# Pharm crops – a super-disaster in the making

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# Pharm Crops: a super-disaster in the making

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## Summary

**Genetically engineered (GE) "pharm" crops are designed to produce drugs and vaccines in the plant. The growth of such GE crops in the environment could potentially contaminate the human food supply and domestic animal food supply and as a consequence may cause harm to health. Pharm crops could have harmful ecological consequences if crossed with wild plants or eaten by wildlife. Therefore, Greenpeace demands a ban on the cultivation of pharm and other GE crops in the outdoor environment.**

## Introduction

Some companies are currently in the process of genetically engineering plants so that they can literally "grow" drugs and vaccines in the plants. This process to make pharmaceuticals in plants has been dubbed "biopharming" and the crops are called "pharm" or "pharma" crops. The idea behind using GE (genetically engineered) plants to make pharmaceuticals is based on the fact that there is a potential to make large quantities of pharmaceuticals this way and produce them at a low cost (Miller 2003, Anon 2002). However, such GE crops pose dangers to the environment, human and animal health and many scientists are now speaking out about these dangers.

Already, researchers have produced some vaccines and human proteins for use as drugs in pharm plants (Ma *et al.* 2003), although none have yet been licensed for commercial medical use. The plants being used for pharm crops include usual food crops such as maize (corn), soybean (Ma *et al.* 2003) and also rice. Some vaccines have been produced in pharm crops that are designed to be taken by simply eating the plant. The idea is that such 'edible' vaccines could enable developing countries to produce cheap vaccines that could be stored without refrigerators (Anon 2005b). However, there are concerns about the variability of the concentration of the drug or vaccine in plants (e.g. variability with climate), causing uncertainties in dosage (GEN, 2000). In other cases, such as some GE plants producing human proteins, the protein may be purified from the plant so it can be subsequently used as a pharmaceutical.

There is a wide array of pharm plants being researched. For instance, antibodies have been produced to treat tumours, tooth decay and prevent sexually transmitted diseases (Ma *et al.* 2003). Vaccines include those for hepatitis B, rabies, cholera, HIV and Norwalk virus (Alli *et al.* 2002, Ma *et al.* 2003). Pharm crop medical products are not yet at the stage of being commercially grown. However, two proteins from genetically modified plants, avidin and β-glucuronidase, used as laboratory reagents, are now commercially available (Ma *et al.* 2003). Companies involved in producing pharm crops include Diversa, Dow, Epicyte, Meristem Therapeutics and ProdiGene (Anon, 2004). Monsanto decided to discontinue its GE pharm crop research in late 2003 (Fox News, 2003)

## Dangers of Pharm Crops

The production of cheaper vaccines and beneficial drugs by pharm crops may sound very attractive but there is growing scientific concern about using pharm crops. There are great dangers, which could occur when pharm crops are grown in the environment.

There are two main concerns:

**(1) Possibility of contamination to human food and domestic animal foods with potentially harmful consequences**
Pharm crops grown outdoors (i.e. in fields) could contaminate other food crops and end up in normal human produce. In this way, humans could be exposed to potentially toxic pharmaceuticals in their food that could harm them (Andow *et al.* 2004). And the same is true for domestic animals (pets or livestock) – their food could be contaminated with potentially toxic drugs. If a food was contaminated with a vaccine for example, it is possible that a person or animal could have an allergic reaction to it.

**(2) Threats to the environment**
If pharm crops are grown in the open, then plant-eating animals, pollinating insects and microorganisms in soil surrounding the plants would be exposed to potentially harmful pharmaceuticals in the crops (Ma *et al.* 2003). Wild relatives of pharm crop plants could also be affected if the genes for the pharmaceuticals were passed to them by pollen from the pharm crop and cross pollination occurred. In this way, the unwanted pharmaceutical gene could persist in populations of the wild relatives and may have negative ecological consequences (Stewart *et al.* 2003), such as adverse effects on plants and wild animal populations. Furthermore, if the pharm gene persisted in wild plants, the gene could again be transferred back to related food crops by pollination (Andow *et al.* 2004).

