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February 7, 2003

Dockets Management Branch (HFA-305)
Food and Drug Administration
5600 Fishers Lane, rm. 1061
Rockville, Maryland 20852

Re: Docket No. 02D-0324, Draft "Guidance for Industry: Drugs, Biologics, and Medical Devices Derived From Bioengineered Plants for Use in Humans and Animals"

To Whom It May Concern:

The North American Millers' Association (NAMA) is pleased to respond to the request for comments on the "Guidance for Industry: Drugs, Biologics, and Medical Devices Derived From Bioengineered Plants for Use in Humans and Animals" drafted by the U.S. Food and Drug Administration (FDA) in collaboration with the U.S. Department of Agriculture (USDA). The issue of using bioengineered plants to create drugs, biologics, and medical devices is a timely and critical one. NAMA commends the FDA and USDA for beginning the process of looking at the system and controls necessary to govern a new technology that promises major benefits and at the same time creates new risks for domestic agriculture. As the national association representing 46 milling companies and over 90% of the U.S. milling capacity for wheat, corn, oat, and rye, NAMA members are a critical link in the U.S. food chain and have a vested interest in maintaining the safety of the U.S. food crop. To this end, NAMA offers the following comments on the FDA guidance document for review and consideration.

It is clear that the production of pharmaceutical crops is very different from the production of food crops or other bioengineered crops intended for food and feed. Pharmaceutical crops are not intended for consumption in the food and feed chain and, therefore, should be regulated according to a separate set of criteria than other crops that are intended for food and feed use. As currently drafted the FDA guidance only begins to provide a framework for the use of bioengineered plants to create pharmaceutical crops (including drugs, biologics, medical devices, therapeutic proteins, and animal biologics). NAMA's primary comment regarding the FDA guidance is that it must only be part of an overall regulatory framework that includes mandatory rules, monitoring, and penalties that will guarantee the 100% containment of all pharmaceutical crops. Based on the

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current tolerance level of zero for pharmaceutical crops, 100% containment is absolutely necessary. NAMA will continue to insist on 100% containment from the food and feed supply for any substance not approved for human consumption.

By itself the FDA guidance is ineffective in addressing the risk to the food chain and consumers of food products. The major issues of concern are addressed in the guidance, but do not have the binding power of regulations and detail no enforcement or punitive actions due to the inherent nature of their issuance as "guidance" and not regulation. NAMA recommends that future controls be issued in collaboration with USDA as regulations that are enforceable under penalty.

FDA should also consider a change in the title of its guidance to better reflect the audience it is intended to address. The current title only refers to "industry" which could be misleading since the term typically means private industry. The production of plant-made pharmaceuticals is not only done by private industry but also by various groups including universities, farmers, and any person or organization handling the bioengineered products. The title should be expanded so there is no mistake that the guidance should apply to all working with plant-made pharmaceuticals.

NAMA believes that recommendations in the FDA guidance document represent a step in the right direction toward the overall containment of plant-made pharmaceuticals. In particular, NAMA supports several of the recommendations in Section III-C that list some logical controls and procedures that should be a part of a confinement system for any pharmaceutical crop production. Points 1, 2, 3, and 4 of Section III-C contain components of a strict confinement system that would begin to lend confidence in the ability to have a system of 100% containment and should be included in future regulations.

However, points 5 and 6 of Section III-C fail to fully guarantee that the pharmaceutical crop will in no way enter the food and feed chain. While the guidance says, "Source plant materials should not be processed in facilities that also are used for the production of food or feed, such as grain mills," it also continues on to say, "without prior consultation with USDA/APHIS/BRS and FDA." NAMA believes that it should be made clear in this guidance and all future documents that absolutely no material from pharmaceutical crops should be processed in food and feed facilities. Furthermore, point 6 that discusses the control of waste material makes a similar assertion that all waste material must "be disposed in a manner to ensure that the material will not enter the human or animal food chain unless you have specifically consulted with FDA for the use of this material in food or feed products." Under the regulatory framework that exists today there should never be an instance where the disposal of plant-made pharmaceutical waste material can enter the human or animal food chain and therefore such a statement implies incorrectly that in certain cases such practices might be tolerable.

In addition, the FDA guidance does not address the possibility of intentional sabotage of pharmaceutical crops creating the possibility for spread of pollen or mixing

of mature crops with those intended for food and feed. The FDA and USDA must consider procedures and methods to prevent intentional acts of sabotage when looking at confinement measures.

NAMA would also like to recommend that FDA and USDA consider the following for inclusion into any regulatory proposals for pharmaceutical crops in the future.

- An expansion of current physical confinement system procedures to include a physical separation from all like-commodities or containment under monitored greenhouse conditions, sufficient to guarantee a 100% effective isolation from like-commodities used in food and feed.
- A temporal separation at pollination based on growing and planting periods. While we have less scientific confidence in temporal separation, we would advocate the redundancy of a separation that assures zero tolerance by taking into account different planting and growing conditions.
- Security procedures that prevent deliberate contamination.
- Mandatory liability insurance coverage to indemnify all downstream traders, handlers, processors and food manufacturers for the full cost of recall, destruction and brand degradation as a result of gene flow, or other release of genetic material into the food or feed industries.
- The use of dedicated equipment in all steps of the plant-made pharmaceutical manufacturing process including seed production, seed distribution, planting, harvesting, conveyance, and storage.
- The creation of USDA/GIPSA validated test methods for the presence of the specific plant-made pharmaceutical products before approval of field test permits.
- Compliance and enforcement procedures that guarantee a zero level of contamination including the creation of a third party auditing system of compliance.
- A procedure that would require the discontinuation of all activity in a plant-made pharmaceutical field including planting, harvesting, and transportation, immediately upon the discovery of any regulatory violation until such violation is resolved to the satisfaction of the regulatory authority.
- A requirement that all outdoor plant-made pharmaceutical production fields remain fallow for at least one crop year after harvesting and any volunteer material be documented and disposed of according to established regulations.

The recommendations of NAMA do not intend to include all necessary measures, but rather a basic framework that should be considered in all regulatory deliberations. Several of these points were mentioned or suggested in the FDA guidance, but others such as methods to prevent volunteers from a previous year's crop from mixing with a subsequent food and feed crop are not addressed at all.

A final and important subject that is not addressed in the FDA guidance is the use of plants to derive industrial products. Industrial products are no more intended for food and feed uses than pharmaceutical products and present as many risks to food safety.

NAMA would therefore ask the FDA and USDA to develop regulations for industrial crops in the near future using similar criteria to that used for pharmaceutical crop regulation.

Thank you for the opportunity to comment on this important issue. We look forward to working with the FDA and USDA as the guidance and other regulations are formulated. Please contact Mr. Jim Bair, Vice President, North American Millers' Association, at 202/484-2200, ext. 107 if you have any questions.

Sincerely,

Betsy Faga

Betsy A. Faga
President