

# PHARMING THE FIELD:

A Look at the Benefits and Risks of Bioengineering Plants to Produce Pharmaceuticals

Proceedings from a workshop sponsored by the Pew Initiative on Food and Biotechnology, the U.S. Food and Drug Administration and the Cooperative State Research, Education and Extension Service of the U.S. Department of Agriculture.





## INTRODUCTION

The power of biotechnology now allows scientists to use plants as “factories” to produce a wide range of new products. One of the most exciting developments is the ability to use plants to produce human pharmaceuticals useful in treating cancer, cardiovascular disease, infectious diseases and other conditions. Developers hope this technology will lead to safer, more abundant and more affordable new medicines.

This powerful new application of biotechnology also raises questions about whether plant-made pharmaceuticals pose risks to humans and the environment, particularly if they are produced in plants that also serve as food or feed crops.

To shed light on these issues, the Pew Initiative on Food and Biotechnology, the U. S. Food and Drug Administration, and the Cooperative State Research, Education and Extension Service of the U. S. Department of Agriculture co-sponsored a two-day conference entitled *Pharming the Field*. This event brought together a broad range of interested parties to share information and exchange views on the potential benefits and risks associated with plant-made pharmaceuticals and to review the current laws and regulatory policies that apply to these plants.

The views that emerged from the conference are captured here to demonstrate the broad diversity of perspectives and to provide context for future dialogue on this very important issue. It should be noted that the exchanges among participants reflect only their opinions and not necessarily those of the sponsoring organizations.

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## EXECUTIVE SUMMARY

The Pew Initiative on Food and Biotechnology, the Food and Drug Administration (FDA) and the Cooperative State Research, Education and Extension Service of the United States Department of Agriculture (USDA) held a workshop in July 2002 in Washington, D.C., to explore an emerging sector of the biotechnology industry that involves engineering plants with genes that allow them to produce pharmaceutical substances.

The event drew government officials, biotechnology and food industry representatives, scientists, patient advocates, environmentalists and members of public interest groups. Discussions addressed why some companies believe these new types of transgenic plants, often referred to as “pharma plants,” could provide a cost-effective and abundant source of biological material currently in demand for a new generation of medicines. Participants also focused on whether the technology poses risks to humans, animals and the environment, particularly if drugs are produced in plant varieties that also serve as food or feed crops. Finally, participants considered what steps industry and government regulators are taking to minimize these risks and whether these actions are sufficient.

Scientists from biotechnology companies described their ongoing efforts to develop genetically modified (GM) crops—corn is a leading candidate though investigators also are experimenting with other species, including tobacco—capable of producing specific human antibodies, enzymes and other biological material for a class of drugs known as biologics. In most cases, the material would have to be extracted from the plant before it could be used in a drug. Scientists once envisioned developing drugs that could be administered through the consumption of raw plants serving as “edible vaccines.” However, most scientists now believe that in order to assure dose consistency, all pharma plant products will require some level of processing.

Currently, biologics, which account for an increasing percentage of pharmaceuticals, are manufactured with material grown in mammalian cell cultures. Some industry observers warn, however, that production via mammalian cells is so costly and inefficient that without the development of alternative production systems, promising new treatments for a range of conditions may never make it to market.

Though there are not yet any FDA-approved drugs containing material from pharma plants, presentations at the conference revealed a growing interest in developing alternatives to mammalian cells systems has spurred industry to move rapidly toward commercial applications of pharma plants, with a variety of field tests and clinical trials now underway. This quickening pace has heightened interest from the food industry, environmental groups and some consumer advocates who worry about how these crops will be “contained” so that they are not inadvertently consumed by humans or animals or allowed to spread into the surrounding ecosystem. For example, discussions at the conference focused on what the government should require and what industry is currently doing to prevent crops engineered to produce pharmaceuticals from spontaneously breeding with varieties intended for food or feed.

One USDA official indicated that the agency has responded to public concerns by instituting requirements for pharma plant cultivation that are more rigorous than those applied to other GM varieties and that, unlike many other GM crops, pharma plants will always be under USDA regulatory scrutiny. Officials from USDA and FDA also spoke of how they will coordinate their oversight efforts.\* One reason the agencies are seeking close cooperation is that, in addition to assessing the safety and efficacy of plant-derived drugs, FDA will set its own standards for field operations, as it plans to give field cultivation of pharma plants the same sort of regulatory scrutiny that it applies to conventional drug manufacturing facilities.

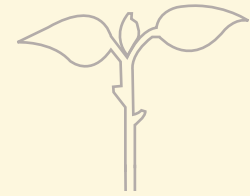
Critics of the status quo focused on what they view as a lack of transparency that inhibits independent efforts to assess whether pharma plants are a threat to humans, animals or the environment. For example, some participants noted that USDA-issued permits for pharma plant field tests rarely disclose what substance the plant has been engineered to produce or how much acreage is under cultivation. This sparked a discussion about the tension between the desire for public disclosures that would facilitate an independent evaluation of potential health and environmental hazards and a company’s right, or even its fiduciary duty, to protect confidential business information.

In her keynote address, former FDA Commissioner Jane Henney noted that the introduction of pharma plants would benefit from a frank and open airing of all concerns, no matter how controversial. She cautioned against approaching this new technology with either “blind faith” or “irrational fear.” Rather, she advised all stakeholders to seek common ground through an objective, evidence-based assessment of the issues.

\* In September 2002, USDA and FDA jointly published a draft “guidance document” outlining what they will be seeking from producers of “drugs, biologics, and medical devices derived from bioengineered plants.” The document is available on the Internet at: <http://www.fda.gov/cber/gdlns/bioplant.htm>.

## PLANTING THE FUTURE:

### The Benefits and Reasons for Using Plants to Produce Pharmaceuticals



The reason some companies are engineering plants with genes that allow them to produce drugs is relatively simple. A growing number of cutting edge treatments that target a range of conditions such as arthritis, herpes, cancer and infectious diseases require human and viral proteins—mainly antibodies but also enzymes and other biological material—that must be derived from living systems. Currently, drug makers synthesize this material in animal cell cultures (Chinese hamster ovary cells are commonly used) that must be carefully nurtured inside sophisticated fermentation vats or “bioreactors.”

But as Richard McCloskey, vice president of medical research at the biotechnology firm Centocor, explained, there is concern in the industry that this system may have two fundamental limitations. First, production of high-quality biological material via mammalian cells is very expensive and results in drugs that may be too costly for patients to afford. Second, there are not enough of these bioreactors available to meet existing, much less future, demand for drug production.

For example, Mitch Hein, president and director of Epicyte Pharmaceutical Inc., pointed out that four pharmaceutical products that require human antibodies currently consume about seventy-five percent of today’s mammalian cell fermentation capacity. Hein noted that a review of therapies currently in the development pipeline reveals that by 2010 there could be 30 or more antibody-dependent products competing for these same facilities. In an effort to deal with this dilemma, Centocor’s McCloskey said his firm, and other pharmaceutical companies as well, are exploring whether deriving the raw materials they need from genetically engineered plants could lower costs while simultaneously boosting manufacturing capacity.

“Lower costs for me as a clinician are potentially translated into more affordable products for more patients sooner rather than later,” he said.