## How Could Contamination of Human or Domestic Animal Food Occur?

There are two principal ways in which the pharm crop products could contaminate food. Firstly, the gene for the pharmaceutical could be passed to neighbouring crops of the same or closely related species by cross-pollination. If fertilisation with this pollen occurred in the normal crop, then the resulting seed, and therefore food meant for the table, would be contaminated (Anon 2005a). In the words of a scientist from the Union of Concerned Scientists:

> "*If genes find their way from pharm crops to ordinary corn, they or their products could wind up in drug-laced cornflakes*" (Pearce 2004).

This is a legitimate possibility. Scientists have already found that genes from other GE food crops (i.e. non pharm GE crops) have ended up in conventional (non GE) crops growing in the US. Over half the batches of seed from maize, soybeans and oil seed rape (canola) that were tested in one study contained some GE contamination (Pearce 2004).

A hypothetical example that illustrates another problem is to imagine that a crop was engineered to produce a non-edible commercial biochemical, with a relatively low toxicity to humans. If the gene for the biochemical outcrossed into a neighbouring crop, one where the seed was saved and exchanged by farmers, the gene for the biochemical could increase in frequency such that the commercial biochemical reached toxic levels in the harvested seed and this could have human health impacts. Although this scenario is unlikely, none of the steps of the process are unrealistic (Ellstrand 2003).

The second way that food could become contaminated is via the physical mixing of seed or grain. For example, pharm seed could be spilled in the field or mixed with normal crop seed during seed production, harvest, storage, transport or handling. Every step along the harvesting and processing trail has potential for contamination. Indeed, a study in the U.S. has concluded that the current agricultural system for corn and soybean are set up to mix grain from various sources and such a system cannot protect normal food crops from contamination with pharm crops (Andow *et al.* 2004).

What is more shocking is that accidents involving the mixing of pharm crops with food meant for human use has already happened. Seeds from a GE corn pharm crop

containing a pig vaccine were left in fields in Iowa and Nebraska and grew the following year amongst normal soybean crops (Cohen 2002, Cohen 2003b). The seeds had been left by the Texas-based company Prodigene and under current regulations should have been removed by the company. A scientist from the Union of Concerned Scientists commented that,

> "*This is a failure at an elementary level. They couldn't distinguish corn from soybeans and remove them from a field. That's like failing nursery school*" (Cohen 2002).

Action was taken by the U.S. government to prevent the crops reaching the food chain. 155 acres of corn that was surrounding the soybeans in Iowa was destroyed in case it had cross-pollinated with Prodigene's pharm crop (Fox 2003). 500,000 bushels of harvested soybeans that were mixed with the pharm maize (or corn) crop were withheld from entering the food chain (Cohen 2002, Fox 2003). Prodigene were ordered to pay US$3 million for the clean-up costs and fines for violating its permit (Cohen 2003a). This example highlights a potential problem of food contamination that has occurred after growing pharm crops on the land. A plant geneticist at the University of California commented that the government were lucky to find the Prodigene pharm crops, and he said,

> "*What if the GM corn had come up inside a corn field? It could have cross-pollinated and you'd have no idea where it was*" (Cohen 2002).

There are currently no tests available to find out whether conventional crops are contaminated with pharm crops (Pearce 2004). In most cases, the pharm crop is experimental and the information required for independent testing of pharm crops is classified as confidential business information.

The problem of pharm crop seeds being mixed with normal seed after harvesting is also a real possibility. Mistakes have already been made with other GE crops. For example, a variety of GE corn meant only for animals feed known as Starlink, turned up in foods across the U.S. (Anon 2005a). Considering all the potential routes for contamination of food with pharm crops, it is a frightening possibility that the Union of Concerned Scientists believe that contamination of the food system may already have occurred (Mellon & Rissler 2004).

