National Grain and Feed Association

February 6, 2003

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

RE: Docket No. 02D-0324

The National Grain and Feed Association (NGFA) is pleased to respond to the Food and Drug Administration's (FDA) request in the September 12, 2002 Federal Register (FR) for comments on a draft document, developed in conjunction with the U.S. Department of Agriculture (USDA), entitled "Guidance for Industry: Drugs, Biologics and Medical Devices Derived from Bioengineered Plants for Use in Humans and Animals." As noted in the FR notice, the draft guidance is intended to provide recommendations to sponsors, manufacturers, licensees and applicants on the use of bioengineered plants or plant materials (bioengineered pharmaceutical plant) to produce biologic products, including intermediates, protein drugs, medical devices, new animal drugs and veterinary biologics.

The NGFA consists of 1,000 grain, feed, processing and grain-related companies that operate about 5,000 facilities that store, handle, merchandise, mill, process and export more than two-thirds of all U.S. grains and oilseeds. Also affiliated with the NGFA are 36 state and regional grain and feed associations.

Preface to Comments to the Proposal

While NGFA is responding to the FDA's proposal in the below comments, we want to preface these comments with our strong reservations regarding the likelihood of achieving zero contamination of existing grain and food supplies in the U.S. through a combination of corporate responsibility and regulatory control, whether through a voluntary or a mandatory system. As many quality control experts will attest, developing a fail-proof system that includes a strong dependence on human performance is an unrealistic expectation. Accidents occur, and any legal or regulatory approach that is chosen should contemplate both the probability of failure to meet zero contamination under specified parameters as well as the cost of such occurrences.

Even among some informed regulators, the expectation is a probability greater than zero that contamination of the U.S. grain-based food system will occur at some

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point. This obviously is not satisfactory since the commercial grain and related food products must achieve zero tolerance, and will no doubt be subject to a certain amount of (at least) random testing of grain and products both domestically and internationally.

The costs of an occurrence of contamination will depend on the extent of the contamination, its dispersion in the grain and food system prior to discovery, as well as consumer reaction (in addition to any real health threat that may or may not be present in such occurrence). While not a perfect analog, the StarLink™ situation in 2000 has resulted in an estimated $500 million loss (based upon informal survey work) directly to Aventis. Market damage, in terms of lost markets to the U.S., is in addition to this level. And, because grain-marketing systems in the U.S. are so fluid with intermingled commodities, it is expected that small levels of StarLink may be detectable for years to come. Thus the conclusion is that the cost exposure to the grain and food industry from another contamination incident is potentially huge, with a long-term impact over many years. So that even a small probability of an accident occurring is a highly significant risk exposure to the existing grain and food industry.

Given the heavy financial exposure of not just the grain handling industry, but even more so in wholesale and retail processed products, we would urge that the administration support a policy change (either through regulation or legislation if that is deemed necessary) to ensure that companies, academic institutions and others involved in the research and commercial production have demonstrated financial resources or financial backing to be able to cover potential losses from accidental or other forms of adulteration that might be caused by a confinement breach in pharmaceutical or industrial crop production.

Specific Comments on the Proposal

As noted previously, because the food and feed industry face a "zero tolerance" standard in both domestic and international markets for the presence of any unauthorized bioengineered plant or plant material in general commodity crops, it is imperative that FDA (and USDA) develops and enforces stringent confinement and processing standards for bioengineered pharmaceutical plants and plant material. In this regard, we offer the following suggestions to improve the draft guidance document:

- The guidance document should include a statement immediately before the **Introduction** stating there is a current "zero tolerance" policy for the presence of bioengineered pharmaceutical plants in general commodity food and feed crops, i.e., the guidance document should clearly state that strict segregation sufficient to achieve zero tolerance is mandatory for those bioengineered pharmaceutical plants and plant material that lack harmonized domestic and international tolerances for the presence of such material in food and feed. We believe such a statement would send an important message to both domestic and international consumers regarding the continued strength of the U.S. regulatory system.

- Title "Guidance for Industry: Drugs, Biologics..." should be changed to "Guidance for the Production of Drugs, Biologics..." to make it clear that the provisions of the document apply to all groups – private, public, and academic – that may be involved in the research, production and processing of bioengineered pharmaceutical plants. Similar text should be added to the body of the Guidance.