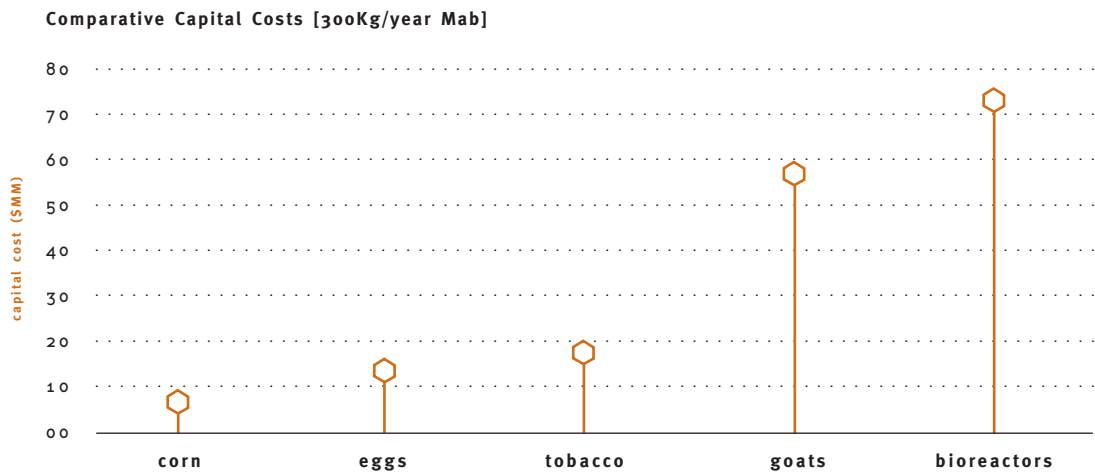
Pharmaceutical products derived from transgenic plants have yet to reach the market. McCloskey noted that while the field is progressing rapidly enough that some plant-derived products are in early-stage clinical trials, there are not yet enough data to definitively state that GM plants will provide a viable alternative to mammalian cells. With high costs and insufficient capacity threatening to slow the rollout of powerful new medicines, McCloskey believes that companies must aggressively seek out alternative systems.

“If the patients for whom these biologics are intended can’t pay for...the drugs...and the healthcare system refuses to do so, there will be no research or development with these agents,” he said.

Underscoring Hein’s point about production capacity, McCloskey estimated that fourteen percent of new medical treatments now in clinical trials are biologics, i.e., therapies such as antibodies or other proteins that now must be derived almost exclusively from mammalian cells. Furthermore, he expects that percentage to grow, but he worries that a bottleneck may soon occur in the drug pipeline when companies seek to scale-up production from clinical trials to general distribution.

Unlike conventional pharmaceutical companies, McCloskey explained, most biotech companies outsource production. They have valid concerns, he noted, about whether the manufacturers they depend upon possess the capacity to fulfill their needs—and whether patients and their insurance companies would be willing to pay the price required to recoup the costs of building additional facilities.

**CHART** 1 **Comparing Costs of Antibody Production Systems**



**SOURCE:** Watler: Amgen. Adapted from a slide prepared by Richard McClosky, Centocor, Inc.

**RICHARD MCCLOSKEY**

Centocor, Inc.

“If the patients for whom these biologics are intended can’t pay for ...the drugs...and the healthcare system refuses to do so, there will be no research or development with these agents.”

“For instance, if there is a demand for 2.5 million liters of mammalian cell capacity, even at a low estimate of \$2 million for each kiloliter, that’s \$6 billion needed for new [facilities] to make these biologics,” he said.

McCloskey observed that industry publications are “replete with alarms” about a pending shortfall in production, with estimates that “20 to 50” products could be delayed by a lack of manufacturing capacity. Building a new mammalian cell bioreactor facility takes about five to seven years at an average cost of about \$600 million. It also requires an expectation that the investment can be recouped through drug sales, and this makes transgenic plants an attractive alternative, he said.

McCloskey said producing 1000 kilograms of human antibodies in hamster cells costs about \$105 to \$175 per gram. Transgenic plants might be able to produce the same amount for \$15 to \$190 per gram. He explained that the wide range in cost estimates for production via transgenic plants indicates that plants might not provide savings in all instances but that in some cases, the savings could be substantial. For example, McCloskey cited figures showing that it costs \$80 million to produce 300 kilograms of antibodies in mammalian cells, but genetically modified corn might be capable of producing the same amount for \$10 million.

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In addition, McCloskey believes that producing pharmaceutical substances in transgenic plants could allow companies to rapidly boost capacity in response to increased demand, since they could simply cultivate more acreage, as opposed to constructing new bioreactor facilities. That is particularly important, he said, because some biologics under development will be intended for “hundreds of thousands of patients” or might be administered in large doses or, in the case of chronic afflictions such as arthritis, the therapy could be required for years. All of these factors would increase demand for significant quantities of raw material.

“It may be naive, but I conceive that the husbandry principles for 100,000 acres of a plant are not much different than for 1,000 acres of a plant,” he said, “where I can tell you that going from an 8 liter (mammalian cell) reactor to an 800 liter or a 1,000 liter reactor is not sometimes so simple.”

Centocor, McCloskey noted, is particularly interested in engineering corn with genetic material that will allow it to produce the substances the company needs. Transgenic corn, he said, appears capable of producing pharmaceutical-grade material in a way that will allow extraction and purification “using very simple methods.” According to McCloskey, “the simpler the purification scheme, the greater the savings.”

Overall, McCloskey said answers to questions about the therapeutic quality of biological material extracted from transgenic plants are coming rapidly, and by next year, industry should have a better sense about whether pharma plants can play a significant role in drug manufacturing. Transgenic plants may fall short of their potential, he said, if there are “unanticipated purification problems,” if therapeutic substances made in plants are not as effective as those made in mammalian cells, or if cost savings do not pan out.

In addition to these pitfalls, McCloskey believes the development of pharma plants could be hampered by legal barriers or by marketing issues related to negative public perceptions that have surrounded the entire field of genetic engineering. He thinks that, ultimately, “somewhere at this intersection of benefit-to-risk and economics...lies the contribution of transgenic plants for making human products.”

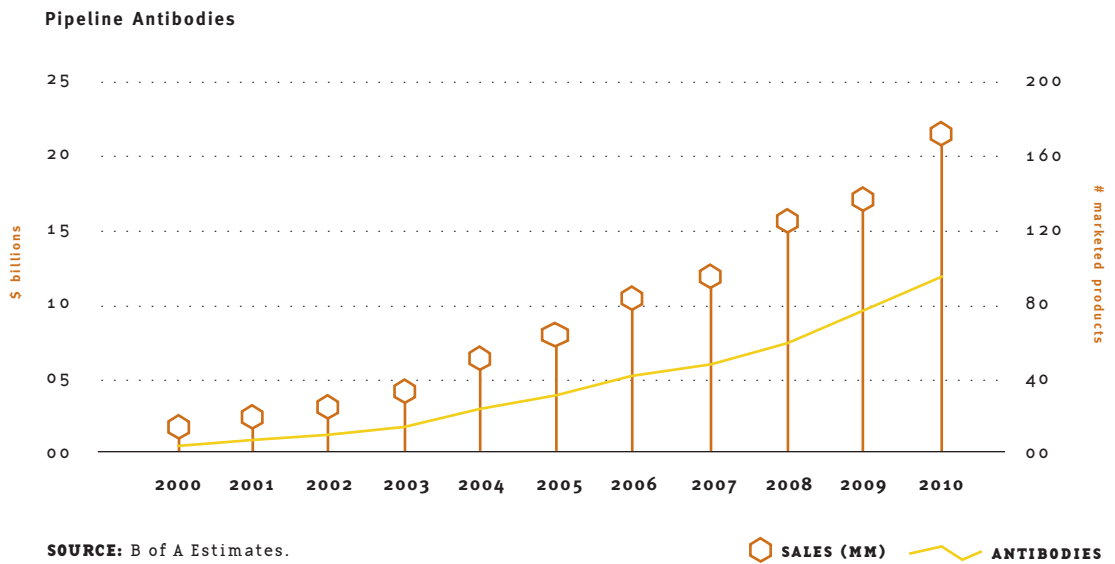
Hein, with Epicyte, a company developing several pharmaceutical products in transgenic plants, believes therapies requiring large quantities of human antibodies at low costs, such as those targeting inflammatory diseases or intended for topical applications, “have the most to gain from plant-based pharmaceutical manufacturing.”

**CHART**

**2**

**Demand for Biological Material Production: Antibodies in the Pipeline**

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**SOURCE:** B of A Estimates.  
Adapted from a slide prepared by Mich Hein,  
Epicyte Pharmaceutical, Inc.

## Resolving Scientific and Stewardship Concerns

Hein explored two issues that will be important to determining whether plants can help industry avoid a production bottleneck. One is whether human biological material produced in transgenic plants is safe and effective. The other involves the quality of company “stewardship,” i.e., industry’s ability to grow, harvest and process pharma plants in a way that addresses public concerns about potential exposures to humans and the environment.

