

WASHINGTON, D.C.—New concerns over resistance to *Bacillus thuringiensis* (Bt) insecticides in targetcrop pests are bringing together researchers, environmentalists, and other specialists, who are trying to devise strategies for "resistance management." Optimists have been saying that Bt sales could grow ten-fold to top \$1 billion by 2000. However, if the resistance problem is not faced immediately, say pessimists, the useful lifetime and sales of Bt could fall far short of those projections.

BEATING BUGS

"We cannot afford to wait on the problem of insect resistance to Bt.' assert staff members of the National Audubon Society (Washington, DC), who recently convened a workshop on the topic here. Participants-including officials from the U.S. Environmental Protection Agency (EPA, Washington, DC) and representatives from the biotechnology industryseem agreed that resistance-management programs are needed. Participants from several environmental groups also say that approach is essential, but contend that even careful use of Bt will likely reduce its efficacy and thus lead to renewed dependence on traditional chemical pesticides.

Different strains of Bt, a soil-dwelling bacterium, produce a family of endotoxin polypeptides with activity against a range of insects. Typically, it is protoxins that are consumed by susceptible insects, partly digested, and then bound as active toxins to receptors along insect cell membranes of the gastrointestinal tract where they destroy membrane integrity. Reduced affinity of receptors for Bt molecules apparently is the means by which an insect acquires resistance.

Currently, Bt insecticides are formulated as partly purified protein products, or they are encapsulated in killed bacterial cells, which serves to prolong the product's effective field life. In addition, biotechnology researchers in universities and at companies in the U.S. and Europe are introducing Bt genes into a wide variety of agriculturally important plants. Although anticipated use of such transgenic plants intensifies concerns that insecticide resistance will develop more rapidly, the extended use of any Bt-containing products could promote resistance in insects.

Some resistance already is occurring. For example, Bruce Tabashnik at the University of Hawaii (Honolulu, HI) found Bt resistance in diamondback moths, whose larvae infest watercress and cruciferous vegetables throughout the state. A few years ago, no such resistance was noted. Now three distinct populations of moth are moderately resistant to this insecticide. "All had been heavily treated with Bt," says Michael Caprio of the University of California (Berkeley), who worked with Tabashnik.

RESISTANCE PROMPTS EARLY PLANNING

Similarly, Bt resistance is found among Colorado potato beetles in Florida and New York, according to Rich Rousch of Cornell University (Ithaca, NY). Other reports indicate Bt-resistant insects on crops in Japan,

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the Philippines, Thailand, and Taiwan. In all such cases, Bt products were applied to plants much like conventional pesticides.

No transgenic Bt-producing plant is yet being marketed. However, several kinds are being field tested. For example, cotton plants that produce Bt were well-protected against a variety of insect pests during field tests conducted over several years, according to David Fischhoff of Monsanto (St. Louis, MO). In cotton plants, the transgenic insecticide performed better than did chemical pesticides against the potentially devastating pink bollworm. Moreover, in other field trials, Bt-producing transgenic potatoes showed "good resistance" to the Colorado potato beetle, says Fischhoff. In some cases, the transgenic delivery of the insecticidal protein appears so much more effective than conventional applications that the new approach eventually might be incorporated into particular pesteradication programs, he notes.

Despite obvious enthusiasm over Bt's performance in transgenic plants, Fischhoff acknowledges the potential for target insects developing Bt resistance. One technical strategy to avoid resistance would be to deploy transgenic plants that can make two distinct Bt-type insecticidal products. Other strategies noted by workshop participants include use of refuge plants on which Bt-susceptible insects could survive, thereby reducing selection for Bt-resistant insects. Inclusion of some seeds that contain no Bt genes would provide such refuges within the crop itself. The selective use of other types of pesticides is a possibility, as is greater reliance on crop rotations as ways of avoiding the selection of Bt-resistant insects.

No one seems clear on who holds the responsibility for establishing such practices. For example, workshop participants discounted industry's Bt Management Group-a consortium of companies working on Bt-which at first glance seems a likely candidate. The group manages a fund for Bt research, but its members seem reluctant to broaden the organization's scope, saying that fear of Justice Department (Washington, DC) scrutiny for potential antitrust violations is a major source of that reluctance. Moreover, not all Bt producers are members of the management group, and it also lacks any authority to set industry standards.

Another possibility is that EPA officials set policies to preserve Bt's future utility. At best that prospect is unusual for the agency, which traditionally has concentrated on "keeping horrific things out" of the marketplace, says Ann Lindsay of EPA's Office of Pesticide Programs. In addition, the agency may not have adequate statutory authority to enforce resistance-management programs, which is more typically in the province of growers and agriculture-extension officials. However, Lindsay says, "I think there are things EPA could do," noting that for resistance management it would make sense to consider Bt products generally rather than to examine each company's products individually.

Monsanto's Fischhoff argues that a desire to assure long-term returns on Bt products will lead companies to adopt prudent resistant-management policies on their own. Moreover, the "court of public opinion" is carefully weighed within companies, serving as another incentive to use Bt products carefully.

"If we're ever to be successful at EPA in promoting the safer use of pesticides, it will only work if we have an integrated team with industry," EPA's Lindsay says. However, points out Edward Bruggemann, a staff scientist for Audubon, "We see no financial incentives for resistance management. We don't expect to avoid resistance altogether. But once resistance is in the field, there's not a whole lot one can do." — Jeffrey L. Fox