these standards raises both policy and empirical questions. *Bt*-corn technologies will impact the environment in qualitatively different ways than OP soil insecticides. How does one weigh such different risks in judging which one is "worse"? Worse to whom, compared to what, measured how?

Corn insecticides impose well documented, relatively easy to monitor effects on non-targets that are largely contained and reversible, assuming a species is not driven to extinction. *Bt*-transgenic corn is likely to impose a greater range of more subtle impacts, some with lower probabilities, but the consequences could be broader and the impacts more uncontained. Judging which set of risks are "worse" is a challenge for policy-makers that they have yet to seriously grapple with.

If EPA registers *Bt*-corn for rootworms, the experiment will proceed and a key, unstated policy decision will have been made. If a precautionary approach prevails, how to settle the question of "what is worse" will evolve through an open, consultative process. Many analytical hurdles will remain, but the process and the precautionary framework will provide a basis to channel research and shape consensus.

A third important area of concern is now attracting long-overdo attention – impacts of *Bt*-crops on non-target beneficial insects that play a role in biological control mechanisms. Work by Swedish scientists led by Angelica Hilbeck demonstrated the subtle effects of *Bt*-corn on general predators like lacewings. Her team's work demonstrating tritrophic effects on non-target beneficials in 1988-1999 added another ecosystem and pest management related concern to a growing list.[34]

Stotzky's research on the persistent of *Bt* toxins from transgenic plants in soil added a fourth dimension in the list of ecological concerns in need of much more field research (see <http://www.biotech-info.net/risks.html#soil> for his key December 1999 *Nature* article and a commentary by Benbrook).

The core elements of a precautionary approach to these new concerns are the same as those that should govern the other concerns addressed earlier –

[34] See (Hilbeck, A., et al., 1998a, 1998b, 1999). This work is summarized in the March 1999 *A Seed* article "*Bt* Crops and Their Impacts on Insects and Food Webs," accessible at http://www.biotech-info.net/insects2.html. Further discussion of the significance of this work appears in the summary of the March 2000 meeting at U.C. Berkeley organized by Miguel Altieri, accessible at http://www.biotech-info.net/summary1.pdf.

- Proceed incrementally and only if registrants and others agree to abide by the rules and principles established to assure a positive outcome in the face of uncertainty (i.e., adherence to a precautionary approach).
- The goals underlying performance standards must be clearly stated and explicitly linked to policy objectives and priorities.
- As a legal prerequisite prior to approvals, registrants and stakeholders with an economic interest must agree to do their share in paying for needed research and monitoring and cooperating with independent scientists.
- Approvals should be based on evidence that the technology has and will meet certain standards of performance.
- A plan to monitor performance and potential risks via properly designed independent field research should be agreed upon, practical, and funded.
- Some of the fieldwork should be done under worse case scenarios. If careful research fails to validate the basis of a risk concern under such circumstances, the level of concern should be downgraded and monitoring resources invested elsewhere or reduced.
- When performance standards are not met, there should be a clear and non-litigious process for cutting back on commercial plantings until outstanding issues are resolved.
- As encouraging results are obtained and as confidence grows, plantings should be allowed to expand, while also initiating the necessary experiments to answer new questions that arise as the level of adoption increases. (Some problems will not be pressing in the early stages of adoption, but if and as the technology moves toward a major place in corn production, new issues will surely warrant analysis).

Parting Thoughts

Assessing how the U.S. EPA managed the process leading to the commercialization of *Bt*-corn engineered to control the ECB provides important insights into structural and legal shortcomings in the review and approval process. In this paper, we offer a taxonomy of these shortcomings and find that the precautionary principle provides a useful framework for defining a course of action that falls between wide-open commercial approvals and “Just Say No” denials.

We are particularly impressed with the extent to which a precautionary approach, if adhered to early in the process, would have led to a consensus on several core scientific questions that needed immediate attention. Suppose the USDA and EPA, along with the private sector and NGOs had met at the table in 1995 to set forth a research agenda and assure that well-supported and independent scientists carried it out. Under this scenario, there is at least a chance that answers and insights for many of the issues described above would have emerged prior to or in step with approvals allowing widespread commercial plantings. This would not have eliminated all tensions nor settled all policy debates, but it would have helped channel debate to issues involving choices, values, goals and tradeoffs.

Lessons learned would have provided a much firmer foundation for review of and action on the new generation of *Bt*-corn technologies targeting the corn rootworm. In government, precedent is often the enemy of progress. The U.S. government is still in denial regarding its "substantial equivalence" policy and has not acknowledged the scientific shortcomings of past decisions. Perhaps the recent steps taken by USDA and FDA to solicit public input will help the agencies find reasons and a way to move beyond what they have said and done in the past.

Without concerted action and a significant investment in new science, the weight of uncertainty and public skepticism will continue to impose mammoth costs on those wishing to bring forward the benefits of biotechnology in food production. The U.S. government must play a major but very different role in this new phase. In order to restore confidence in agency objectivity and scientific acumen, the approval process must become much more rigorous and cautions. This will not be easy since precedent carries so much weight in the U.S. legal system.