Exploring the quality of biological material derived from transgenic plants, Hein noted that there is evidence that plant-produced antibodies can be effective. He cited a 1998 study published in *Nature Medicine* describing a clinical trial in which a plant-derived antibody was effective in preventing tooth decay. He also noted a 1998 study in *Nature Biotechnology* offering evidence from animal tests that a human antibody derived from a transgenic plant (in this experiment, soybeans were used) may prevent vaginal transmission of the herpes virus.

For scientists, a key topic of discussion, according to Hein, is that while transgenic plants can manufacture antibodies that are nearly identical to those expressed in human and animal cells, there is one potentially important difference. Although the protein components of the antibodies are identical, he said, plants, animals and human cells each attach a different type of carbohydrate to the antibody known as a glycan. Glycans are of interest to scientists, he said, because they can play a role in stimulating an immune response. As Hein explained, in some cases they are important to signaling the immune system that “there’s a bad thing over here, so come over and let’s take care of it.”

The issue, Hein said, is that if the glycan in the plant-produced antibody looks different from what would naturally occur in a human, then “there’s a possibility the body might recognize it as foreign and eliminate it from the system, thereby influencing the efficacy of the drug.” Hein said there is a lot of research exploring the impact of this difference and, “in the end, that needs to be determined on a drug-by-drug basis.”

While companies are focused on whether transgenic plants can produce effective pharmaceuticals, Hein noted that they are also aware that they must pay close attention to “stewardship issues,” to “monitoring the product, process and technology so that public safety and environmental safety are protected.”

“We need to focus on the public benefit and risks so that we clearly understand what’s at stake,” he said.

**Cultivating the Cure: A Patient Perspective**

Nancy Loving, co-founder and executive director of WomenHeart: The National Coalition of Women with Heart Disease, said companies developing pharma plant products should make patients their “partners in this adventure.” She asserted that, in general, patients are “always on the side of advancement, on the side of scientific research, on the side that searches for the cure, on the side that can provide us with safer, cleaner, more effective medicines.”

As for medicines derived from transgenic plants, she expects a variety of reactions from patients. She believes some will consider pharma plant products “more natural and pure” because they come from plants. At the other extreme, she said, are patients who distrust any pharmaceutical products and, therefore, will be leery of pharma plant products. Overall, she believes “most patients will not be concerned about the source of the protein or the source of the pharmaceutical product.”

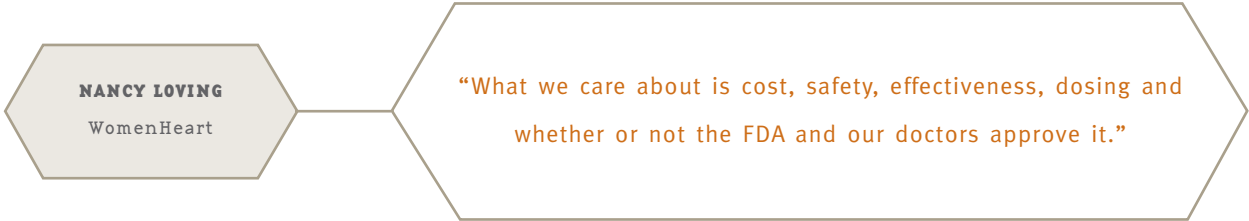
“What we care about is cost, safety, effectiveness, dosing and whether or not the FDA and our doctors approve it,” she said.

According to Loving, patients are like everyone else in that they “care about the safety of food crops” and will rely on industry, government and the advocacy community to make sure pharma plants are produced in a way that does not endanger the food supply.

She implored companies developing pharma plants to work in collaboration with patients and not assume that patients are “too demented or too dumb to discuss or understand scientific advances.” She said patients today are, in general, “highly educated and well informed” and “extremely comfortable with technological innovation.”

“I read the New England Journal of Medicine, I read JAMA [Journal of the American Medical Association], and I even read the footnotes,” she said. “I haven’t gotten to Chemical Engineering News, but I’ll get there and I’ll get your vocabulary down.”

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## Discussing Costs, Acreage, Crop Choice, Waste and Vaccines

In the discussion that followed, Bill Freese with the environmental group Friends of the Earth questioned whether industry's cost assumptions for pharma plants account for expenses incurred in containing the crops (so that they do not co-mingle with food crops) and potential liability costs should containment fail.

Hein asserted, "The people engaged in this are not going to put their enterprise at risk, so they will calculate these costs on the front-end."

Melvin Mathias with USDA was curious about how much farmland might be devoted to growing pharmaceutical plants. Hein responded that it is difficult to project "because we don't know how many of the drugs that have the potential to be produced in plants actually will be."

Hein noted that scientists trying to produce antibodies in transgenic corn believe they eventually could produce 10 kilograms per acre. McCloskey offered that one can get a feel for the scale required by considering an example in which satisfying the therapeutic needs of 10,000 patients would require 15 kilograms of plant-produced antibodies a year, which, under Hein's projection, could potentially be derived from an acre and a half of corn.

"You can see that if you were going to treat a million or five million people or something like that, the numbers of kilograms of antibodies grow very greatly," McCloskey said. "But at the kind of estimates (Hein) just mentioned, the number of acres consumed is really quite small."

Richard Caplan with U.S. Public Interest Research Group (USPIRG) questioned whether, after the pharmaceutical products have been extracted, any part of the crop would be used in human food or animal feed. Hein said his company would use the crops only as a "production vehicle for drugs" and not "in any other chain of commerce."

On another topic, Ann Marie Thro, who works with plant breeding and genetics at USDA, asked what might prompt industry to look at a wider range of transgenic crops for producing pharmaceuticals. Most companies are working with corn. According to Thro, there could be benefits from pursuing a more diverse group of crops, such as allowing more rural farm communities to gain income via production of transgenic pharmaceutical plants.



Hein noted that while it might be interesting to consider incentives that would prompt industry to look at other crops, industry’s singular focus at the moment is to “develop drugs that are safe and effective for human use.” To accomplish this goal, Hein said industry has decided to work with crops “where we have the most data, we know the most, and we can control the system the best.”

Ellen Kennedy with Calvert Asset Management Company asked how developing countries might benefit from pharma plants. Hein responded that, in general, one benefit might be a “broader availability of medicines.”

He said that when the field was in its formative stages, some envisioned the emergence of pharma plants would allow vaccine production to be moved into developing countries, with the idea that edible crops engineered to produce vaccines could be grown and consumed wherever they were needed. Hein noted, however, that while edible vaccines might one day become a reality, they might fall short of initial expectations.

It was once thought that a vaccine incorporated into an edible plant could be administered simply by having patients eat, say, a raw banana or potato. It now appears that in order to make sure the vaccine is administered in the proper dose, some level of processing will be needed. While the vaccine might still be edible and easier to distribute than conventional vaccines because it could be packaged in small jars like baby food, thus eliminating requirements for cold storage, Hein noted that producing the vaccine would still involve both state-of-the-art manufacturing facilities and careful regulatory review, neither of which are generally available in the developing world. Therefore, Hein said, the benefits pharma plants may hold for developing countries may be less dramatic than what was contemplated several years ago.



## LEAVES OF CHANGE: Potential Environmental Impacts and Containment Strategies

Companies developing pharma plants understand that there are concerns about potential risks to humans, animals and the environment posed by open cultivation of pharmaceutical substances in transgenic crops, particularly when food crops are involved, said Philip Eppard, head of regulatory affairs at Monsanto Protein Technologies.

He said industry recognizes the need to keep pharma crops “contained,” i.e., separate from non-pharma varieties, at all stages of production, whether it is in the laboratory where seeds are developed, in the field as the plants mature, or during harvesting, transport, and processing.

“The key point here is that this is a closed-loop production system, totally outside the commercial grain channels,” he said. “It’s not like I put this in my mom or dad’s grain wagon and send it down the street.”

He said companies developing pharma plants approach their work with a mindset that “there is a broad difference between commodity grain production and plant-made pharmaceutical production.”

“The standards that are enforced, the standards we drive towards are pharmaceutical quality standards,” he said. “Our goal is the same as any other pharmaceutical production system: to have a well-characterized, stable, and safe production of medicine.”

