NFPA
The Food Safety People

NATIONAL
FOOD
PROCESSORS
ASSOCIATION

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February 6, 2003

VIA EMAIL (www.fda.gov/dockets/ecomments)

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

RE: Docket No. 02D-0324. Guidance for Industry: Drugs, Biologics, and Medical Devices Derived from Bioengineered Plants for Use in Humans and Animals
67 Federal Register 57828, September 12, 2002

John R. Cady
President and
Chief Executive Officer

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Dear Sir or Madam:

The National Food Processors Association (NFPA) is the voice of the $500 billion food processing industry on scientific and public policy issues involving food safety, nutrition, technical and regulatory matters, food security and consumer affairs. NFPA's three scientific centers, its scientists and professional staff represent food industry interests on government and regulatory affairs and provide research, technical services, education, communications and crisis management support for the association's U.S. and international members. NFPA members produce processed and packaged fruit, vegetable, and grain products, meat, poultry, and seafood products, snacks, drinks and juices, or provide supplies and services to food manufacturers.

General Comments:

NFPA appreciates the opportunity to submit comments on FDA's and USDA's guidance to provide recommendations to sponsors, manufacturers, licensees, and applicants of products derived from bioengineered plants or plant materials. The food industry has grave concerns with respect to the use of bioengineered food and feed plants and plant materials to produce non-food products, whether they are pharmaceuticals or industrial chemicals. NFPA's concerns center on the clear possibility and consequences of adulteration of food/feed crops, and associated food/feed products, due to the contamination of such crops and products by those food/feed crops that have been genetically

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engineered to produce PMPs and industrial compounds unapproved for food/feed use. For the purpose of these comments, the term "plant made pharmaceuticals (PMPs)" is used to represent PMPs themselves, as well as industrial chemicals and other products not intended to be included in the general food supply or food products. The term "food" is used to represent both human food and animal feed.

NFPA believes it is necessary, at the outset of these comments, to make clear our view on the use of food crops for PMP production. In a perfect world, and if the food industry had complete control of this promising technology from the beginning, the food industry would never have supported the use of food crops for the production of PMPs. The risk of contamination to the food supply is simply too great, as the food industry learned through our experiences with commodity products such as Starlink™ corn, which was not approved for human food. Unfortunately, PMP technology has already been implemented in food crops.

Given that consideration, NFPA strongly opposes the use of food crops to produce PMPs without the necessary effective controls and procedures to ensure against any contamination of the food supply. The U.S. experience with Starlink™, and recent permit violations within the PMP sector itself, demands placing a high burden of proof on this technology sector for robust control systems. The record to date, especially in view of past human errors, necessitates the requirement of proof that sufficient controls can be put in place to achieve 100% protection against any PMP contamination. Unless this is the case, then applications should be allowed only in non-food crops segregated from food crops.

The food industry is clearly an affected stakeholder in this issue. The food industry believes that the use of bioengineered food and feed crops for the production of products not intended to be in foods for the general public constitutes a practice that must be addressed in a manner that clearly and comprehensively protects the integrity of the food supply. As discussed in the following comments, it is NFPA's position that PMPs, industrial compounds, and like products not approved or intended as general human or animal food or food ingredients, must be subject to mandatory regulatory oversight that is directed to preventing adulteration of the food supply, including being subject to permits from USDA's Animal and Plant Health Inspection Service (APHIS). NFPA acknowledges that such mandatory regulatory oversight is and must be the responsibility of different federal agencies acting together in a coordinated, comprehensive way.

Food Industry Issues Associated with PMP Production:

NFPA acknowledges that the current and potential benefits of biotechnology clearly call for and justify the broad pursuit of this technology. However, maintaining a safe, wholesome and unadulterated food supply must remain the primary goal of the government as it is for the food industry. Government and industry must take clear and meaningful actions that prevent damaging the integrity of the food supply in every aspect of PMP production, including

propagation, cultivation, production, harvesting, distribution, and waste disposal at field testing and commercialization stages.

NFPA believes that the use of major food and feed crops for production of PMPs that are not approved for human foods or animal feeds is not appropriate without protective, mandatory and effective controls and procedures that ensure against the contamination of the food/feed supply. FDA has a zero tolerance for articles of food that are not approved for human consumption. The entire food chain, including agricultural producers and food processors, are subject to this standard. Anything less than 100% prevention of PMP adulteration of the food supply could expose segments of the food chain to liability and regulatory risks that are not of their making or within their control. Consequently, it is our position that if 100% prevention against adulteration is not achievable, food and feed crops must not be used in the production of PMPs. Because we live under a zero tolerance (i.e., 0%), we must demand nothing less than 100% protection from PMP contamination.

