Should We Be Pharming With Food Crops?

THOMAS A. LUMPKIN
Asian Vegetable Research and Development Center
Tainan, Taiwan

The field release of food crops genetically engineered for production of non-food products may be publicly perceived as an unacceptable risk, for scientific or other reasons. Of special concern are commodity food crops, such as corn, that are transformed to produce pharmaceutical or other industrial products possibly detrimental to humans. If such a transgenic product moved accidentally, or as a result of malicious intent, into the human food supply and was eventually detected, the perceived human-health risk—whether real or imagined—could cause a catastrophic disruption of the food industry. Such an incident could result in loss of livelihood for thousands of farmers, commodity handlers, food processors, *etc.*, even though the vast majority did not participate directly in, or benefit financially from, the production of the genetically engineered (GE) crops.

WHY PHARMING?

The in-depth knowledge that has been accumulated over years of study of the genetics, biology, biochemistry, cultivation, storage, and processing of food crops means that much of the information needed for genetic engineering, "pharming" (cultivation of a GE organism to produce a pharmaceutical product) and processing is already known, *i.e.* there is relatively little need for knowledge-base investment. Reduced need for funding is the main reason why food crops are attractive hosts for production of GE non-food products. Apparent low capital-investment costs of pharming are especially attractive for the pharmaceutical industry. "As Centocor vice president for medical research," Richard McCloskey stated, "the top four reasons to make Mabs (monoclonal antibodies) in transgenic plants are capital avoidance, capital avoidance, capital avoidance and capital avoidance" (Dry, 2002). The cost of field production is estimated to be about one eighth of the capital needed for construction of a fermentation factory (Pew Charitable Trusts, 2002). However, while the pharmaceutical industry may see reduced need for capital investment, in some cases farmers may be penalized for the pharming of food crops.

Liability Concerns

A wide range of arguments can be made for avoiding food crops as sources of non-food products. In nearly every case, concerns about liability can be raised. This is certainly the case with commercial pharming of corn. For example, the negative impact of pharming on sales of non-GE corn can be predicted from experience with first-generation crops engineered for herbicide tolerance: markets for US corn and soybean have shrunk, especially in Europe and Africa, and have cost farmers billions in sales. StarLink™ and other accidents have fueled consumer concerns about corn. Other crops have not been spared. Outcrossing by herbicide-tolerant GE canola in Canada has destroyed the limited organic canola industry. Proteins of transgenic origin found in Canadian honey in the European Union (EU) have resulted in a drop in honey exports to Europe by 55% (Smyth et al., 2002). Thus, savings in capital investment by the pharmaceutical industry may be shifted as risk to the food industry, but ultimately may be brought back to the pharmaceutical industry by insurance claims via the courts.

The food industry has taken a stance on production of non-food products in food crops (Cady, 2002):

> *We will not be satisfied with anything short of zero risk to the food supply by substances not approved for human consumption. We must be convinced that it is possible to design systems for absolute confinement and containment of crops producing non-food substances and that a mandatory regulatory framework is in place to assure all necessary protective measures will be taken by producers and users of these crops.*

Concerns have been raised also about environmental risks (National Research Council, 2002):

> *(T)he production of non-edible and potentially harmful compounds in crops such as cereals and legumes that have traditionally been used for food creates serious regulatory issues. With few exceptions, the environmental risk that will accompany future novel plants cannot be predicted. Therefore they should be evaluated on a case-by-case basis.*

Some feel that contamination is inevitable due to human behavior (Anonymous, 2002):

> *Current gene-containment strategies cannot work reliably in the field. Seed companies will continue to confuse batches, and mills will continue to mix varieties. Although "buffer zones" may theoretically control pollen dispersal (and gene spread), in practice farmers will be unable (or unwilling) to follow planting rules.*

For example, 30% of farmers failed to comply with refuge protocols required to maintain effectiveness of *Bt* corn (Dove, 2001). Thus, with existing confine-

ment methods, it seems inevitable that GE products unintended for human consumption will enter the food chain.

Regardless of the danger of any technology and the rigor of its standard operating procedures, humans are prone to errors of judgment and to failure to follow procedures. Atomic energy production is certainly one of the world's most highly regulated industries, yet for all of the tens of billions of dollars spent on safety, there have been thousands of accidents and victims, most notably at Chernobyl and Three Mile Island. For all the dangers of radioactivity, it does decay, even if the half-life runs to tens of thousands of years. In comparison, transgenic organisms are alive and have the potential to multiply themselves and their genes, possibly undetected, for years. Thus, even if confinement were a disciplined and well funded safety system with multiple layers of redundancy, accidents would be likely, and, in rare cases, GE plants could sustain and broaden their spread as an altered life form, with possibilities of harm to mankind and the environment.

Catastrophic Risk

The pharmaceutical industry has examples that allow us to focus on another aspect of human behavior that raises the potential of catastrophic risk: the intentional sabotage of a product. Pharmed commodities, especially if they are handled outside the confines of the factory, raise numerous opportunities for sabotage. The Tylenol®-tampering incident in the United States and similar occurrences around the world, including Japan, are examples. A stolen truckload of a pharmed commodity could be used by one of the millions already opposed to pharming, to shut down sales. The confines of pharmaceutical fermentation plants, greenhouses (Traynor *et al.*, 2001), growth chambers, and screen houses offer far more inherent security than field and farming operations that are frequently unguarded.