At Monsanto, where transgenic corn is the primary crop being pursued as a pharmaceutical production system, Eppard said containment begins in the laboratory where the plants are transformed with genetic material that allows them to produce pharmaceutical substances. “Small numbers of people” are involved in the work; their products never leave company control, and there is no sale of the seed.

Once under cultivation, Eppard explained, containing the pharma plants involves a range of practices designed mainly to reduce the risk of pollen spreading from, for example, a field of pharma corn to a field of corn intended for food or feed.

**PHILIP EPPARD**  
Monsanto Protein  
Technologies

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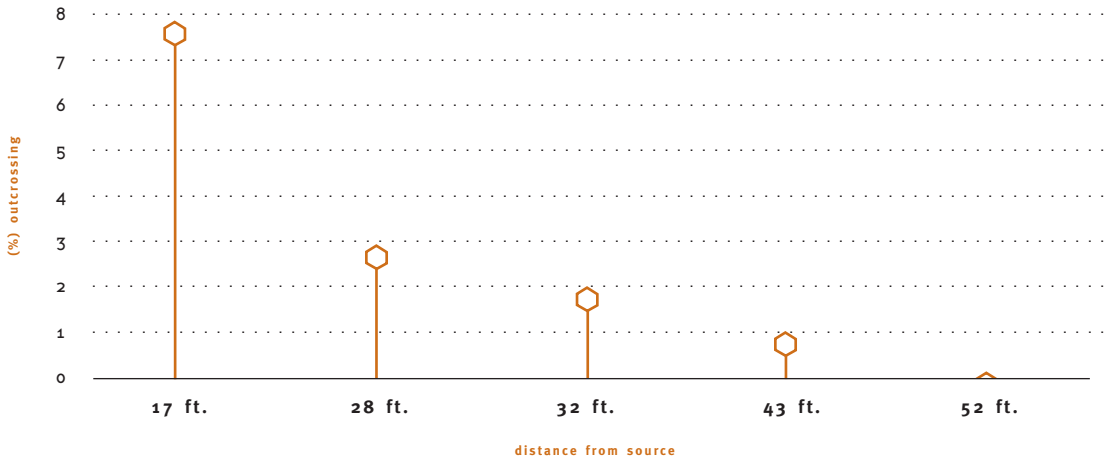
He said Monsanto has worked with regulatory officials to review data on how far corn pollen can travel and remain viable, data that is used to set minimum separation distances between fields of pharma corn and corn intended for food, feed or seed. Pharma crops are also planted and harvested at different times than food and feed crops, he said, so that neighboring crops are not receptive when the pharma crops are producing pollen.

He further stated that Monsanto seeks to limit pollen flow by “detasseling” the corn, which requires removing the portion of the plant where most of the pollen is stored, and by planting rows of non-transgenic corn next to the pharma corn to catch any pollen that might be emitted from the pharma plants.

Finally, so called “sentinel” plots of corn are planted at a certain distance from the pharma crops and are routinely checked for evidence of pharma corn pollen in order to confirm that the containment measures are working, Eppard explained. Once it is harvested, Monsanto procedures call for delivering the pharma crops to production facilities via “secured transport” and “bonded couriers.”

“We do this during research and development and there’s every intent at Monsanto to do this in commercial scale as well,” Eppard said.

**CHART** 3 **Viable Pollen Movement Decreases with Border Width**



**SOURCE:** Halsey et al. 2002. Adapted from a slide prepared by Philip Eppard, Monsanto Protein Technologies.

## Concerns about Containment: A Food Industry Perspective

Food producers have a range of concerns about what would happen if containment systems like those described by Eppard should fail and allow pharma plant products to enter the food supply, said Jeffrey Barach of the National Food Processors Association. These include concerns that such co-mingling could result in illness, injury, product recalls, lasting damage to brand names, and international market disruption.

Barach also noted that accidents could engender what he referred to as “consumer distress.” Should there be a mishap, he said, consumers could react by avoiding certain food brands and categories and becoming distrustful of food processors.

Barach stated that, in an ideal world, pharma plant producers would eliminate such risks by using only non-food plants, such as tobacco and grasses. He acknowledged, however, that food producers “have to accept the conclusion that, at least initially...there will be food plants involved.”

“If we do use food plants, we would suggest...that they always be grown in containment in isolated locations,” he said. “The initial constraint here is to segregate it from food crops.”

He stated that food producers would also like to see developers of pharma plants explore an assortment of strategies to reduce the risk of co-mingling. For example, he suggested food plants used for pharmaceutical production could be engineered so that the desired proteins are expressed in the “leaves, stems or other parts” as opposed to the “edible part of the food plant.” Although he acknowledged that it has proven controversial in the other applications, Barach would like plant developers to explore using the so-called “terminator gene” to engineer sterility into pharma plants. Other potential measures, he explained, could include engineering the plants with “visual markers” that distinguish them from crops intended for food, the use of “atypical” growing seasons, and cultivation in locations that are far removed from areas where food crops are grown.

“All of these strategies get us to looking at several degrees of separation between the traditional food plant and the food plant used as drugs,” he said. “That’s what we’re looking for as a food industry, more degrees of separation than just containment and isolation steps.”

Barach noted that the Biotechnology Industry Organization (BIO) has developed detailed guidelines for keeping pharma plants out of the food supply. He said it was important to make sure those guidelines are adhered to not just by the big companies, but also by smaller operations and by academic researchers and institutions experimenting with pharma plants. Barach called existing government regulations “adequate” but noted that “there’s going to be some room for improvement.”

“This represents something we never want to see,” Barach said, showing a mock-headline that read “Medical Carrots Containing Vaccine Found in Baby Food: Recall Underway.”

“I would strongly recommend and strongly expect that any industry, any group that’s pursuing this to get it right the first time and to get it right every time,” he said.

Barach said he does not expect food processors to ask regulators to establish tolerance levels so that a certain amount of pharma plant products in food, should there be inadvertent mixing, would be considered safe. He said the food industry does not envision a situation in which it would accept any amount of co-mingling between pharma plant products and food products.

**JEFFREY BARACH**  
National Food Processors  
Association

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any group that’s pursuing this to get it right the first time and to get it  
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## Potential Environmental and Human Health Risks

Jane Rissler of the Union of Concerned Scientists called plants engineered to produce drugs the “second generation” of GM crops and said they have the potential to be both more rewarding but also more risky to consumers than “first generation” GM crops, such as those engineered with herbicide tolerance and pest resistance.

Gauging the risk associated with pharma plants, she said, ultimately will require data on the amount of the product that might find its way into humans, animals or the ecosystem (i.e., exposure levels) and the safety profiles of particular plant-produced substances. She illustrated this as an equation in which risk is equal to the “potential of exposure times the potential for harm.”

“If either one of those is zero or near zero, we need not worry,” she said.

Exposure considerations begin, she said, with who or what might inadvertently come into contact with the pharma plant. People might be accidentally exposed, she said, “if the product were to get into the food supply.” Rissler noted that domesticated or wild animals could be exposed if they end up feeding on the pharma crop. She said soil organisms could absorb secretions from the plant and insects could come into contact by absorbing pollen or chewing on the leaves or stalk.

Determining the significance of any exposure, she explained, will depend on the “intended use of the” pharma plant product. For example, if a pharma plant were to produce a protein intended as a blood-thinning agent, then one would need to know how it is activated. Safety assessments also would need to consider how the protein would affect animals or insects.

“As I’ve looked at the limited amount of information that I have and tried to inform it with some work on websites and so on, it looks to me that it’s reasonable to conclude that some, perhaps many, pharmaceutical producing food crops might pose risks to humans,” she said. “It seems like it is reasonable to conclude based on what I know that many pharmaceutical producing crops may pose risks to the environment.”

Rissler conveyed that it is hard for scientists to conduct independent and more definitive assessments of risks because companies consider much of the data about their plants, such as acreage under cultivation and the pharmaceutical product involved, to be confidential business information (CBI). Furthermore, she noted that the key agency responsible for monitoring field cultivation, USDA’s APHIS, has not conducted a formal Environmental Assessment or EA of a pharma plant field trial since 1998, even though in the last four years “there’s been an increase, we think, in the variety and certainly the number of field tests.”