## What Concerned Scientists Say Should be Done

The Union of Concerned Scientists (UCS) commissioned a report by experts on pharm crops in relation to their use in the current farming system of the USA (Andow *et al.* 2004). They concluded from that report that it was necessary to stop production of pharm crops outdoors in order to protect the food supply (Mellon & Rissler 2004):

> "*UCS recommends that the U.S. Department of Agriculture halt the outdoor production of genetically engineered pharma and industrial crops immediately, until a system is in place to produce drugs and industrial substances without putting the food system at risk*".

The UCS warn that widespread contamination of food crops with pharm genes will undermine the value of gene banks, that is, seed stores of traditional crop varieties (Pearce 2004). UCS recommended that the US Department of Agriculture explore indoor cultivation of pharm crops such as secure greenhouses in conjunction with a specialised management system to prevent the mixing of pharm crops with normal foods. UCS also recommend putting greatest effort into using alternative methods to pharm crops:

> "*The best way to reap the benefits of pharma crops and simultaneously protect the food system is to stop now and begin investing in other methods of*

*biopharmaceutical production such as alternative crops and fermentation and cell culture systems*".

The 'alternative' crops referred to in this quote are non-food crops. While such crops would reduce the risk of contamination of the food chain they still may pose a risk to the environment if grown outdoors. There would also be the risk of pharm crop debris and seeds being mixed with food crops. UCS recommended selecting plants that would pose minimal risks to foods and the environment.

One pharm product produced in a food crop, potato, has been abandoned amid fears that it might get mixed up with normal potatoes in the human food chain (Anon 2005b). This pharm crop produced the hepatitis B vaccine and had already been tested as successful in humans in a clinical trial. The vaccine is instead now going to be produced in a relative of a tobacco plant and given as pills containing the preserved ground up leaves. The UCS have commented on the use of tobacco plants as pharm crops noting that a special management system would be necessary to segregate it from normal tobacco that is chewed or smoked by the public and would still pose unknown environmental risks (Mellon & Rissler 2004).

The concern about potentially toxic substances in food due to contamination from pharm crops was highlighted in a recent editorial of a scientific journal:

"*After all, is this really so different from a conventional pharmaceutical or biopharmaceutical manufacturer packaging its pills in candy wrappers or flour bags or storing its compounds or production batches untended outside the perimeter fence*?" (Anon 2004).

## Prospects for food companies

The food industry fears that pharm crops could contaminate the food supply with vaccines and drugs (Miller 2003). Contamination could result in costly recalls (Miller 2003) and damage brand names (Mellon & Rissler 2004). If humans consumed contaminated foods they could direct lawsuits against companies that sold them the food. Companies selling organic food are especially at risk because consumers expect organic produce not to contain contamination from any GE crops (Mellon & Rissler 2004).

Food companies have been taking action. For instance, officials of the Grocery Manufacturers of America are urging the US Department of Agriculture to use "non-food crops" in their research and development of pharm crops (Fox 2003). Fearing another contamination incident like the Prodigene accident where a maize pharm crop contaminated soybean crops the following year (see above), a spokesperson for the Grocery Manufacturers of America commented that,

"*There is no room for trial and error in plant-made pharmaceutical regulations*" (Cohen 2003b) and

"*Incidents like these can have ripple effects. We don't want to lose international markets because we can't assure the safety and integrity of the food supply*" (Cohen 2002).

## Current Regulation of Pharm Crops

Since cultivation of pharm crops began, about a decade ago, they have been placed under progressively stronger regulatory regimes (Mellon & Rissler 2004). Currently, regulations set by the US Department of Agriculture state that there must be a buffer zone of one mile between pharm crops and traditional crops of the same variety, that land used to grow pharm crops should lie fallow for a year and that separate farm equipment be used for planting and storing and harvesting pharm crops (Miller 2003). However, the UCS warns that the regulations are not good enough because they have not been designed to meet the goal of complete protection of the food supply:

> "*The only acceptable goal of US pharma crops policy is to keep pharmaceutical and industrial substances out of food altogether*" (Mellon & Rissler 2004).