The adverse consequences of intentional or unintentional adulteration of food and feed that PMP production could introduce include loss of consumer confidence in the safety of the food supply, loss of international trade in food commodities and processed foods, and regulatory and civil liability charges against the food industry, as well as damage to brand and product standing in the market place. The food industry expects and calls on federal agencies to consider these impacts as well as food safety and public health issues in crafting biotechnology regulations and industry guidance.

Scope of the Guidance:

NFPA recognizes that the proposed guidance document is not currently drafted to address comprehensively all the issues associated with PMPs. The vast majority of the draft guidance concerns issues relating to the safety, purity, and efficacy of vaccines and drugs, which are relevant concerns. However, FDA, in cooperation with USDA, and other federal agencies as appropriate, should use this opportunity to provide specific guidance and/or statements of relevant federal policy and plans, particularly with respect to preventing adulteration of the food supply. These issues can be covered in the Introduction section of the Guidance. FDA should make clear the Guidance's relationship and contribution to the existing and proposed Coordinated Framework and coordinated federal actions described in the Office of Science and Technology Policy notice of August 2, 2002 (67 FR 50578), as well as the government plans to introduce additional regulation including the scope of such regulations.

The Purpose and Scope section of the draft Guidance states types of compounds produced in bioengineered plants, such as non-protein drugs, botanicals or allergenic products for human use are not covered under these guidelines. NFPA feels it is essential that these guidelines (and any future regulations) cover compounds that may cause the food supply to be considered adulterated if present. Specifically, we are concerned with compounds commonly referred to as "industrial

products" (e.g. trypsin, lipase, biopolymers, etc.) where there is an adulteration risk, similar to that of pharmaceuticals, for these compounds to become part of the food supply through contamination if food crops are used for production. We believe the full range of proteins and compounds that could be produced in food crops should be addressed by the guidance, particularly with respect to environmental considerations. NFPA believes that proteins and chemicals not intended to be eventual components of food and/or feed, yet that are grown in food crops, are of a major concern to food processors and to the public and should be addressed in this guidance. We believe that "industrial products," just as pharmaceutical products, should be handled and treated as regulated articles, and should not be considered, at any time of development or commercialization, for an "un-regulated status" by USDA.

Environmental Considerations:

The opening sentence under General Considerations of the Environmental Considerations section points out that the use of bioengineered pharmaceutical plants to produce regulated products raises a number of environmental issues that should be addressed, including "confinement measures that may be needed to control the spread of the bioengineered pharmaceutical plants and to keep them from entering the food or feed supply." While NFPA strongly agrees with this point, we believe it does not go far enough in drawing attention to the range of possible ways in which PMP production could result in contamination of the food supply and the consequences if this occurs. FDA should make clear the full scope of the processes, activities, or events that would result in adulteration of food, and the Agency should articulate its expectation that controls must prevent such an occurrence.

FDA's enforcement role is only briefly addressed, with mention that the presence of the target gene or gene product in food or feed could render such products adulterated. Further, reference is given to FDA's Center for Food Safety and Applied Nutrition (CFSAN) or Center for Veterinary Medicine (CVM) for more information about the legal implications of any such material getting into food or feed. A more direct and explicit discussion of these "legal implications" should be given. FDA should indicate the stringent standards it maintains and the consequences for those responsible for the PMPs. Also, the explicit requirements imposed, such as performance requirements under permits, through application of APHIS's regulations during field trials, transport, and commercialization should be described.

NFPA believes that FDA should recommend in the Guidance, and consider for inclusion in a mandatory requirement, a systematic approach to determining the potential avenues for adulteration of food crops/foods and the relevant prevention controls. NFPA believes the Hazard Analysis and Critical Control Point (HACCP) approach offers a potential model.

The Guidance should include expanded discussion of the manner in which FDA and USDA can and will use the National Environmental Policy Act (NEPA) requirements to ensure the agencies adequately address relevant environmental concerns. FDA and USDA should indicate how the

NEPA process would be used by the agencies to confirm that environmental concerns, particularly potential adulteration of food products, have been adequately addressed. NFPA strongly supports the inclusion of the Confinement Measures section in the Guidance. NFPA, however, believes this element of the Guidance must be the subject of mandatory regulations, and strongly urges the agencies not only to implement this section of the Guidance immediately, but to initiate expeditiously a rulemaking on this provision.