**JANE RISSLER**  
Union of Concerned  
Scientists

“The question for those looking from the outside is ‘do the current regulations protect against the human health and environmental risks? I’m disappointed to have to say that they don’t. We don’t have public involvement, we don’t have scientific rigor, we don’t have information.”

Absent the EA’s, which require agencies to solicit public comment, Rissler said that for the last four years scientists have not had “any opportunity to find out what’s happening” or to comment on containment standards.

“The question for those looking from the outside is ‘do the current regulations protect against the human health and environmental risks?’ she said. “I’m disappointed to have to say that they don’t. We don’t have public involvement, we don’t have scientific rigor, we don’t have information.”

Rissler said industry and the government should “work together to develop the kind of regulatory scheme that would inspire confidence and be protective.”

“And we would urge that there be a zero tolerance in food crops,” she said, “until the government has a comprehensive, transparent, scientifically rigorous program in place to control the risks and until the public and scientific community are fully informed and involved in the regulatory process.”

Tony Laos, president of the crop biotechnology company ProdiGene, asked Rissler what it would take to “show that these products are safe.” Rissler responded that there is a need for such things as public meetings with government officials and independent scientists to evaluate what companies plan to do and how the regulators set their standards for pharma plants.

“Once that process is established, once we can take a look at your risk assessments and proposals, once we have a system for assuring that there is protection, then I think you should have no problem,” Rissler said.



## SOWING THE SEEDS OF REGULATION:

### Analysis of the Laws and Regulations that Govern the Use of Pharmaceutical Plants in the U.S.

The cultivation and production of drugs in transgenic plants is conducted under the regulatory scrutiny of the Food and Drug Administration (FDA) and the U.S. Department of Agriculture (USDA). The USDA is generally the first agency pharma plant producers encounter, because it must approve any field tests. The FDA's main area of expertise is assessing the safety and efficacy of new medicines that might emerge from those field tests. However, as agency officials explained, there are overlapping areas of jurisdiction, and to address these, USDA and FDA are preparing a guidance document to articulate how each agency will apply its authority to pharma plants.

#### FDA: Following Pharma Plants from the Farm to the Patient

Keith Webber with FDA's Center for Biologics Evaluation and Research (CBER) pointed out that in dealing with pharma plants, FDA would do more than evaluate the safety and efficacy of a plant-produced drug.

The FDA gets involved in the oversight of pharma plants, Webber said, when a company or investigator seeks its approval to use a pharma plant product in a human clinical trial. As part of that oversight, Webber said, FDA will assert its broad authority to regulate drug manufacturing facilities to set standards for farming operations.

"We are essentially viewing the farm as a facility," Webber said.

According to Webber, FDA's authority to conduct oversight early in the drug production process is rooted in the agency's long-standing regulations requiring pharmaceutical facilities to follow a proscribed set of "good manufacturing practices" or GMPs. For pharma plant producers, adhering to GMP regulations will require documentation that they have exercised tight control over all aspects of planting, cultivation and harvesting.

Webber said producers would have to provide evidence to FDA that they possess "clearly written procedures for all activities" and "written documentation of everything you've done, and generally, that requires two signatures." They would not be allowed to delegate the responsibility for developing and following such "standard operating procedures" to a grower.

“It will be against the law essentially to just give seed to a farmer to grow and give us the bushel when you are done,” he stated.

One area FDA will be monitoring is the relationship between seed and yield, or, as Webber explained, “how much you put in...and how much you got back.”

“This is of value because if there is a large discrepancy in yield somewhere, that means that there would be a loss of seed...and companies don’t want to do that,” he said, adding that companies will need “written procedures in place to monitor yield.”

Such requirements for pharma plant producers, Webber explained, are analogous to what is required of conventional drug manufacturers, who “have to keep track of every vial they fill.”

GMP standards also must cover “handling of the waste stream” Webber said, noting that what pharma plant producers do with waste material from their fields “must be approved by the government.”

As for judging the safety and effectiveness of the plant-made pharmaceutical, Webber noted that FDA regulatory standards essentially would be the same as those applied to any new drug. He explained that pharma plant products, like any other drug under agency review, would require animal pre-clinical testing and human clinical trials to answer questions about such matters as toxicity and dose response.

Webber indicated that there would be issues specific to plant-produced drugs that will be considered by FDA reviewers. These include concerns about whether pesticides were used during cultivation, or whether “plant-associated toxicants” are present in the “host system.”

Webber said FDA’s regulatory activities are being coordinated with USDA efforts. For example, USDA provides FDA with “confidential copies of all permits for plant drug biologics,” he said, and the agencies have conducted joint inspections of field trials.

## USDA: Singling Out Pharma Plants for Special Scrutiny

Jim White, senior operations officer with Biotechnology Regulatory Services (formerly the Biotechnology Assessment branch) of USDA’s Animal and Plant Health Inspection Service (APHIS), noted that APHIS is giving transgenic plants that produce pharmaceuticals a particularly rigorous review.

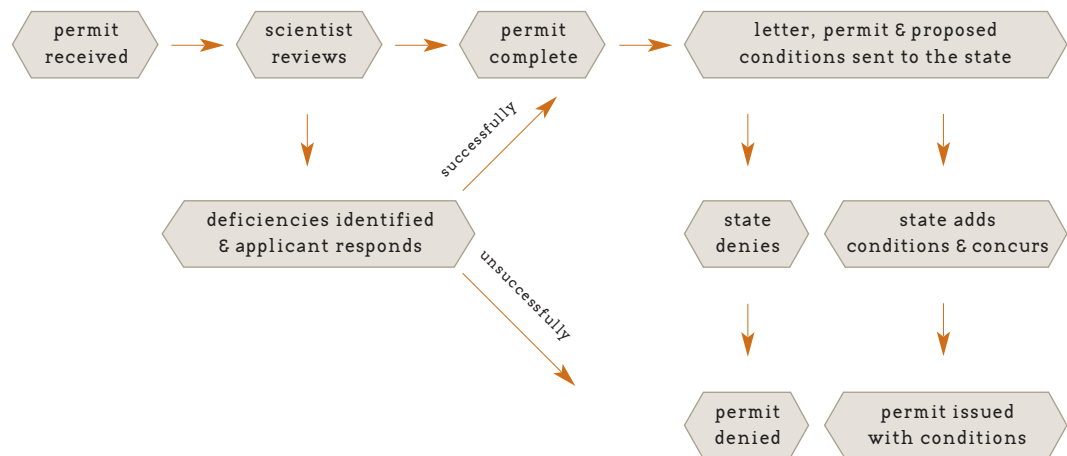
For example, while APHIS has decided that many transgenic crops are safe enough to be grown free of regulatory control (these are known as “nonregulated” plants), White said that pharma plant cultivation “will always be under federal oversight.”

The goal of APHIS’s oversight, White pointed out, is to make sure pharma plants “are kept separate from any other similar plant.”

“We inspect laboratories and greenhouses to ensure they are contained,” he said. “We inspect and control field sites to ensure that they are confined.”

### CHART 4 APHIS Permit Process for Pharma Plants

Permit Process 120 days



SOURCE: Adapted from a slide prepared by James White, USDA Animal and Plant Health Inspection Service (APHIS).

According to White, under the permitting process, anyone—a company, a scientist, an academic institution—that plans to cultivate pharma plants must first submit a permit application, which is then reviewed by agency scientists. Once the agency is satisfied that the field trial meets its regulatory standards, the permit is forwarded to state officials, who can then add conditions or, as has happened in the past, reject the permit. Once cultivation is underway, White said, APHIS conducts inspections of all pharma plant field sites.

A key task for APHIS scientists reviewing a permit, White said, is an assessment of what the grower plans to do to keep the pharma crop from spreading its genes, something scientists refer to as “gene flow.” In the case of corn, thus far the most widely used pharma crop, the challenge for the grower, he explained, is to ensure that pollen from the pharma plant does not fertilize a sexually compatible non-pharma plant.

