Biotech Companies Lobby for Federal Regulation

The lack of rules for marketing and testing agricultural biotechnology products is holding up research and investment

THE FIRST PRODUCTS of the brave new world of agricultural biotechnology—crop plants genetically engineered to resist plant pathogens and herbicides—are almost ready to move into full-scale testing. But whether U.S. farmers will actually be able to plant any of the new varieties of these novel crops in the next few years may depend as much on the federal government as on the companies developing them.

Six years after the Reagan Administration began trying to hammer out regulations governing outdoor testing and marketing of organisms produced with recombinant DNA technology, federal agencies have yet to agree on such basic issues as how to determine which plants and microorganisms should be subject to special review, and which should be exempt.

Part of the holdup has been that six of the biggest federal agencies—three on a side—have taken conflicting views of whether genetically engineered organisms should be singled out for special regulation. But the wrangling may finally be coming to an end: The White House says it will be stepping in to resolve the controversy and that a basic agreement may be hashed out within a month.

At present, the Environmental Protection Agency (EPA) and the U.S. Department of Agriculture (USDA) are approving small-scale field trials involving genetically engineered plants and microorganisms on a case-by-case basis. But there are no overall rules governing large-scale testing and it's unclear what companies will have to do to gain approval to market some biological products.

Consequently, many companies are unable to make long-range plans because they cannot predict how much time and money it will take to get a new crop variety or biological pesticide on the market. Some, such as Eastman Kodak, have even decided to avoid using any recombinant DNA technology that might get a potential product stuck in regulatory quicksand. "Without knowing what is going to be required," says Kodak's director of agriculture, Zenas B. Noon, Jr., "you can risk losing millions of dollars."

Others are nervously hoping that their competitors will not steal a march on them while they wait for agencies to provide written guidance or regulations mapping the route to commercial production. Pioneer Hi-Bred International, for example, is concerned that regulatory delays may prevent it from marketing seeds for genetically modified sunflowers, soybeans, and corn ahead of its competitors. Rod Townsend, regulatory affairs manager for Pioneer, says some of these crop varieties may be overtaken by hybrids produced through traditional breeding techniques. Says Townsend, "Quite honestly, it is not clear to most of us where we go from [small-scale] contained field tests and how we move toward commercialization."

Resistant squash. *An inserted gene makes this plant, developed by Upjohn, resistant to two viruses but subject to regulation.*

Asgrow Seed, a division of the Upjohn Company, finds itself in the same predicament. Asgrow wants to start large-scale seed production by 1994 for transgenic varieties of cantaloupe and squash engineered for virus resistance. But, says John Sorenson, the company's executive director of vegetable research, although the EPA and USDA have approved dozens of small field trials, neither agency has fully defined what additional testing requirements there may be.

Regulatory uncertainties are also holding back university research, says Eric Triplett, assistant professor of agronomy at the University of Wisconsin at Madison. Although he has received approval for a small field test of engineered microbes that colonize plant roots and assist in nitrogen uptake, Triplett says that, without an overall regulatory framework, "the system for getting approval for tests involving microorganisms can be a bit strange." Consequently, "many researchers are simply not trying to do these sorts of experiments."

As the federal process has stalled, agricultural biotechnologists are faced with the possibility that the states will fill the regulatory vacuum with rules for the testing of engineered organisms within their borders. Some 22 states are currently considering various forms of legislation. Says Pamela J. Bridgen, executive director of the Association of Biotechnology Companies, "We are concerned that 50 different states are going to come out with different sets of regs if the feds do not get their act together."

North Carolina, in fact, has already passed a bill (*Science*, 4 August 1989, p. 466). And a few weeks ago, Hawaii was dissuaded from following suit only when the USDA dispatched an official to the state to lobby against proposed legislation. Among other things, that bill would have required additional environmental assessments on an engineered organism to be carried out if state officials thought the federal assessment was inadequate.

To avoid the threat of a state-by-state regulatory patchwork, the biotechnology industry is doing something unusual: pleading with the federal government to come up with regulations. In mid-March, Richard Godown, the president of the Industrial Biotechnology Association, wrote James B. Wyngaarden, assistant director of life sciences at the Office of Science and Technology Policy, imploring the Bush Administration to do something to break the gridlock. The matter now has been elevated to Vice President Dan Quayle's Council on Competitiveness.

What's holding the feds up? One obstacle is a long-running squabble pitting officials from the EPA, the USDA, and the National Science Foundation (NSF) against their counterparts in the Food and Drug Administration (FDA), the Department of Health and Human Services (HHS), and the Na-

tional Institutes of Health. The issue: Should genetically modified plants and microorganisms be regulated any differently from organisms bred by traditional means?

One attempt to answer that question is now before Quayle's council in the form of a proposal that would establish a detailed framework to determine which types of organisms should be regulated. Under that proposal genetically engineered organisms would be subject to special regulation, the determining factor being the types of genetic changes introduced by recombinant DNA. This approach is supported by the EPA, USDA, and NSF. Terry Medley, director of the USDA's Office of Biotechnology Coordination, says there's good reason to look more carefully at genetically engineered organisms. "It is not that you are regulating because of the process that was used to make the organism. It is because there are unknowns about the resulting organisms. When something has been added, there can be a lack of familiarity with the end product and how it behaves."