Ironically within a few years, the business community may have to shelve its skepticism about the precautionary principle and work to gain passage in the U.S. of legislation incorporating the core provisions of the precautionary principle into basic environmental laws. Why? Because new legislation may emerge as the only way to liberate agencies from the need to dance around and defend early miss-steps. If EPA continues to spend most of its time and political capital dealing the first generation of agricultural biotechnologies, the second generation will pay the price.

percent acres treated, i.e. 2.0 equals 2%]							
Active Ingredient	**Likely Target Pest**	**1971**	**1982**	**1991**	**1995**	**1998**	**1999**
lambda-cyhalothrin	ECB					2.00	3.00
permethrin	ECB			2.00	4.00	2.00	3.00
cyfluthrin	ECB						2.00
dimethoate	ECB		0.00	0.28		1.00	
propargite	ECB			0.18		0.50	
Bt	ECB			0.40			
carbaryl	ECB	1.62	0.17				
diazinon	ECB	2.50	0.18	0.20			
esfenvalerate	ECB			0.44			
fenvalerate	ECB		0.07				
malathion	ECB	0.20					
methomyl	ECB		0.40				
methoxychlor	ECB	0.08					
Subtotal ECB Control		**4.39**	**0.82**	**3.50**	**4.00**	**5.50**	**8.00**
One-half Acreage Treated with Rootworm + ECB Products		1.41	2.43	5.67	5.50	6.50	4.50
Total Acreage Treated for ECB		**5.80**	**3.25**	**9.17**	**9.50**	**12.00**	**12.50**
terbufos	Rootworm		9.40	8.00	6.00	6.00	5.00
tefluthrin	Rootworm			2.00	5.00	5.00	7.00
tebupirimiphos	Rootworm						2.00
carbofuran	Rootworm	4.97	6.66	3.00	2.00	1.00	1.00
chlorethoxyfos	Rootworm					1.00	1.00
fonofos	Rootworm		6.88	4.00	1.00	1.00	
phorate	Rootworm	4.53	4.57	2.00	1.00	0.50	
aldrin	Rootworm	10.18					
bufencarb (RE-5353)	Rootworm	5.98					
chlordane	Rootworm	0.72					
DDT	Rootworm	0.01					
endrin	Rootworm	0.10					
ethoprophos	Rootworm		0.84				
flucythrinate	Rootworm			0.15			
heptachlor	Rootworm	2.57					
isofenphos	Rootworm		1.15				
paraquat dichloride	Rootworm		0.25				
toxaphene	Rootworm	0.19	0.37				
trimethacarb	Rootworm			0.17			
Subtotal Rootworm		**29.23**	**30.12**	**19.32**	**15.00**	**14.50**	**16.00**
chlorpyrifos	Rootworm + ECB		4.13	9.00	7.00	6.00	5.00
bifenthrin	Rootworm + ECB			0.34	1.00	2.00	2.00
fipronil	Rootworm + ECB					1.00	1.00
parathion-methyl	Rootworm + ECB	0.06	0.19	2.00	3.00	1.00	1.00
cyfluthrin + tebupirimiphos	Rootworm + ECB					3.00	
disulfoton	Rootworm + ECB	0.70	0.01				
monocrotophos	Rootworm + ECB		0.07				
oxydemeton-methyl	Rootworm + ECB		0.47				
parathion	Rootworm + ECB	2.06					
Subtotal Products Both Pests		**2.82**	**4.86**	**11.34**	**11.00**	**13.00**	**9.00**
% Acres Treated All Chemicals, All Target Pests		**36.4**	**35.8**	**34.2**	**30.0**	**33.0**	**33.0**

Source: Compiled by Benbrook Consulting Services, based on data in USDA/NASS field crop chemical use surveys, multiple years.

References

Benbrook, C., Groth, E, Hansen, M., Halloran, J., and S. Marquardt. Pest Management at the Crossraods, Consumers Union of the U.S.. 1996. (To purchase a copy call 208-263-5236, or send an e-mail to Karen@hillnet.com>).

Buchanan, R. L., and M. P. Doyle. "Foodborne disease significance of *E. coli* 0157:H7 and other enterohemoorrhagic E. coli," *Food Technology*, Volume 51: 69-76. 1997.

Clegg, C.D., Anderson, J.M., Lappinscott, H.M., VanElsas, J.D., and J.M. Jolly. "Interaction of a genetically modified pseudomonas flourescens with the soil-feeding earthworm Octolasion cyaneum," *Soil Biology and Biochemistry*, Vol. 27: 1423-1429.

Donegan, K. K., and R. Seidler. "Effects of transgenic plants on soil and plant microorganisms," *Recent Res. Devel. Microbiology*, Volume 3: 415-424. 1999.