White said agency requirements for containing corn engineered to produce pharmaceuticals are based on what scientists have learned from several decades of studying corn’s reproductive behavior. For example, he pointed out that corn generally sheds pollen for ten to fourteen days, that the pollen is viable from three to twenty-four hours, and that corn plants are generally receptive to fertilization for three to fourteen days. Thus, one way to keep pharma corn from spreading its drug-producing genes to non-pharma corn is to schedule planting so that pollen production occurs before or after other corn plants would be receptive to fertilization.

White said APHIS also has considered research indicating that gene flow between corn crops is reduced by 99.5 percent when they are a quarter of a mile apart.

Armed with information about when pollen is shed and how far it travels, APHIS has come up with containment standards that prescribe when pharma corn can be planted and how far it must be from other corn plants. White said there could be no corn of any type within a half-mile of the pharma plants and no corn intended for seed production within a mile. In addition, the pharma corn must be planted at least twenty-one days before or after any corn that is between half a mile and a mile away.

**Open pollination confinement measures for 2002 Growing Season**

- Sites are at least 1 mile away from corn seed production
- No other corn plants are grown within a radius of 0.5 miles of the transgenic test plants at any time during the field test
- Transgenic corn must be planted no less than 21 days before, or 21 days after, the planting dates of any other corn that is growing within a zone extending from 0.5 to 1.0 mile of the transgenic test plants

**SOURCE:** Adapted from a slide prepared by James White, USDA Animal and Plant Health Inspection Service (APHIS).

White said agency scientists believe the standards are “quite rigorous” and will be “difficult or virtually impossible to meet” in the major corn producing region of the U.S., a wide swath of the Midwest known as the “corn belt.”

White noted that APHIS has developed similar, science-based standards for containment of other pharma crops and, in the interest of transparency, has posted them for public review on its web site. Failure to comply with confinement or other agency regulations for pharma plants, which include a requirement that APHIS must be notified within 24 hours of any “unusual event,” can result in fines “upwards of a half a million” dollars, White said.

White pointed out that APHIS has endeavored recently to provide the public with more information on what pharma plants are actually producing, a difficult task because so much information about what these plants make is not publicly disclosed, as producers consider it to be confidential business information.

“It’s not the easiest thing to write a description about the safety of a gene that is confidential, but we are trying and will try,” White said, adding that the agency plans by the end of the year to have fact sheets posted on its Web site, which will provide information on products being produced in the pharma plants currently under agency jurisdiction.

Overall, regardless of the safety profile associated with a particular pharma plant product, White declared, “APHIS is committed to doing what is humanly possible to keep these products out of the food supply and to do the best job possible of ensuring the safe field testing of these products.”

**JIM WHITE**  
USDA Animal and Plant Health  
Inspection Service (APHIS)

“APHIS is committed to doing what is humanly possible to keep these products out of the food supply and to do the best job possible of ensuring the safe field testing of these products.”

**Industry Seeks Validation Via Regulation**

Bradley Shurdut, who leads government and regulatory affairs for biotechnology for Dow Agrosciences, said companies producing pharma plants understand that “without proper control” they will be unable to protect, nurture and realize the exciting benefits of this extremely valuable opportunity. An important aspect of managing the process, he said, is a strong regulatory presence from regulatory agencies such as USDA and FDA bolstered by a deep corporate commitment to stewardship.

“We need regulations tough and we need them transparent,” he said. “We have and continue to work with government to move this thing forward quickly and in a way that is comprehensive, so we are willing to raise the bar.”

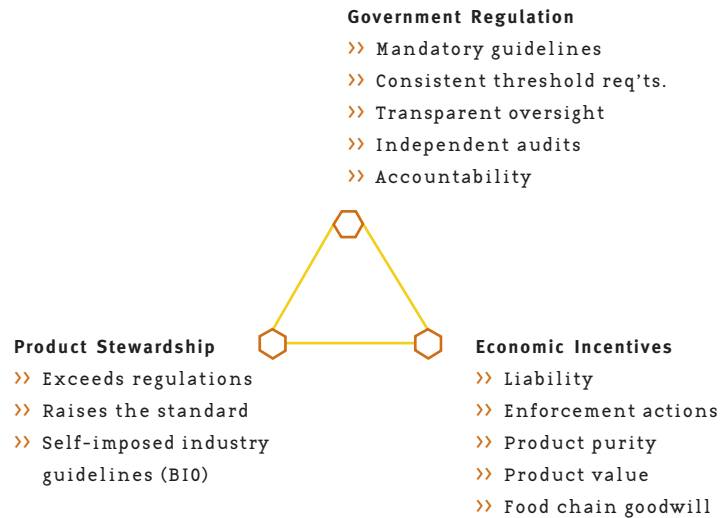
Shurdut agrees that regulations should focus on avoiding unintended pollen flow “off the site,” as well as the inadvertent commingling of biopharma grain. This dovetails, he said, with industry’s interest in maintaining the purity of the product by keeping non-pharma pollen and seed away from the pharma crops, where its presence could compromise the integrity of the highly regulated finished pharmaceutical product.

“We need to protect these crops from pollen flowing either into or out of the biopharma sites,” he said.

Shurdut said industry members agree on the principle that for the time being pharma plants should be developed in regions outside of commodity production areas. To stress that ‘biopharming’ is a highly regulated, specialized business opportunity for companies, he argued that it is important to dispel notions that pharma crops are a “value-added” opportunity for a significant number of farmers. He said the need to carefully control seed distribution would limit the financial opportunities presented by pharma crops to a select group of highly trained growers who are either corporate employees or enter into a close contractual relationship with a company.

**BRADLEY SHURDUT**  
Dow Agrosciences

“We need regulations tough and we need them transparent. We have and continue to work with government to move this thing forward quickly and in a way that is comprehensive, so we are willing to raise the bar.”



**SOURCE:** Adapted from a slide prepared by Bradley Shurdut, Dow Agrosiences.

“...To that end, we will never sell a single seed to a farmer and I think that goes for the whole industry,” he said.

Shurdut noted that pharma plants are expensive products and it is in a company’s self-interest to maintain complete control of all aspects of the process. This is imperative to delivering a cost-effective, quality product while minimizing potential losses attributed to lost product, liability claims, damage to corporate “good will,” and costs associated with government enforcement actions.

Overall, Shurdut believes industry would benefit from adopting “product stewardship” practices that compliment federal standards. For example, he described how Dow’s current business plan calls for the conduct of experimental work in the Southwest—a high-yield area that is far from corn production areas.

## Potential Gaps in the Oversight Scheme

Greg Jaffe, a lawyer with the Center for Science in the Public Interest, said that despite assurances from both government and industry, protecting humans and the environment from risks posed by pharma plant products requires an “overhaul” of the existing regulatory structure.

A key flaw in the current regulatory practices, Jaffe indicated, is that the government almost never requires a formal Environmental Assessment (EA) before a pharma plant is approved for open-air cultivation. He pointed out that when they are required, the assessments are “not adequate” because they “don’t deal with all of the environmental risks,” a criticism, he noted, that originally came from a National Research Council (NRC) report on transgenic plants and environmental safety.

White, with APHIS, responded that while his agency considers environmental issues for every permit involving pharma plants, there is a reason it rarely conducts a formal EA. As White explained, while in general many federal agency decisions must be supported by an EA, USDA has carved out an exemption for agency actions involving field trials that would include procedures for containing the crop. Furthermore, APHIS requires containment measures for all pharma plant field tests.

In addition to his criticism of the environmental reviews, Jaffe contended that, overall, the APHIS process “lacks both transparency and public participation.”

For example, Jaffe argued that when APHIS developed containment standards for pharma crops, it allowed industry, but not the general public, to participate.

“We weren’t given an opportunity to comment on those before they were put out and my understanding is that industry and other people were given an opportunity to comment,” he said. Jaffe claimed that in the original draft of the containment standards, pharma corn was to be kept five miles from seed corn but in the final draft it ended up being one mile.

“I’m not sure why that was changed, I’m not sure what the scientific implications were behind that, but that lack of transparency, that lack of public participation in those kinds of decision-making things gives me cause to be concerned about this process,” he said. “Even if, in the end, we have a good permit and so forth, it doesn’t lend itself to having a lot of confidence in the process and a sense that everybody’s views are being considered.”