Theft of intellectual property rights is a common occurrence within the chemical and pharmaceutical industries. Notably, countries such as India and China (before WTO) have not respected some US pharmaceutical patents. Theft for commercial purposes from pharming field operations must be recognized as highly probable, leading to the possibility of a dangerous transgenic organism being produced outside of its original protective regulatory framework.

Risks From Environmental Factors

Beyond inconsistencies in human behavior, a vast array of environmental factors could result in a contamination or poisoning. Violent weather phenomena—hurricanes, storms, tornados, dust devils, and floods—must be expected to disseminate pollen, seed and even viable whole plants or plant parts, perhaps even to seed-production fields of the same crop type. Even spring frosts, which can emasculate self-pollinating crops, can dramatically expand the range of out-crossing beyond mandated buffers for pharmed crops.

Concerns about herbivores consuming product-bearing plant parts are rarely addressed. These include deer and game birds feeding for extended periods in pharmed fields and then taken for human consumption. A similar and all-too-common occurrence is escape of livestock—which could feed in pharmed fields.

Pharmed compounds may accumulate in predators, especially those feeding within an area of pharming that is large relative to their hunting range or which has a concentrated food source. A compound can be further concentrated over time in herbivores, predators, and micro-fauna if the pharmed crop is produced year after year in the same feeding range and is expressed in vegetative parts left in the field.

Contamination of groundwater or runoff through decay of product-expressing plant parts raises other liability concerns, especially where relative concentration and toxicity combine with resistance to decomposition.

The possibility of a recurrence of transgenic plants in a new location or in the same field could result from environmental factors. Rodents and birds can be expected to harvest, transport and store at distance, seeds produced in pharmed fields. No-tillage fields used for corn and soybean often have high populations of rodents since their nests remain undisturbed. Seeds buried by rodents or plowed below the wetting zone in irrigated regions can be expected to germinate at some point in the future. Similarly, seeds will remain dormant in irrigated desert fields if irrigation is discontinued for one or more growing seasons, perhaps long after oversight of the field is terminated. Environmentally induced and genetic seed dormancy can result in seed remaining viable for years under dry or low-oxygen conditions.

MORATORIUM

The unpredictability of nature and human behavior makes the possibility of absolute confinement, under current approaches, unrealistic, especially under field conditions. The financial risks and liabilities involved in producing non-food products in food organisms have already been demonstrated by the recent $3 million fine levied on ProdiGene. A more dramatic example is the StarLink™ accident, involving production of GE corn with the *Bt* Cry9C gene, which should have been restricted in use to animal feed (www.starlinkcorn.com). The eventual liability in this case could approach $1 billion. Facing claims of this magnitude, insurance companies may ultimately dictate a ban on the use of food organisms, at least for companies that seek to produce such crops in developed countries.

These concerns justify consideration of a moratorium on the use of food crops to produce non-food products. Research may eventually create the ability to stack many redundant biological confinement mechanisms into GE food organisms such that risk can be acceptably eliminated. If this becomes possible, reasonably safe production in some situations might become possible. Thus,

a moratorium rather than a permanent ban on the use of all food organisms is justified.

Conclusions and Recommendations

Pharmaceutical and industrial product companies are attracted to corn and other common food organisms as carrier organisms for GE products because of the in-depth accumulated scientific knowledge. In addition, positive changes have been made to these organisms over thousands of years of domestication, including large seed size, non-shattering seed heads, high yield, non-lodging, determinate maturation, lack of seed dormancy, photoperiod insensitivity, male sterility, and apomixis. This accumulation of knowledge and acquired characteristics could take decades of research and billions of dollars to reproduce in a potential non-food organism targeted for use as a carrier for production of non-food products. The United States and other governments and institutions should support knowledge-base and biological character development of non-food carrier organisms—such as castorbean or tobacco—to make them attractive to pharmaceutical and chemical companies for transformation and synthesis of GE products.

References

Anonymous (2002) Going with the flow. Nature Biotechnology 20 527.

Cady JR (2002) NFPA Forms Industry Force to Protect Integrity of Food Supply From Adulteration by Plant-Made Pharmaceuticals and Industrial Chemicals. http://www.nfpa-food.org/News_Release/121102_News_Release.htm

Dove A (2001) Survey raises concerns about Bt resistance management. Nature Biotechnology 19 293–294

Dry LJ (2002) The case for plant-made pharmaceuticals. BIO News April/May. http://www.bio.org/pmp/BIONews200204.pdf

National Research Council (2002) Environmental Effects of Transgenic Plants: The Scope and Adequacy of Regulation. Washington, DC: National Research Council, The National Academies Press.

Pew Charitable Trusts (2002) Pharming the Field: A Look at the Benefits and the Risks of Bioengineering Plants to Produce Pharmaceuticals, Proceedings of the Conference, July 17–18, 2003. Washington, DC: Pew Charitable Trusts.

Smyth S *et al.* (2002) Liabilities and economics of transgenic crops. Nature Biotechnology 20 537–542)

Traynor PL *et al.* (2001) A Practical Guide to Containment: Greenhouse Research with Transgenic Plants and Microbes. Blacksburg, VA: Virginia Tech.