Union of Concerned Scientists
Citizens and Scientists for Environmental Solutions

February 5, 2003

Dockets Management Branch (HFA-305)
Food and Drug Administration
5630 Fishers Lane
Room 1061
Rockville, MD 20852

Re: Docket No. 02D-0324

To Whom It May Concern:

Please accept the attached comments from the Union of Concerned Scientists concerning "Guidance for Industry: Drugs, Biologics, and Medical Devices Derived from Bioengineered Plants for Use in Humans and Animals" (docket number 02D-0324).

Sincerely,

Jane Rissler

Jane Rissler, Ph.D.
Senior Staff Scientist

Attachment

02D-0324

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Union of Concerned Scientists
Citizens and Scientists for Environmental Solutions

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February 5, 2003

Honorable Anne Veneman
Secretary
US Department of Agriculture
Whitten Building
14th and Independence Avenue, SW
Washington, DC 20250

Honorable Mark B. McClellan, M.D., Ph.D.
Commissioner
Food and Drug Administration (HF-1)
5600 Fishers Lane
Rockville, MD 20857

RE: ZERO-CONTAMINATION INITIATIVE ON PHARMCROPS

Dear Secretary Veneman and Commissioner McClellan:

On behalf of the Union of Concerned Scientists (UCS), we hereby submit the following comments on the regulation of crops engineered to produce pharmaceuticals (pharmcrops). UCS is a nonprofit, public interest partnership of citizens and scientists working to achieve practical, sustainable solutions to human health and environmental problems.

Pharmcrops represent an application of biotechnology that may deliver lower-priced drugs, a substantial benefit in the era of high medical costs. At the same time, however, these crops may present risks to people who inadvertently consume them in contaminated food; also, they may present environmental risks.

Below are UCS's comments on the contamination risks of pharmcrops (our comments on environmental risk will follow later). We are focusing on food contamination first not only because food safety is a vital concern, but also because addressing these risks is essential to the advancement of the technology. We believe that even one discovery of a food product contaminated with engineered drugs would hobble the technology, if not stop it in its tracks.

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To ensure that the food supply is completely protected against contamination from pharmcrops, UCS recommends the following four steps:

1. ***USDA and FDA should jointly set zero contamination of the food supply as the goal of the agencies' pharmcrop policy.***

Exposing consumers to drugs though food crops is an unacceptable risk to human health. In addition, and also important, the discovery of drugs in food items would cause momentous and costly disruptions in the food system. Company brands could be damaged and huge costs incurred in testing products and conducting recalls. In addition, the grain and oilseed pipelines would have to be purged of the contaminant. The StarLink episode gives an idea of how expensive those disruptions can be. Costs associated with that incident total something like one billion dollars[1]—even though the trait was not likely to cause harm if consumed in food. To ensure against another StarLink, the USDA and FDA need to set zero contamination of the food supply as the goal of the agencies' pharmcrop policy and then judge the adequacy of required containment measures against that goal.

2. ***USDA and FDA should establish a public scientific advisory committee on pharmcrops to consider and advise the agencies on the full range of measures available to meet the goal of zero contamination of the food supply.***

To determine which measures—or combination of measures—can achieve a zero-contamination goal, USDA and FDA should convene a panel of experts. The agencies should charge the committee with defining and evaluating all available measures and approaches, including at a minimum the ones listed below, for their contribution to preventing contamination of the food supply. The panel should consider measures crop by crop and both alone and in combination. The experts should then rank the measures—or combinations of measures—that will meet the zero-contamination goal for each major crop. Special emphasis should be given to corn, currently the most popular crop for pharmaceutical production.

Pharmcrop contamination of the food supply is likely as a result of outcrossing via pollen and physical mixing. Outcrossing occurs as pollen from pharmcrops is carried by wind or insects into nearby fields and fertilizes crops destined for human consumption. Pharmcrop seeds left behind after harvest may germinate the next year and cross pollinate with food crops. Physical mixing may happen at several points in the food chain—on the farm during planting, cultivating, and harvesting and off the farm at the grain elevator or in transport.

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[1] Smyth, S., G.C Khachatourians, and P.W.B. Phillips, Liabilities and economics of transgenic crops, *Nature Biotechnology* 20:537-41, June 2002.

A range of options, including those presented below, could be considered to prevent contamination from both routes. Meeting the goal of zero contamination would probably require combining a number of methods and tailoring a different combination for each crop.

Potential measures include:

- *Zoning*—Growing pharmcrops in designated areas, perhaps states or counties, where they would not encounter food crops. Zoning could prevent outcrossing and severely reduce opportunities for physical mixing.

- *Spatial separation*—If pharmplants are grown at a sufficient distance from food crops, viable pollen will not reach food crops.