He said public participation also is limited by the fact that much of the data contained in an APHIS permit is labeled confidential and hence unavailable for outside review. He noted that authors of the NRC report had difficulty assessing the risks posed by pharma plants because much of the information submitted to APHIS was labeled confidential.

Andrew Baum, head of SemBiosSys Genetics, said he understands the need for transparency but wondered how that can be reconciled with “the legitimate need to keep our programs confidential.” Jaffe responded by arguing that if companies faced more stringent requirements for justifying why certain information must be kept confidential, more data would end up in the public domain while legitimate trade secrets still would be protected. He also suggested that companies consider procedures that might allow individuals outside the process to view certain information on permits with the stipulation that it be kept confidential.

Rissler, with the Union of Concerned Scientists, told Baum that companies “have to think about how to gain the public’s confidence and not lose (their) commercial advantage.” She said there would be greater public acceptance of pharma plants if “we had some independent scientists under government offices looking at some of these containment measures.”

“I would like to, as the EPA (Environmental Protection Agency) has done on many occasions (involving transgenic crops), bring together a scientific advisory panel of outside scientists to look at things like your containment strategy,” she said. “That would improve confidence and that would be an important thing to do.”

As it now stands, according to Rissler, when it comes to assessing pharma plant safety, “we don’t know what’s being done, we don’t know where it’s being done, we don’t know how much of it is being done.”

## A LOOK AT FUTURE RESEARCH NEEDS AND THE ROLES OF PUBLIC AND PRIVATE INSTITUTIONS IN FILLING THEM

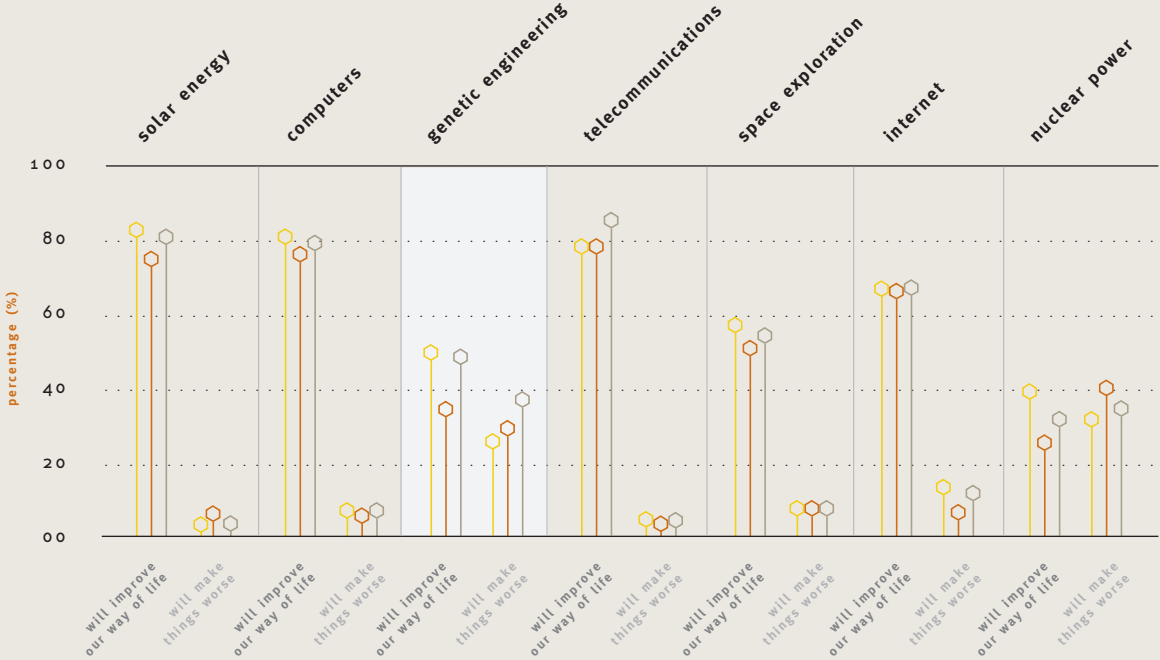


Mary Clutter, assistant director of the National Science Foundation, sought to place the development of pharma plants into a broader context by discussing the challenges to what she referred to as “21st century biology.” Among those, she said, are dealing with the public’s understanding of science in general, and genetic engineering in particular, as well as the lack of funding for basic research on plant biology.

Clutter presented results from a survey published this year by the National Science Board, which assessed public attitudes in Europe, the U.S. and Canada toward several technologies. The survey detailed whether respondents thought the innovations would “improve our way of life” or “make things worse.” She pointed out that while large majorities expressed enthusiasm for computers, telecommunications and the Internet, there was a degree of ambivalence about genetic engineering. In fact, public skepticism about genetic engineering, she said, was at about the same level as its distrust of nuclear power.

CHART 7

Public attitudes toward selected technologies in the United States, Europe, and Canada



SOURCE: National Science Board, Science and Engineering Indicators-2002  
Adapted from a slide prepared by Mary Clutter, National Science Foundation.

● UNITED STATES (2000)  
● EUROPE (1999)  
● CANADA (1999)

In the U.S., for example, about 50 percent of those surveyed thought genetic engineering would make things better, but almost 30 percent thought it would make things worse. In Europe, less than 40 percent of the respondents saw improvements emerging from genetic engineering while more than 30 percent believed the technology would be detrimental.

“So we have a major challenge there,” Clutter said.

Clutter also discussed the need for more government funding of basic research, especially for plant biology. She said USDA “has not been making major investments in this area” and that last year, all federal sources combined provided \$350 million for plant biology research, with the NSF being the largest contributor. That is not a lot of money, she said, when considering the importance of such basic research to fueling advances in biotechnology, and the fact that government spending last year on medical research topped \$20 billion.

Clutter said dealing with challenges such as public perceptions of science and inadequate funding for basic research would require better partnerships between the public and private sector.

“We need to develop effective partnerships that would involve the public and private sector,” she said. “We’re not going to solve any of these major challenges without an effective partnership.”

**MARY CLUTTER**  
National Science  
Foundation

“We need to develop effective partnerships that would involve the public and private sector. We’re not going to solve any of these major challenges without an effective partnership.”

## Plant Promiscuity and Its Implications for Containment

Norman Ellstrand, an expert in plant population genetics at the University of California, Riverside, noted that basic research in plant biology is critical to understanding how plants exchange genetic material. Better insights into gene flow between plants, Ellstrand said, will lead to greater confidence in measures designed to prevent pharma plants from spreading their novel traits to food and feed crops and to wild plants.

Ellstrand discussed several ways agricultural crops can move beyond their intended areas of cultivation and breed with other crops or wild plants. Seed dispersal is one avenue of “escape,” Ellstrand said, while some plants, such as strawberries, are capable of breeding when fragments of the plant disperse. But he said pollen is the “most effective mechanism” used by plants to exchange genetic material.

In agriculture settings, Ellstrand said, drifting pollen routinely produces hybrids between different varieties of the same crop and between crops and wild relatives that exist nearby.

Regardless of how it occurs, Ellstrand said there is evidence that most crops—and it makes no difference whether they are transgenic or conventional—“spontaneously mate with other varieties of the same species (crop-to-crop gene flow) and mate with wild relatives (crop-to-wild gene flow) somewhere in the world.” For example, in the U.S. there is evidence of crop-to-crop gene flow from farm to farm between crops of corn and between crops of canola. Although corn has no wild relatives in the U.S., Ellstrand noted that it does have wild relatives in Mexico.

Overall, the effect of gene flow, whether crop-to-wild, or crop-to-crop, depends on the particular genetic traits that might be passed along, Ellstrand said. For example, he noted that in Europe, production of domesticated sugar beet suffered when they spontaneously bred with wild sugar beets because the union produced hybrids that were unsuitable for harvest. In northeastern California, Ellstrand said, spontaneous breeding between “range grass and rye led to the evolution of a new weed which caused farmers to abandon wheat and rye production.”

