

# Engineering Crops to Resist Weed Killers

*Plants that resist herbicides could be a boon to chemical companies; a prototype may soon be field tested*

**I**N the near future the U.S. Department of Agriculture is expected to announce its approval of the first outdoor test of a plant that has been genetically engineered to tolerate a herbicide. Although the experiment is modest, it is part of a major race by many biotechnology and chemical companies to redesign the genetic code of seeds and create crop plants that can withstand weed killers.

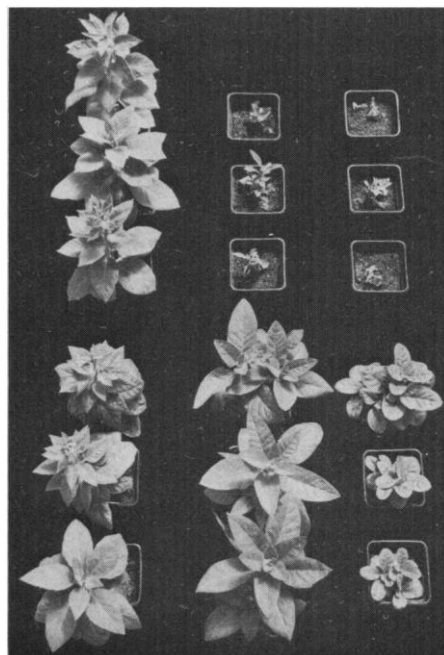
These new kinds of plants will not be on the market for at least several years, but there is already considerable speculation about their potential economic and environmental impact. Chemical companies, whose worldwide herbicide sales totaled almost \$4 billion in 1984, may jockey for each others' markets by creating seeds tailored to tolerate their own brands of weed killers. Farmers may be able to trim their production costs and reduce the need for tillage. On the other hand, some environmentalists are concerned that the new plants will prompt farmers to flood their fields with more herbicides, leading to more pollution.

Robert Goodman, a senior scientist at Calgene, Inc., in Davis, California, the company that is about to get the nod from USDA to proceed with a field test, says that the new technology "makes it easier to respond to environmental and agricultural concerns." The creation of herbicide-resistant plants is virtually impossible with conventional breeding techniques and, as a result, herbicides traditionally have been created to match the tolerance of a certain plant. Now, with genetic engineering, the reverse is true, according to John Fulkerson, senior scientist at USDA. Plant characteristics can be sculpted to fit an herbicide. The alteration is relatively simple, involving a single gene mutation. Howard Schneiderman, Monsanto Company's chief scientist and a senior vice president, says enthusiastically, "Genetic engineering allows us to enter a partnership with mother nature. We don't have to force-fit herbicides to plants any more."

Calgene and Monsanto, for example, are competing to develop plants that are resistant to Monsanto's glyphosate product known as Roundup. Roundup is one of the

most widely used herbicides in the world and is regarded as one of the most environmentally safe. Calgene, in its field test, will analyze a noncrop variety of tobacco plant that tolerates glyphosate, and plans to build herbicide tolerance into several other species, such as tomatoes, cotton, and poplar trees, which are important in the paper industry.

Herbicide-resistant plants may help a farmer reduce expenses indirectly. Although seeds are a small part of total farm costs, a farmer may save money if the new seeds are paired with herbicides that are cheaper because their patents have expired and have to compete with generic versions. But the biggest potential lies with designer seeds matched with new, more efficient proprietary chemicals, according to Charles Benbrook, executive director of the Board of



## Designer plants

*Calgene's new tobacco plants are genetically altered to tolerate glyphosate. The top three rows are unmodified plants and the bottom three are the modified ones. The two right rows have been sprayed with different concentrations of herbicide.*

Agriculture at the National Academy of Sciences.

Such a combination, he says, could reduce the need for tillage, which is done mainly to control weeds, and have a ripple effect in money savings. Less tillage cuts soil erosion and the costs of energy, fertilizer, and water. According to a market analysis by Calgene, the creation of glyphosate-resistant tomatoes could save farmers in California's Central Valley \$30 per acre by reducing the expense for mechanical tillage and hand hoeing and other pesticides.

Herbicide-resistant seeds might also help to solve the problem of "carryover," in which the chemical lingers in the soil and is toxic to the next crop to be planted. The designer seeds "could give the farmer flexibility in his crop rotation," Schneiderman says. The new plants "will almost certainly be designed with multiple resistance" to give the grower even more choices to match his needs, says Charles Arntzen, Du Pont's director of plant sciences and microbiology.

Carryover is a major problem with atrazine, the main herbicide used to treat corn. It is, however, toxic to soybeans, which are often planted in rotation with corn. The chemical persists in the soil from one season to the next, reducing the yields of soybeans, says John Duesing, senior scientist at Ciba-Geigy, the principal manufacturer of atrazine. Ciba is trying to develop an atrazine-resistant soybean, other sources say. (The gene for atrazine resistance could theoretically be transferred from corn to soybeans but gene expression would be limited because corn is monocotyledonous, while soybeans are dicotyledonous.)

For chemical companies, herbicide resistance is a smart way to protect their current markets or expand into new ones. Most, if not all, of the major herbicide manufacturers are engaged in some research to develop herbicide-resistant plants, according to Jack Doyle in his book, *Altered Harvest*. Doyle is director of the agricultural resources project at the Environmental Policy Institute in Washington, D.C. Part of the attraction lies in the fact that the gene alteration "is doable now," says Dilip Shah, a molecular biologist at Monsanto.

Ralph Hardy, former head of research at Du Pont and now president of Biotechnica, Inc., said that herbicide-resistant plants can help a chemical company enlarge its market for proprietary products and also guard its market share for herbicides that are off-patent. Biotechnica is conducting a considerable amount of research in herbicide resistance.

