# *Paper Presented to the Research and Development Perspectives Workshop*

DANIEL JONES
*National Program Leader, Biochemistry/Biotechnology*
*US Department of Agriculture*
*Washington, DC*

This workshop is on research and development perspectives on genetically modified crops containing pesticidal substances, and the possible development of pest resistance to those substances through biological selection.

Modern biotechnology has the potential to provide highly specific biopesticides for protection of agricultural crops from the ravages of pests that were formerly controlled by conventional chemical pesticides. The use of chemical pesticides can result in negative outcomes such as: 1) toxic residues in soil, water, and food; 2) emergence of secondary pests; 3) development of pest resistance; and 4) pest resurgence following the development of resistance. In addition, certain uses of some chemical pesticides may be discontinued as a result of the Food Quality Protection Act enacted by Congress in 1996.

Whether these same problems will plague the use of biopesticides will depend on the nature of the biopesticide, and may depend on how it is used. For example, should biopesticides be expressed in plants at high levels to maximize killing of pests, or at low levels to minimize selective pressures for the development of pest resistance?

The most widely used biopesticides at the present time are those derived from insecticidal proteins of a soil bacterium called *Bacillus thuringiensis* (Bt). These insecticidal proteins act by binding to receptors in the insect gut thereby disrupting digestion and leading to the insect's death within a few days. There are more than 50 different Bt proteins with differing toxicities for caterpillars, beetles, flies, and nematodes. Bt insecticidal protein can be applied to plants either as an external spray, as it has been for about 40 years, or inserted into the genetic blueprint of crops by the newer transgenic techniques.

The growing acreage planted to Bt crops has caused some scientists and interest groups to express concern about the development of pest resistance to Bt insecticidal proteins. In 1997, for example, there were close to four million acres of Bt corn, two million acres of Bt cotton, and 25,000 acres of Bt potatoes. In the next few years, alfalfa, canola, soy, sorghum, and wheat containing Bt genes are expected to reach the market.

The economic costs of losing Bt as a viable biopesticide due to the emergence of resistance in large populations of insects would be enormous. Organic farmers would be particularly hard hit. Resistance to Bt insecticidal proteins has been reported in insect populations that are exposed extensively or continuously to the toxins. Resistance to Bt in the diamondback moth has been documented in field populations in Asia, Central America, and the United States (Hawaii, Florida, and New York). Researchers from the US Department of Agriculture (USDA) have shown that the Indianmeal moth can become resistant to Bt if it lacks a key enzyme needed to activate Bt toxins.

There are a number of strategies to minimize or delay the development of pest resistance. In general, limited use and rapid degradation of biopesticides after release decreases selection pressures for the development of pest resistance. Specific strategies to delay the development of pest resistance include:

- Multiple toxins
- Low expression levels
- Partial resistance
- Timed expression
- Tissue-specific expression
- Mixtures of resistant/susceptible seed
- Provision of refuges

To protect the continued use of Bt-based biopesticides, the US Environmental Protection Agency (EPA) currently requires companies developing transgenic crops to submit and implement pest resistance management (PRM) plans as a condition of product registration. The major components of the current PRM plans are a high dose of the insecticidal protein to kill as many insects as possible, and the mandate of refuge areas where nonresistant insects can grow and breed with any resistant ones that might arise.

Some interest groups and scientists have taken issue with the EPA-approved PRM plans. They contend that some insects are not getting sufficiently high doses of insecticidal protein in the field to be killed, and that the refuge areas provided are not large enough relative to the area planted with transgenic crops. These interest groups have asked the EPA to suspend current transgenic plant registrations, and stop new ones on the basis of their belief that the transgenic plant varieties will worsen the pest-resistance problem.

There is an apparent lack of consensus among academic, government, and other scientists about many aspects of PRM. Knowledge gaps in basic pest ecology clearly exist, but there is also disagreement about:

- How the knowledge gaps should be filled
- What assumptions can be made now
- How quickly resistance will develop
- What regulatory and farming practices should be followed in the meantime

One solution for pest resistance to Bt is to develop a more diverse array of insecticidal proteins for agricultural use. In addition to Bt, there are a number of insecticidal proteins being studied, but they are not as far along commercially. These include lectins, antibodies, protease inhibitors, insect peptide hormones, vegetative insecticidal proteins, and wasp and spider toxins.

The USDA has funded research that transfers insecticidal genes from soybeans to corn to combat crop damage from corn rootworm. This research identified a whole series of inhibitor genes with different modes of action that are available for use in case the corn rootworm acquires resistance to the original inhibitor now in the field. The USDA National Research Initiative has a major research area entitled Pest Biology and Management. This includes a subarea on Biologically Based Pest Management that solicits proposals for a variety of biological pest management research including resistance management studies.

We at the USDA are open and receptive to suggestions developed at this workshop on directions that future research on pest resistance management could take.