Fear of Pharming
Controversy swirls at the crossroads of agriculture and medicine

By Alla Katsnelson

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Farming, one of the world's oldest practices has suddenly found itself entangled with modern medicine. Imagine this: at your child's appointment for a routine vaccination, the doctor proffers a banana genetically engineered to contain the vaccine and says, "Have her eat this and call me in the morning." Though still far-fetched, the scenario is getting closer to reality, with the first batch of plant-made medicines--created by genetically modifying crops such as corn, soy, canola and even fruits such as tomatoes and bananas to produce disease-fighting drugs and vaccines--now in early clinical testing.

Splicing foreign genes into plants is nothing new--biologists have been doing it for about 25 years. Using the technology to produce protein-based medicine could revolutionize the drug industry, proponents say. Plants are inherently safer than current methods of using animal cell cultures, which carry a risk of spreading animal pathogens; plants also provide a much cheaper means of production. But fears that these "pharma crops" will contaminate the food supply are casting shadows on the promise of the technology.

The problem is that containing genes from GM plants seems to be harder than scientists expected. Recent data suggest that bioengineered genes spread more widely than previously thought. A pilot study released in February by the Union of Concerned Scientists (USC) found that more than half of native species of corn, soybean and canola tested contained low levels of DNA from strains engineered to confer resistance against herbicides. An analysis published in March established that genetically engineered corn had found its way into Mexico despite that country's six-year-old ban on growing GM varieties of the crop. And a major review of biologically modified organisms conducted last year by the National Academies of Science stressed the need to develop better confinement techniques. These findings and others illustrate the reality that experts are starting to acknowledge: the way things are going, maintaining zero levels of contamination from GM plants may be impossible.

Leaks of pharma crops have occurred as well. Two years ago, USDA inspectors found experimental corn plants containing a pig vaccine growing in nearby conventional fields in two separate incidents in Nebraska and Iowa. ProdiGene, the Texas biotech company responsible for the mishaps, was heavily fined for violating its permit and ordered to destroy 500,000 bushels of soybeans and 155 acres of corn plants. But perhaps more importantly, the leak shook the public's confidence in the technology. So far, no one has shown that current
GM crops carry any health risks. But pharma crops, the new generation of GM plants, raise the safety stakes: the proteins spliced into these plants are specifically chosen to target physiological function.

The USDA Animal and Plant Health Inspection Service (APHIS), which oversees crops, responded to the ProdiGene incident by revising its regulations for growing pharma crops. Companies must now use designated equipment for planting and harvesting, provide better crop containment training for growers, and undergo at least five inspections a year. The new rules also require that pharmaceutical corn be grown at least one mile away from any other fields and planted at least 28 days before or after surrounding corn crops are planted. Lisa Dry, spokeswoman for the Biotechnology Industry Organization (BIO), says the new rules make drug pharming so distinct from producing commodities crops that future contamination is preventable. And industry, keen to avoid any further negative publicity, takes contamination very seriously. In fact, according to Neil Johnson, regulatory programs director at APHIS's Biotechnology Regulatory Services, many if not most companies running field tests for pharma crops currently operate under tighter restrictions than government regulations demand.

But even with stringent compliance by industry, the science of gene flow could flout APHIS's rules. Corn in particular, which accounts for about two thirds of pharmaceutical crops being tested, has a strong tendency to cross-pollinate. "Corn is the world's worst organism for this," says Norman Ellstrand, a plant geneticist at the University of California at Riverdale and director of the Biology Impacts Center. "When I heard about this, my first thoughts were, 'What were they thinking?!' Corn pollen is viable for only a few days, and the 28-day segregation requirement provides a good deal of additional protection against contamination. But the problem, Ellstrand observes, is that there is little actual data on how far genes can travel.

"We're working on isolation standards based on research done in the 1950's," declares Joseph Burris, an emeritus professor of seed science at Iowa State University who now owns a consulting company specializing in gene containment issues. "A lot of things have changed." More recent work is starting to suggest that genes can travel farther than previously thought. One report presented at the First European Conference on the Co-existence of Genetically Modified Crops with Conventional and Organic Crops last November found viable corn pollen as high up in the atmosphere as 2,000 meters. If pollen is present that high, the researchers say, there may be a chance that it can spread over dozens of kilometers if there is enough convection to maintain it aloft. "Our fields are factories without walls. We can't control the environment," Burris asserts. "With isolation distances of [1 mile], our odds of having a problem are very much reduced, but they are not eliminated."
On the other hand, says Michael Pauly of the Chicago-based biotech company Chromatin Inc., current techniques for detecting gene contamination, such as PCR, which measures DNA levels, may be too sensitive for our own good. (Chromatin is developing a novel technique for inserting drug-producing genes into plants.) "You can detect a level of DNA that doesn't actually reflect risk," he explains. Indeed, people and animals ingest foreign DNA with every hamburger they eat. "It's not the nucleic acid that's the problem, but the protein," he says, because it is protein, not the DNA itself, that has a biological effect. Burris, too, notes that the improvement in detection technology has essentially redefined contamination. "We've gotten so abstract about zero contamination. I don't even know what that means," he says.

Many researchers, as well as groups including the Union of Concerned Scientists, the Food Manufacturers of America, and the Consumer Union, contend that the only measure sufficient to ensure zero contamination by pharmaceutical crops would be to avoid developing the technology in plants that can find their way into the stomachs of people or farm animals. But the biotech industry bristles at the suggestion, countering that oilseed crops such as corn not only provide the best medium for obtaining a high level of very pure protein, but are also safer because they are so well studied. "These are the crops that have formed the basis of our culture, our civilization, our economy. This is our knowledge base, and that is fundamentally enabling," Pauly insists.

A consensus about how worried people should be about contamination seems unlikely to emerge in the near future. When it comes to the risk of drugs making their way into the food supply, says Ellstrand, "I wouldn't say zero tolerance for all pharmaceuticals, because presumably some of those things would be totally benign if they got into the food supply." Those products that might not be harmless, he advises, "should be put into non-foods, grown inside of buildings, or simply shouldn't be created in plants at all." Margaret Mellon, head of UCS's food biotechnology program, disagrees. "We can't have a policy which only allows safe drugs in our food. It has to be no drugs."