Furthermore, research in Australia has shown that the suggested buffer zone set by the US Department of Agriculture may not be protective of pollen transfer to traditional varieties of crops. For instance, research showed that pollen from GE oilseed rape was transported to and crossed with traditional oil seed rape varieties in fields up to 2.5 kilometres away (Rieger *et al.* 2002).

## Which Pharm Crops are Being Grown Outside?

Some pharm crops have been grown in the open environment in field trials. In the EU, pharm crop trials include those to a pharm corn to express gastric lipase (http://gmoinfo.jrc.it/). Between July 2001 and June, 2002 the US Department of Agriculture granted 25 permits for pharm crops to be grown and, between May 2003 and April 2004 biotech companies had applied for 16 permits (USA Today 2004). Ventria Bioscience of Sacramento has grown pharm rice in experimental plots in the US (Dalton 2004). The cultivation of pharm rice in the US has attracted much criticism (Freese et al., 2004). Indeed, some companies having threaten to boycott rice grown in a state where pharm rice is also grown (Reuters 2005). It has also been reported that Australia plans to get involved with pharm crops in the coming years (Collins 2004). In addition, a consortium of eleven European countries and South Africa called Pharma-Planta has been awarded 12 million euros by the European Union to develop pharm crops for treating major diseases such as HIV/AIDS, rabies and tuberculosis (European Commission 2004). Field trials from this project are likely to begin in 2006. The growing of the pharm crops in Britain is being considered, but because of factors such as the unfavourable climate it is most likely that the crops will be grown in southern Europe or South Africa (Guardian 2004).

Public access to information about which pharm crops are being grown and their whereabouts has been limited by laws which keep such information as confidential by the business concerned (Mellon & Rissler 2004). Things have recently starting to change in this regard. For example, in August 2004 a judge in Hawaii ruled that the whereabouts of field trials had to be released by the federal government (Honolulu Advertiser 2004). Furthermore, it has been reported that the U.S. Department of Agriculture will release information on the spectrum of risks and environmental impact of pharm crops when a permit has been granted (USA Today 2004).

## Conclusions

**Pharm crops grown in the environment could potentially contaminate the human food supply and domestic animal food supply and as a consequence may cause harm to health. In addition, pharm crops could have harmful ecological consequences if crossed with wild plants or eaten by wildlife. In the light of such fundamental dangers it would be prudent to stop producing pharmaceuticals in food plants altogether and use alternative methods of production such as contained microbial culture or cell culture. Where it was deemed absolutely necessary to produce pharmaceuticals in plants then they should be grown in a way that could be sealed from the environment such as a purpose built greenhouse.**

**Greenpeace is calling for a ban on the cultivation of pharm and other GE crops, since these plants could cause irreversible harm to the natural environment, with potentially devastating consequences for food production and biodiversity.**

## References


Alli, Z., Sardana, R.K., Pierre, B., Andonov, A., Robert, L.S., Schernthaner, J.P., Porter, S.L., Dudani, A.K., Ganz, P.R., Tackaberry, E.S. & Altosaar, I. 2002. Pharming for hepatitis and cytomegalovirus: towards the development of multivalent and subunit vaccines for oral delivery of antigens. Phytochemistry Reviews 1: 55-66.

Anon, 2002. Here we go again. Plans to add drug genes to food crops prove we've learned nothing. Editorial. New Scientist 6 July, 3.

Anon, 2004. Drugs in crops – the unpalatable truth. Editorial. Nature Biotechnology 22: 133.

Anon, 2005a. Too Tempting; there is just one problem with edible vaccines. Editorial. New Scientist 19 February 2005, 3.

Anon, 2005b. Why vaccination by potato got chopped. New Scientist 19 February 2005, 19.

Andow, D., Daniell, H., Gepts, P., Lamkey, K., Nafziger, E. & Strayer, D. 2004. Introduction. In: A growing concern. Protecting the food supply in an era of pharmaceutical and industrial crops. Ch. 1, 21-32. Union of Concerned Scientists, <http://www.ucsusa.org/food_and_environment/biotechnology/page.cfm?pageID=1561>

Cohen, P. 2002. Stray genes spark anger. New Scientist, 23 November 2002, 7.