In the opposing camp are agencies of the HHS, whose most prominent spokesman is Henry Miller, director of the Office of Biotechnology at the FDA. They are arguing for a more flexible approach, based not on how an organism has been modified but on its expected properties and how it will interact with the particular environment into which it will be introduced. The fact that the organism has been produced by recombinant DNA or any other means of genetic manipulation should be irrelevant, Miller contends.

Elizabeth Milewski of EPA's Office of Pesticides and Toxic Substances, which has been fighting the FDA and NIH for 2 years to issue rules governing plants and microorganisms with engineered pesticidal properties, says the disagreement between HHS and other agencies "is largely one of ideological purity." Presidential Science Adviser D. Allan Bromley told *Science* that the White House would attempt to work out an agreement soon—perhaps within a month. But it could still take many months after the basic approach is sorted out to implement specific regulations.

The EPA, for example, is grappling with issues such as whether pesticide-producing genes inserted into crop plants should be registered as pesticides. If so, they may have to go through the same registration process as chemical pesticides. The agency is also trying to establish rules for testing nonpesticidal microbial products such as a nitrogen-fixing strain of *Rhizobium* bacteria.

The unfinished business at the USDA includes rules and guidelines for field tests involving transgenic animals (fish, for example), outdoor experiments conducted at universities with USDA funds, and revisions to rules on open air testing of transgenic plants that may be potential plant pests.

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And the FDA confronts its own questions, among them: Should a chemical produced by a genetically altered plant be regulated as a food additive? Calgene of Davis, California, for example, is hoping to market a tomato engineered to have a longer shelf life and many firms are working on crop plants that will have better nutritional content or disease resistance.

FDA officials are reluctant to regulate genetically engineered products on this basis, but they may not be able to avoid doing so. "Somebody is going to want to see the food safety assessed," observes one USDA official. "Someone is going to have to say they are safe." Public interest groups such as Friends of the Earth and the National Wildlife Federation are watching what FDA does very closely. Says Margaret Mellon of the wildlife federation, "Chemical additives delivered by a gene are no different from those chemicals that are added directly to food."

Biotechnology companies, in fact, may actually prefer to have FDA's stamp of approval. "It's not clear, at least to biotechnology companies, that they will not be open to legal challenge if they do not have an affirmation of product safety," says John Payne, senior staff microbiologist at USDA's Animal and Plant Health Inspection Service. While such oversight may be unnecessary, industry officials, such as Leonard Guarria of Monsanto, say that industry may have to accept it for a time to secure the public's trust in the government.

"Nobody is trying not to be regulated," asserts Calgene Chairman Roger Salquist, who thinks it is time for a compromise to be struck on federal oversight of the industry. In fact, what researchers at universities and industry cannot afford is to have their research and development efforts slowed by further bureaucratic delays. "There is only a limited amount of money in any company for research," says Richard Herrett of ICI Americas. "Unless we get some action, it won't be long before people in the boardrooms start asking about other research opportunities with better payoffs."

■ **MARK CRAWFORD**

NIH Director: The Final Lap?

At last. The committee that has been advising Health and Human Services (HHS) secretary Louis Sullivan to rewrite the job description for the National Institutes of Health director has had its final meeting. A short list of candidates is in Sullivan's hands (*Science*, 20 April, p. 296) and he is ready to start interviewing people for the job now that the advisory committee is through.

The committee's premise from the start has been that the system currently treats the NIH director like a wayward child, the result being that able scientists wouldn't take it on a bet. The proposed solution is to convince Sullivan's assistant secretary for health, James O. Mason, to give the NIH director administrative authority that Mason and his staff currently exercise themselves.

Two examples symbolize the problem. In one case, committee members were arguing that the director of NIH should be able to appoint advisory committees without being second-guessed by HHS staffers.

Mason stepped in. For all practical purposes, he said, that is the way things work now. When a list of potential advisers crosses Mason's desk, he reviews it only for "women, minorities, and geographic distribution." Committee member Maxine Singer, president of the Carnegie Insitution, could barely contain herself. "You illustrate the problem perfectly," she said, adding that anyone smart enough to head NIH ought to be assumed smart enough to take those criteria into consideration without a watchdog.

Anthony S. Fauci, head of NIH's allergy institute, had another example of what NIH sees as petty bureaucratic intrusion. Fauci wanted to give a minor promotion to a senior scientist in his institute—someone who was being courted with outside job offers. Said Fauci, the promotion was "my number one personnel priority." The acting head of NIH made it his number one priority too. But then, in Sullivan's office, "something went wrong. The promotion list came back and this person wasn't even on it," Fauci said. Why? "There wasn't even an explanation."

The advisory committee is sending Sullivan a number of recommendations that all boil down to letting the director of NIH run NIH. How much authority Sullivan will be willing to cede is a question that is yet to be answered. ■ **BARBARA J. CULLITON**