- To the extent possible, the provisions of Sections II, III, and IV should be mandatory and reflective of the current regulatory system for bioengineered plants. While we understand the difficulty in developing guidance that would be applicable to all plants and plant products, the frequent use of terms such as "should" or "may" in some portions of the document leave the impression among domestic and international consumers that compliance with stringent confinement measures is generally voluntary rather than mandatory. To address this concern, the NGFA believes that several portions of the draft guidance document should be amended to reflect the mandatory nature of the Federal Food, Drug and Cosmetic Act (FFDCA) and underlying regulations pertaining to new animal drug and investigational new drug applications. Specifically, the Guidance Document should require the following measures to comply with the FFDCA's prohibition on adulteration of food and feed:

  - ✓ Measures to prevent inadvertent mixing (including cross pollination) of bioengineered pharmaceutical plants with plants intended for food or feed.

  - ✓ Measures to control the production, inventory and disposition of viable seeds to preclude the possibility that such seeds will be used to produce material that could be used for food or feed production.

  - ✓ Measures to account for seed use and documentation of field production sites, pollen drift control measures and destruction of plants in subsequent growing seasons. Such measures should specify the minimum number of growing seasons a field site must be monitored for "volunteer" pharmaceutical crops. In addition, the document should require that personnel be assigned to inspect the fields immediately after harvest for plant material -- such as corn cobs and loose kernels -- that may have been inadvertently left behind, with clean-up of such material as necessary.

  - ✓ The use of dedicated equipment for planting and harvesting as well as dedicated containers for the transportation of bioengineered pharmaceutical plants and plant material. All containers used for such purposes must meet strict standards for integrity to prevent leakage during transportation and be tracked from origin to final destination.

- ✓ The use of separate handling and production facilities for bioengineered pharmaceutical plants and plant material.

- ✓ Measures to control waste material from processing bioengineered pharmaceutical plants to ensure that they do not enter human or animal food. In addition, mandatory procedures should be instituted to verify and document the proper disposition of waste material and by-products.

If FDA does not believe it can use the Guidance Document to require applicants to provide each of the aforementioned assurances to prevent adulteration under the FFDCA, the NGFA believes FDA should implement a rulemaking immediately to implement such requirements.

- Require that bio-engineered pharmaceutical plants that lack harmonized domestic and international tolerances for their presence in food and feed be grown in either: 1) regions of the country where production of its food/feed counterparts is known not to occur; or 2) greenhouse/greenhouse-like conditions that are secured from unauthorized entry and provided with safeguards on ventilation systems to prevent any release of pollen to the atmosphere. As noted previously, we remain unconvinced that such unauthorized crops can be safely grown in general crop production areas.

- Require a comprehensive contingency plan be included as part of the confinement measures for bioengineering pharmaceutical plants and plant material to address an unauthorized release into the environment as well as detection in food or feed. The plan should present a credible and timely response to counteract the release, measures to mitigate any impact on the food and feed sectors. It must also include a commitment of sufficient financial resources to implement the plan, such as a bond or insurance policy.

We also recommend that FDA (and USDA) include a commitment to conduct regular on-site inspections of all field test sites (including public institutions conducting such research) during critical production activities (e.g., planting, growing, harvesting and subsequent handling) of bioengineered pharmaceutical plants and plant material to ensure compliance with confinement and processing requirements.

On the other hand, the FDA should reconsider its recommendation regarding altering the color of pharmaceutical crops as a means to readily distinguish these varieties from their food or feed counterparts. While on the surface this idea appears to have merit, it also has a serious drawback in that it raises the potential for unethical person(s) to sprinkle some food or feed crops dyed the same color into the general commodity stream potentially creating severe disruptions in domestic and export markets. An alternate approach that might prove effective in quickly identifying and preventing inadvertent mixing, at least in the case of corn, would be to require that pharmaceutical

corn be left on the cob until it is delivered using dedicated equipment to the processing facility.

Industrial Crops

Industrial crops (or other crops) not intended to be in food and feed present the same risks to the food and feed industry as pharmaceutical crops and should be subject to equivalent regulations and standards as pharmaceutical crops. Thus, we strongly urge FDA (and USDA) to prepare and publish at the earliest opportunity a similar document for industrial crops that clearly indicates that such crops will be held to the current "zero tolerance" policy as bioengineered pharmaceutical plants for their presence in food and feed, and stringent confinement and processing standards will be enforced.

Thank you for allowing us to comment on this important matter. If we can be of further assistance in this matter, please contact Mr. Thomas C. O'Connor, National Grain and Feed Association, at 202/289-0873.

Sincerely,

Arvid P. Hawk

Arvid Hawk, Chairman
NGFA Food Safety Committee

cc: The Honorable Ann Veneman, Secretary of Agriculture
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