Cohen, P 2003a. Fighting over pharming. New Scientist, 1 March 2003, 22-23.

Cohen, 2003b. Tougher laws on pharm crops 'not good enough'. New Scientist, 22 March, 15.

Collins, B. 2004. Farmers to pharmas. Nature 429 Supplement 3: A10-A13.

Dalton, R. 2004. California edges towards farming drug-producing rice. Nature 428: 591.

Ellstrand, N.C. 2003. The "special" case of genetically engineered plants? In: Dangerous Liasons? When cultivated plants mate with their wild relatives. Ch. 11, 171-186. The Johns Hopkins University Press, Baltimore, USA.

European Commission, 2004. Research and pharmaceuticals: EU 'pharming' solutions to major diseases. Press release, 22 July 2004, IP/04/985. <http://europa.eu.int/rapid/pressReleasesAction.do?reference=IP/04/985&format=HTML&aged=0&language=EN&guiLanguage=en>

Fox, J.L. 2003. Puzzling industry response to Prodigene fiasco. Nature Biotechnology 21: 3-4

Fox News, 2003. Monsanto Posts Loss, to Cut Jobs, Wednesday, October 15, 2003
http://www.foxnews.com/story/0,2933,100172,00.html

Freese, B., Hansen, M. & Gurian-Sherman, D. 2004. Pharmaceutical Rice in California. Potential Risks to Consumers, the Environment and the California Rice Industry. <http://www.foe.org/camps/comm/safefood/biopharm/index.html>

GEN (Genetic Engineering Newsletter) 2000. Edible vaccines. Special issue 3, April 2000. Öko-Institut e.V., Freiburg, Germany.

Guardian, 2004. Medical crops coming soon. Guardian July 13

<http://www.guardian.co.uk/uk_news/story/0,,1259785,00.html>

Honolulu Advertiser, 2004. USDA told to disclose 'biopharm' locations. Honolulu Advertiser August 5 2004. <http://the.honoluluadvertiser.com/article/2004/Aug/05/ln/ln07a.html>

Ma, J.K-C., Drake, P.M.W. & Christou P. 2003. The production of recombinant pharmaceutical proteins in plants. Nature Reviews Genetics 4 : 794-805.

Mellon, M. & Rissler, J. 2004. Introduction, Conclusions, and Recommendations of the Union of Concerned Scientists. In: A growing concern. Protecting the food supply in an era of pharmaceutical and industrial crops. 7-20. Union of Concerned Scientists, <http://www.ucsusa.org/food_and_environment/biotechnology/page.cfm?pageID=1561>

Miller, H.I. 2003. Will we reap what biopharming sows? Nature Biotechnology 21: 480-481.

Pearce, F. 2004. Gene pollution is 'pervasive'. New Scientist, 28 February 2004, 8.

Reuters 2005. Missouri farmers, beer maker, protest biotech rice 12 April 2005.

http://yahoo.reuters.com/financeQuoteCompanyNewsArticle.jhtml?duid=mtfh69639_2005-04-12_17-51-52_n12323952_newsml>

Rieger, M.A., Lamond, M., Preston, C., Powles, S.B. & Roush, R.T. 2002. Pollen-mediated herbicide resistance between commercial canola fields. Science 296: 2386-2388.

Stewart, C.N., Halfhill, M.D. & Warwick S.I. 2003. Transgene introgression from genetically modified crops to their wild relatives. Nature Reviews Genetics 4: 806-817

USA Today 2004. USDA to let public see more info on biotech crops. June 2 2004.

<http://pqasb.pqarchiver.com/USAToday/645354751.html?did=645354751&FMT=ABS&FMTS=FT&date=Jun+2%2C+2004&author=Elizabeth+Weise&desc=USDA+to+let+public+see+more+info+on+biotech+crops>