According to Ellstrand, safety concerns about pharma crops are largely focused on the possibility that a plant engineered to produce drugs might spontaneously breed with a food or feed crop of the same species and pass along its drug making traits in the process. But there also are concerns, he said, that a pharma plant might spontaneously breed with a wild relative and posit into the broader ecosystem a wild, hybrid plant capable of producing pharmaceutical compounds.

Ellstrand said in assessing risks posed by various pharma crops, the “worst possible plant with regards to confining its genes” would be one that:

- » routinely breeds with related crop varieties;
- » produces large amounts of pollen and seed (and the seeds are particularly small);
- » serves as an important food and feed crop;
- » spontaneously mates with wild relatives and
- » is widely planted throughout the world

“That would be the kind of species we would really want to avoid (for pharma crops),” he said. “That species is maize (corn), unfortunately, and there are others as well. Canola would be very difficult (to contain). So if these are going to be planted, we have to go to very great lengths to avoid...contamination problems.”

Ellstrand said the desire to keep pharma crops from exercising their natural ability to breed, either with other crops or with wild relatives, points to a need for more research on the effectiveness of “traditional confinement methods,” such as those recently instituted by USDA for pharma crops, and on other techniques as well. For example, Ellstrand pointed to evidence that planting crops well before or after cultivation has begun for related crops, so called “temporal isolation,” is “a much more effective method” of deterring gene flow than are buffer zones or “spatial isolation.”

Ellstrand cautioned, however, “Research on temporal isolation has been very limited.”

Ellstrand argued that other methods of confinement, such as engineering plants with sterility, also should be studied.

“I think that genetic solutions for containment are ones that should be pursued with regards to future research,” he said.

Whatever method is considered, Ellstrand noted that it must be tested in different environmental conditions and with different plant varieties in order to measure its effectiveness.

Shantu Shantharam of Syngenta, a company that produces both conventional and biotech crops, said that after 15 years of field testing and several years of commercialization he is “not aware of any terrible consequences that people have faced” due to gene escape from transgenic crops.

Ellstrand commented that the only “downside” he has seen so far from gene flow involving transgenic plants has been the spontaneous emergence of canola that possess three different traits for herbicide resistance. While not “an incredible hardship,” he said, the new hybrid does make it more difficult for farmers to control volunteer canola.

Ellstrand said that his research into conventional crops has shown that while problems related to gene flow are rare, when they do occur “they can be doozies.” He expects the situation with transgenic crops to be no different. While problems related to gene flow may be few, he said, when they occur they could be significant, such as creating a super weed or, in the case of pharma crops, adulterating food and feed with drugs.

**NORMAN ELLSTRAND**  
University of  
California, Riverside

“I think that genetic solutions for containment are ones that should be pursued with regards to future research.”

## Understanding What Pharma Means for the Farm Belt

Iowa State's Walter Fehr, a food crop scientist who also focuses on public education and bioethics, discussed how the introduction of transgenic crops in the mid-1990s has impacted the farm belt. Most notably, he said, crop segregation, of little concern less than ten years ago, is now a major issue—and one that will intensify with the arrival of pharma crops.

Fehr explained that in the days before GM crops, while organic producers generally wanted to keep their harvested commodities separate from those who used certain pesticides, there was little concern about co-mingling of seeds or pollen. Then came transgenic crop varieties, such as corn that produces the pesticide known as Bt and soybean engineered to be resistant to the Roundup herbicide. This presented new challenges for farmers whose customers did not want transgenics in their products, Fehr said, since pollen flow or the inadvertent mixing of seeds from GM varieties could lead to lost business.

The desire for crop segregation became even more complex, Fehr observed, when Starlink, transgenic corn approved for animal but not human use, arrived on the scene and ended up co-mingling with crops intended for human food. As a result, Fehr said, all farmers growing food for human consumption, whether they were using transgenic or conventional varieties, wanted their crops segregated from Starlink.

Now pharma crops are entering the picture, he said, presenting another crop variety that will need to be isolated from other varieties.

Pharma crops are an especially provocative topic in Iowa, Fehr noted. He described how local papers have featured news about a new transgenic corn variety that contains an antibody to the herpes virus, and how such stories have provoked strong, often negative reactions. Fehr said some farmers worry that if this pharma corn is accidentally co-mingled with food and feed varieties, it could affect the safety and marketability of their state's main commodity crop.

**WALTER FEHR**

Iowa State  
University

“The point I am making is that this is going to be a very emotional issue for the public. It is so different than what we have ever done before with respect to something in the food supply.”

Mitch Hein, with Epicyte, questioned whether there is a factual basis for such fears or whether people simply have an “emotional” response when they hear the words “antibody” and “herpes.” For example, Hein wondered why someone would be more concerned about corn with a transgene that codes for an antibody as opposed to corn with a transgene that codes for a pesticide, since antibodies are naturally present in a range of food products.

Kathryn Stein of Macrogenics added, “Anybody who has ever had a cold sore has antibodies to a herpes virus.”

Fehr said he used the example of herpes antibodies in corn precisely because it elicits an emotional response. He said he was not suggesting that herpes antibodies are unsafe, but that he was trying to help companies and regulators understand the “dilemma this creates” in terms of convincing the public that pharma plants will not pose a threat.

“The point I am making is that this is going to be a very emotional issue for the public,” he said. “It is so different than what we have ever done before with respect to something in the food supply... As long as you’re aware of how tough it’s going to be to educate the public, then I’m happy.”

Fehr said companies should think about improving public confidence in pharma plants by having safety assessments conducted by independent parties, such as public research institutions.

“If I can say to an audience ‘this is safe based on a federal regulatory agency’s review, it was studied by Pennsylvania State University, the University of Illinois, the University of Maryland, all of which found this to be safe,’ that’s going to make a significant difference,” he said. However, if safety assurances rest solely on industry-supplied data, then the public would be more skeptical.



**KEYNOTE:**

**FORMER FDA COMMISSIONER JANE HENNEY**

Former FDA Commissioner Jane Henney said transgenic plants offer the potential to produce medicines that are safer, cheaper and more easily distributed than what is currently available. She said, however, questions still remain about the effectiveness of plant-derived drugs and consumers will need assurances that government oversight of this new technology is “working in their best interest.”

Henney described the “fundamental reasons” companies are investigating whether pharma plants can produce biological material for new drug therapies. These include the fact that, unlike existing systems, which produce the material in mammalian cells, plants don’t carry the risk of passing on infectious diseases. She also noted that transgenic plants have the potential to lower production costs, savings that could be passed along to the patient. They also offer the ability to scale-up manufacturing much faster than one could do with mammalian cells.

In addition, Henney asserted that plant-produced vaccines could facilitate distribution of preventive therapies by eliminating the need for injections.

Henney, however, also stated that there are still “many issues” that must still be addressed. On the scientific front, Henney pointed out that there are questions about how effective plant-derived products will be at eliciting an immune response and whether certain plant-made substances will be as stable as those produced in mammalian systems. As the field moves forward, she said, there is a need to instill public confidence that pharma plants and their products are safe, something she believes can be abetted by a willingness to engage in a frank, open dialogue.

“Scientists and the public need to find and foster open discussion of even the most controversial topics,” she said. “Never assume that science is too sophisticated for the citizenry to understand.”

Henney noted that, “we often range from faith to fear as we approach anything new in our experience and certainly as we think about technologies.” But she said that “we should not let our faith be that of being blind faith nor our fears be irrational. We should approach our discussion and our openness with facts that could support either.”

Henney encouraged all sides to look for common ground, with the search for “better ways to deliver safe products for patients” as a goal “we might all share.” She also advised regulators to maintain public trust by demonstrating that their decisions are determined by science, not politics.

“The public clearly wants assurances, whether it’s bioengineered food or bioengineered therapeutics from plants, that government bodies and regulatory decision making is working in their best interests and that the decisions made are informed, objective and evidence-based as well as being open to change when further evidence demands,” she said.



**JANE HENNEY**  
Former FDA  
Commissioner

“Scientists and the public need to find and foster open discussion of even the most controversial topics. Never assume that science is too sophisticated for the citizenry to understand.”