Any mandatory regulations should not be limited to codifying the recommendations contained in the Guidance, but should approach the issue of confinement and containment in a detailed and comprehensive way. The issues that should be addressed in both the Guidance, and ultimately in regulations, should include standard operating procedures (SOPs) for comprehensive treatment of biological containment, physical containment, training throughout the development, production, and processing system, identity preservation, security against intentional efforts to cause food adulteration, monitoring and auditing during field tests and commercialization, waste management and disposal, and accident detection and response, including the availability of workable testing methods. Licensing of individuals involved with various stages of PMP production should also be required.

The Guidance and future regulations should provide for innovation and technology developments that further ensure against any adulteration of the food supply from PMPs, with consideration given to those controls and procedures that may not currently be considered. NFPA strongly suggests that the Guidance and future regulations emphasize redundancy in controls and procedures, to provide certain insurance against any possible contamination.

The roles and responsibilities of FDA, USDA, and other agencies, as appropriate, should be established with respect to assessing and concurring with the proposed confinement and containment conditions for field tests and commercialization. FDA must play an integral role in evaluating whether the proposed controls will be 100% effective in protecting the food supply. Since the primary goal of both the food industry and the requisite regulatory agencies is to ensure a food supply that is safe, wholesome and unadulterated, anything less than 100% protection against PMP contamination raises the risk to an unacceptable level. Consequently, in the absence of controls that ensure against any contamination of the food/feed supplies, the use of food and feed crops for the production of PMPs must not be permitted.

Inspections and Monitoring:

Inspections and monitoring of PMP production activities with respect to preventing adulteration of the food supply should be addressed in the Guidance and in future regulations. NFPA is concerned that without a highly active and effective inspection program, the systems designed to protect the food supply from adulteration will not be as vigorous or as stringent as needed. We propose that both the FDA and USDA need to enhance their inspection activities, to include both announced and unannounced inspections. Inspections should occur, at a minimum, at critical

stages of the PMP production (e.g. planting, pollination, harvest, plant processing and plant disposal). NFPA recognizes that providing the oversight and enforcement sought by the food industry may tax available FDA and USDA resources, and the agencies are encouraged to identify and seek sufficient resources. Consideration should be given to regulatory constructs currently available to ensure adequate oversight.

USDA must take full advantage of its strong regulatory authority under the Plant Pest Act and related laws to impose permit conditions that will assure containment of PMPs, including appropriate biological and physical containment measures and HACCP controls. USDA must also use its extensive inspection authority, and bolster the inspection resources dedicated to PMPs, to enable the Agency to closely monitor production of PMPs to assure that permit conditions are not violated. In addition, FDA, which has regulatory authority over PMPs as drugs, should make clear that inadequate containment measures will result in withholding approval of a New Drug Application (NDA), or other sanction under the Federal Food, Drug and Cosmetics Act.

It must be remembered, however, that though regulatory oversight for PMPs is absolutely essential, without effective, redundant and proven controls that are managed properly to ensure against any contamination of the food supply, and the requisite training and auditing of stakeholders engaged in PMP production from propagation to disposal, regulatory oversight of the process is insufficient.

NFPA is interested in working with food chain organizations, policy makers and regulators to review the effectiveness and adequacy of current requirements for segregation and containment of plants designed for production of pharmaceutical agents and industrial chemicals and all such plant-made materials. NFPA will continue its efforts to ensure the necessary regulations and policies are in place to eliminate the risk of contamination to the food supply from PMP production.

Conclusion:

In the absence of effective controls and procedures to ensure against any contamination of the food supply, NFPA strongly opposes the use of food crops to produce PMPs. The use of food crops to produce PMPs must only proceed under systems proven to absolutely prevent any contamination or adulteration of the food supply. Without such systems, the risk to the integrity of the food supply is simply too high, requiring additional liability provisions that will protect, in total, food producers experiencing loss from contamination of the food supply by these materials.

NFPA appreciates this opportunity to comment on the proposed Guidance and the broader policy issues associated with PMP production, and looks forward to working with FDA and USDA on

the issue to ensure the food and feed supplies remain safe, wholesome and unadulterated. This is the primary goal of the food industry, and the mission of both the FDA and USDA.

If you have any questions on the contents herein, please contact us.

Regards,