Monsanto is clearly aiming to protect its market for Roundup, whose American product patent expires in the year 2000.

Jack K. Clark, Bio-Tech Images

Creating herbicide plants "makes good business sense," says Schneiderman. The herbicide is sold in 120 countries. Tests show it has no mammalian toxicity and degrades fairly quickly. The problem is that it "kills anything green," says Schneiderman.

Protecting the Roundup market is very important to Monsanto because the future of its other best-selling herbicide, an alachlor sold as Lasso, is cloudy. Lasso is under special review by the Environmental Protection Agency because of concern over its toxicity. Monsanto is "working furiously" to make soybeans resistant to Roundup, says Sue Tolin, who is a plant pathologist at Virginia Polytechnic Institute and State University and a member of USDA's recombinant DNA advisory committee.

Tolin and others predict that chemical companies, many of which have bought seed companies, will sell seed-herbicide packages in the future. Schneiderman says, "I don't know if we would offer a package, but if we could, we would." Several chemical companies are in a position to do this. Monsanto, W. R. Grace, Royal Dutch Shell, and Stauffer Chemical Company all have purchased seed companies, according to Doyle.

What concerns Doyle is that these kinds of mergers eventually might dampen market competition. But Arntzen says that "the complexity of the market will discourage vertical control." Seed companies at most hold about 30 percent of a crop market, he says. Chemical companies want 90 percent of the acreage for a particular crop. The difference is "incompatible in developing a marketing strategy," Arntzen says.

In addition, not all the major chemical manufacturers have bought seed companies. Du Pont does not own a seed company, but is conducting in-house research to make soybeans and a noncommercial variety of tobacco tolerate its product Glean, a sulfonylurea. American Cyanamid is hoping to create corn to withstand its imidazolinones in collaboration with Molecular Genetics and Pioneer Hi-Bred International, one of the world's biggest corn seed producers.

Will herbicide-resistant crops lead to broader chemical use, which could worsen pollution, such as ground-water contamination? The vast majority of growers in the United States already apply herbicides, so wider use is unlikely, Hardy remarks. Arntzen says that the volume of herbicide used in the United States is actually declining because the more recent weed killers are more potent.

The environmental effects will depend ultimately on the type of herbicides applied. Plants created to tolerate some of the herbicides that are "bad actors" are worrisome, Benbrook says. Atrazine has been found in

## Calgene Breaks New Ground

Calgene, Inc., is the first company to test how the U.S. Department of Agriculture will regulate biotechnology products. The company, based in Davis, California, is passing muster with the federal government far more easily than another California biotechnology firm, Advanced Genetic Sciences in Oakland. The experiment is unlikely to generate the controversy that the AGS experiment has created in recent months.

One difference is that Calgene plans to field test a plant, while AGS wants to release a microbe into the environment. Plants are easier to monitor than microorganisms, so they pose less worry. Second, because the two companies' products have different functions, they are regulated by separate agencies. Plants are governed by USDA. The AGS microbe is regulated by the Environmental Protection Agency because the organism is classified as a microbial pesticide. The test microbe "controls" other bacteria that promote frost.

Calgene plans to test a noncommercial variety of tobacco that is modified to tolerate glyphosate, a broad spectrum herbicide. Glyphosate kills plants by suppressing the production of amino acids that are essential to plant growth. Calgene has overcome this effect by splicing into the tobacco genome a mutant enzyme gene derived from a glyphosate-resistant strain of *Salmonella*. This change prompts the production of the amino acids.

Calgene's experimental protocol is being examined by USDA with the help of its Recombinant DNA Research Committee, whose members include scientists from USDA and other government agencies. University scientists also reviewed Calgene's plan. The research committee's main concern is that the mutant gene might be sexually transferred between the tobacco and other plants in the vicinity, according to Sue Tolin, a member of the committee and plant pathologist at Virginia Polytechnic Institute and State University. The possibility is highly unlikely based on past experience with tobacco, one of the most well-studied species in plant breeding, Tolin says. But to eliminate all possibility, Calgene will snip off the plant flower buds before they bloom. ■ M.S.

ground water at high levels, which Benbrook and Doyle both find troubling. Ciba says the levels found are not harmful.

The environment and public health will benefit if seeds are designed to withstand the newer chemicals coming on the market, Benbrook says. These new herbicides, including the sulfonylureas and imidazolinones, are a "vast improvement" over the older formulations because they show little, if any mammalian toxicity and degrade more quickly, he says.

An important factor that will shape the herbicide market is regulation by EPA. "Old compounds will be displaced by agency decisions," Arntzen says. Benbrook adds that chemical companies will spend more R&D money to invent ecologically safe compounds if EPA develops tough standards on ground-water pollution and can speedup its evaluation of new products.

Although many companies are working hard to design herbicide-resistant plants, not everyone believes this trait alone will be a major selling point or have a profound economic impact. Nicholas Frey, director of

the biotechnology department at Pioneer Hi-Bred says, "We got into herbicide resistance for a number of reasons, but selling herbicide-resistant seeds wasn't a major factor. It isn't a high priority for us."

It takes so long to get new seed varieties to market, Frey says, herbicide-resistant plants are unlikely to be big money-makers. Field tests will have to prove that such changes don't sacrifice a crop's yield. The modified varieties will then have to be mated with parental strains to screen out undesirable traits in the hybrid, a process that takes 4 to 6 years. The earliest any herbicide-resistant plants could be sold will probably be in the early 1990's, Frey and others say.

What is important, he says, is that the research on herbicide tolerance provides important information about basic plant biology and the groundwork to introduce other characteristics into plants such as viral resistance. Schneiderman doesn't disagree on that point, but he adds, herbicide-resistant plants "open up all sorts of possibilities." ■

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