Donegan, K. K., Seidler, R. J., Fieland, V. J., Schaller, D. L., Palm, C. J., Ganio, L. M., Cardwell, D. M., and Y. Steinberger. "Decomposition of genetically engineered tobacco under field conditions: persistence of proteinase inhibitor I product and effects on soil microbial respiration and protozoa, nematode and microarthropod populations," *Journal of Applied Ecology*, Volume 37: 767-777. 1997.

Gebhard, F., and K. Smalla. "Transformation of *Acinetobacter* sp. Strain BD413 by Transgenic Sugar Beet DNA," *Applied and Environmental Microbiology*, Volume 64, Number 4: 1550-1554. 1998.

Gebhard, F., and F. Smalla. "Monitoring field releases of genetically modified sugar beets for persistence of transgenic plant DNA and horizontal gene transfer," *FEMS Microbiology Ecology*, Volume 28, Number 3: 261-272. 1999.

Gray, M. E. "Prescriptive Use of Transgenic Hybrids for Corn Rootworms: An Ominous Cloud on the Horizon?", *Proceedings of the Year 2000 Crop Protection Technology Conference*, University of Illinois at Champaign-Urbana, January, 2000.

Gray, M. E., and K. L. Steffey. "Corn Rootworm Larval Injury and Root Compensation of 12 Maize Hybrids: An Assessment of the Economic Injury Index," *Journal of Economic Entomology*, Volume 91, Number 3: 723-740. 1998.

Fischhoff, D. et al., "U.S. Patent Number 5,763,241," granted to Monsanto Company, June 9, 1998.

Hilbeck A., Baumgartner, A. M., Fried, P. M., and F. Bigler, "Effects of transgenic Bacillus thuringiensis corn-fed prey on mortality and development time of immature Chrysoperla carnea," *Environmental Entomology*, Volume 27: 480-487. 1998a.

Hilbeck, A, Moar, W.J., Pusztai-Carey, M., Filippini, A., and Franz Bigler. "Toxicity of the Bacillus thuringiensis Cry1Ab toxin on the predator Chrysoperla carnea using diet incorporated bioassays," *Environmental Entomology*, Voilume 27: 1255-1263. 1998b.

Hilbeck, A, Moar, W.J., Pusztai-Carey, M., Filippini, A., and Franz Bigler. "Prey-mediated effects of Cry1Ab toxin and protoxin and Cry2A protoxin on the predator Chrysoperla carnea," *Entomologia Experimentalis et Applicata*, Volume 91: 305-316. 1999.

Ho, M.W., Traavik, T., Olsvik, O., Tappeser, B., Howard, C.V., von Weizsacker, C., and G.C. MacGavin. "Gene technology and gene ecology of infectious diseases," *Microbial Ecology in Health and Disease*, Volume 10:33-59. 1998.

Martin, P. "An Iconoclastic View of *Bacillus thuringiensis Ecology*," *American Entomologist*, Volume 40, Summer: pages 85-90. 1994.

National Agricultural Statistics Service (NASS). *Agricultural Chemical Usage: 1998 Vegetable Summary*, USDA/NASS, July 1999.

Saxena, D., Flores, S., and G. Stotzky. "Insecticidal toxin in root exudates from *Bt* corn," *Nature*, Volume 402, December 2, 1999: page 480. Accessible on Ag Biotech InfoNet at <http://www.biotech-info.net/risks.html#soil>.

Shelton, A. M., Tang, J., Roush, R. T., Metz, T. D., and E. Earle. "Field tests on managing resistance to *Bt*-engineered plants," *Nature Biotechnology*, Volume 18: 339-342. 2000.

Smith, K.P., Handelsman, J., and R.M. Goodman. "Genetic basis in plants for interactions with disease-suppressive bacteria," *Proceedings of the National Academy of Sciences*. Volume 96: 4786-4790. 1999. http://www.biotech-info.net/genetic_basis.html.

Schubbert, R.., Renz, D., Schmitz, B., and W. Doerfler. "Foreign (M13) DNA ingested by mice reaches peripheral leukocytes, spleen, and liver via the intestinal wall mucosa and can be covalently linked to mouse DNA," *Proceedings of the National Academy of Sciences*, Volume 94: 961-966. 1997.

Sorensen, S.J., Schyberg, T., and R. Ronn. "Predation by protozoa on *Escherichia coli* K12 in soil and transfer of resistance plasmid RP4 to indigenous bacteria is soil," *Applied Soil Ecology*. Volume 11: 79-90.

Tappeser, B., Jager, M., and C. Eckelkamp. "Survival, Persistence, Transfer – An Update on Current Knowledge on GMOs and the Fate of Recombinant DNA," Institute for Applied Ecology, Germany, May 1998, <http://www.oeko.de/english/gentech/gmo.htm>.

van der Heijden, M.G.A., Klironomos, J.N., Ursic, M., Moutgolis, P., Streitwolf-Engel, R., Boller, T., Wiemken, A, and I.R. Sanders. 1998. "Mycorrihzal fungal diversity determines plant biodiversity, ecosystem variability and productivity," *Nature*. 396:69-72. http://www.biotech-info.net/mycorrihzal.html.