- *Temporal separation*—Outcrossing can also be prevented by planting pharm and food crops so that they flower at different times. If plants do not flower in the same time period, pollen produced by the pharmplants will not encounter receptive eggs to fertilize in the food crops.

- *Disallowing food crops*—Both physical mixing and outcrossing would be substantially reduced if only nonfood (and nonfeed) crops were used for pharmaceutical production. For example, kenaf, an a plant grown for its fiber, might be considered. Or pharmcrop companies could develop other nonfood crops explicitly as pharmcrops. The best candidates would be ones that are not ingested, as is tobacco.

- *Dedicated machinery and infrastructure*—Requiring farmers to have planters, combines, trucks and other on-farm equipment dedicated solely to pharmcrops would decrease the likelihood of physical mixing on the farm. A dedicated grain-handling infrastructure—elevators, trucks, railroad cars—for moving and storing grain once it leaves the farm would also reduce co-mingling.

- *Indoor production*—Growing pharmcrops indoors would eliminate outcrossing and, if the facilities were used solely for pharmcrops, would also avoid physical mixing. Large greenhouses or lighted caves and mineshafts[2] might be adapted for the task.

- *Sterile pollen*—Requiring that pharmcrops produce sterile or no pollen would help reduce outcrossing.[3]

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[2] Pharming plants underground, *Nature Biotechnology* 19:802, September 2001.
[3] Daniell, H., Molecular strategies for gene containment in transgenic crops, *Nature Biotechnology* 20:581-86, June 2002.

- *Engineering chloroplasts*—Splicing drug genes into chloroplasts would reduce outcrossing substantially because pollen typically contains few, if any, chloroplasts. The method is not one hundred percent effective because of the pollen grains that do carry chloroplasts.[4]

- *Suicide genes*—Genetic engineers may be able to devise suicide-gene cassettes that would reduce the viability of pharmcrop seeds.[5] Although sterile, such seeds would still carry the drug products of interest and would be a food contamination problem if moved into the food system. Suicide genes would also not inhibit the expression of drug genes if transferred to neighboring crops via pollen.

The USDA/FDA pharmcrop advisory committee should meet and deliberate in public. Its members should be selected for their expertise in relevant scientific disciplines and crop production. The panel should be balanced to include representatives from academia, the food and pharmcrop industries, consumer and environmental organizations, and organic and conventional commodity crop grower groups. The committee's report should be written by its members and made public in a timely fashion.

3. *USDA and FDA should use the advisory committee's report to devise regulatory requirements to be imposed on growers, handlers, and transporters of pharmcrops.*

Once the government has the results of the committee's work, it should evaluate the cost and feasibility of adopting the options or combinations of options that meet the goal of zero contamination of the food supply. The government should choose the options that are least expensive and most likely to encourage a commercially viable pharmcrop industry. Once it has selected the appropriate measures, the government should impose them as mandatory conditions on the field testing and commercial growth of pharmcrops.

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[4] Maliga, P., Plastid engineering bears fruit, *Nature Biotechnology* 19:826-27, September 2001.
Ruf, S., M. Hermann, I.J. Berger, H. Carrer, and R. Bock, Stable genetic expression of tomato plastids and expression of a foreign protein in fruit, *Nature Biotechnology* 19:870-75, September 2001.

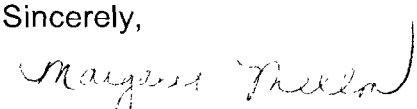
[5] Daniell, H., Molecular strategies for gene containment in transgenic crops, *Nature Biotechnology* 20:581-86, June 2002.
Smyth, S., G.C. Khachatourians, and P.W.B. Phillips, Liabilities and economics of transgenic crops, *Nature Biotechnology* 20:537-41, June 2002.

4. ***USDA and FDA should impose a moratorium on field tests and commercial production of engineered pharmcrops until they have convened the scientific advisory committee and established a regime that the scientific community believes will assure the goal of zero contamination of the food supply.***

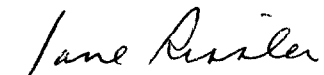
The pharmcrop industry is already struggling in the wake of the StarLink and Prodigene episodes. Too much is at stake to allow more such incidents, which remain possible as long as pharmcrops are grown without adequate confinement. To avoid a "StarLink with drug genes," USDA and FDA should impose a moratorium on field tests and commercial production of engineered pharmcrops. That delay should last until they have convened the scientific advisory committee and established a regime that the scientific community believes will assure the goal of zero contamination of the food supply. Such a moratorium would likely keep fewer than thirty pharmcrops out of the field for the next growing season. That is a small price to pay for setting this industry off on a solid scientific footing.

Thank you for your consideration of our comments.

Sincerely,



Margaret Mellon, Ph.D., J.D., Director
Food and Environment Program



Jane Rissler, Ph.D.
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