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regulators, university scientists, and environmentalists broadly agree that *Bt* proteins comprise a safe, environmentally friendly family of insecticidal agents. Even so, the huge extent of the land devoted to corn raised concerns about the potential emergence of *Bt*-resistant strains among target insects.

Environmentalists contend that widespread use of *Bt* in a high-acreage crop such as corn will greatly accelerate the appearance of resistance to this family of agents and lead to them becoming useless to all farmers. They point to several still-circumscribed growing areas, particularly in Hawaii and various regions of Asia and the Pacific island nations, where high use of *Bt* is associated with resistance development in target insects and consequent loss of effectiveness.

Margaret Mellon and Jane Rissler of the Union of Concerned Scientists (Washington, D.C.) argue that because corn is grown on such a vast scale, if the corn borer is exposed regularly and at near-constant levels to *Bt*, the loss of *Bt*'s effectiveness is "virtually ensured." David Andow of the University of Minnesota (St. Paul, MN) says "The development of resistance to *Bt* is not necessarily inevitable. But our experience indicates there's no reason to expect otherwise."

Industry representatives, however, think otherwise. "We're not convinced resistance will arise," says Mycogen's director of corporate communications, Michael Sund. Because the transgenic plant produces insecticide where pests feed, "the delivery system solves some of the problem," points out Lotstein. Moreover, according to Sund and his colleague Joseph Panetta, director of environmental and regulatory affairs at Mycogen, because trans-genic corn is producing such high levels of *Bt* and insect killing is so efficient, resistance is not likely to emerge. Mycogen's corn produces *Bt* at levels 20 times higher than needed for a 100% kill of the European corn borer.

This "high-dose" strategy for avoiding resistance evokes skepticism elsewhere, however. "If the high-dose strategy does not kill 100% of the insects, it won't work," Andow says. "Maybe, if there is enough *Bt* in the corn, it will become a nonhost plant and insects will avoid it. But as long as the corn borer lays eggs on corn, my gut feeling is that, sooner or later, they will feed. And the key [to resistance emergence] may be that not every plant will produce a high-enough dose to kill all the insects."

Andow and several other university researchers favor the testing of another insecticide efficacy-prolonging strategy in which susceptible insects are encouraged to thrive on untreated plants that serve as insect refuges. The hypothesis is that, by allowing some insects to live without selective pressure from *Bt*, there is less likelihood that the population will develop wholesale resistance to it.

EPA has responded to these concerns by issuing the Mycogen and Ciba product registrations for a provisional five-year period, with a requirement that the companies monitor the development of resistance in target insects and take other steps to develop resistance-management programs. Indeed, the two company's applications may have accelerated EPA's development of resistance management policies. An EPA working group recommended applying a resistance management approach to "those pesticides we'd most like to extend the life of, including some chemical pesticides," says Elizabeth Milewski of the EPA Office of Pesticides and Toxic Substances (Washington, D.C.).

But the need to rule on the Ciba and Mycogen applications arose before a comprehensive policy was formed. "Corn is really a major crop," Milewski says. "The possibility of resistance to *Bt* emerging and having an impact on foliar (spray) applications of *Bt* is higher, so [these applications] became the first compelling cases for a resistance management program."

Industry representatives would prefer a voluntary, rather than a mandatory, program. "We may lose the flexibility we need to manage resistance," Mycogen's Panetta says. Meanwhile, academic scientists are waiting to see whether industry will call upon them to conduct some of the monitoring and research activities that the EPA-mandated program seems to entail. And outside critics complain that the research and monitoring should have been undertaken with some of the analysis completed before EPA approved the *Bt* corn for such widespread use.

—Jeffrey L. Fox

Insect rules take shape

A "transgenic arthropod team" has been formed in the Biotechnology, Biologics, and Environmental Protection division of the U.S. Department of Agriculture's Animal and Plant Health Inspection Service (APHIS-BBEP; Washington, D.C.). According to Orrey Young at APHIS, the agency has received inquiries from several researchers looking at transgenic biocontrol arthropods. Ultimately, the researchers plan to use these organisms to control crop pests. At this stage, says Young, the agency "merely wishes to be ready to provide appropriate assistance when an application arrives proposing release of a transgenic arthropod."

For most arthropods, especially those of medically important species like the mosquito and the tsetse fly, recombinant DNA delivery and expression systems are still in development. Researchers at the University of Illinois (Urbana, IL) plan to develop "mariner" transposable elements—like those used in *Drosophila*—as transformation vectors. PCR studies have already shown that such elements are present in many insects.

An example of the type of project that might eventually come under any new regulations is work at Yale University (New Haven, CT) that aims to express antiparasitic genes in tsetse flies so that the flies cannot function as hosts.

By the end of September, APHIS-BBEP hoped to have made announcements on both the regulatory requirements and the issues associated with the introduction of recombinant arthropods. Interested parties can contact Orrey Young via the APHIS World Wide Web site (http://www.aphis.usda.gov/) or by e-mail (oyoung@aphis.usda.gov).

— John Hodgson