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February 6, 2003

Dockets Management Branch (HFA-305)
U.S. Food and Drug Administration
5600 Fishers Lane - Rm. 1061
Rockville, MD 20852

Re: Guidance for Industry: Drugs, Biologics, and Medical Devices Derived from Bioengineered Plants for Use in Human and Animals (67 *Federal Register* 57828, Sept. 12, 2002).

We are on the verge of a time in which fields historically devoted to agricultural crops will become drug and chemical manufacturing facilities, dramatically different from those used to date. Plant-based drug development technologies promise substantial therapeutic and economic benefits. However, if not subject to stringent controls, the same technologies also threaten the integrity and safety of the United States food supply. It is up to the U.S. Government, and the U.S. Food and Drug Administration (FDA) and the U.S. Department of Agriculture (USDA) specifically, to ensure that we do not sacrifice food safety to technological progress. The proposed guidance fails to strike this balance and, in the process, fails to inspire confidence among U.S. food companies about the integrity of U.S. commodity supplies and the ability of current regulations to isolate and contain these products.

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The undersigned U.S. trade associations, including the Grocery Manufacturers of America ("GMA"), American Bakers Association ("ABA"), Biscuit & Cracker Manufacturers Association ("B&CMA"), Food Marketing Institute ("FMI"), Institute of Shortening & Edible Oils ("ISEO"), International Dairy Foods Association ("IDFA"), National Confectioners Association ("NCA"), National Council of Chain Restaurants ("NCCR"), National Restaurant Association ("NRA"), and National Soft Drink Association ("NSDA"), appreciate the opportunity to provide these comments to the U.S. Food & Drug Administration in response to the Agency's proposed guidance regarding the use of bioengineered crops for the development of drugs, biologics, and medical devices (*67 Federal Register 57828*, Sept.12, 2002).

GMA is the world's largest association of food, beverage and consumer products companies. With U.S. sales of more than \$460 billion, GMA members employ more than 2.5 million workers in all 50 states. The organization applies legal, scientific and political expertise from its member companies to vital food, nutrition and public policy issues affecting the industry, including the critical issue of biotechnology. Led by a board of 42 Chief Executive Officers, GMA speaks for the food and consumer product manufacturers and sales agencies at the state, federal and international levels on legislative and regulatory issues. The association also leads efforts to increase productivity, efficiency and growth in the food, beverage and consumer products industry.

ABA is the national trade association representing the wholesale baking industry. The Association's membership consists of approximately 300 bakers and bakery suppliers who together are responsible for the manufacture of approximately 80 percent of the baked goods sold in the United States.

B&CMA represents more than 70 national and international biscuit and cracker manufacturers and over 150 bakery suppliers. Cookies and crackers include a wide variety of distinctive products with retail sales in the United States of more than \$10 billion.

FMI is a non-profit association that conducts programs in research, education, industry relations and public affairs on behalf of its 2,300 member companies — food retailers and wholesalers — in the United States and around the world. FMI's U.S. members operate approximately 26,000 retail food stores with a combined annual sales volume of \$340 billion — three-quarters of all food retail store sales in the United States. FMI's retail membership is composed of large multi-store chains, regional firms and independent supermarkets. Its international membership includes 200 companies from 60 countries.

IDFA is the dairy foods industry's collective voice in Washington, D.C., throughout the country and in the international arena. IDFA has become a leading player in the formation of positive domestic and international dairy policies. Today, IDFA represents more than 500 dairy food manufacturers, marketers, distributors and industry suppliers across the United States and Canada, and in 20 other countries. IDFA is the umbrella organization for three constituent organizations: The Milk Industry Foundation (MIF), National Cheese Institute (NCI), and International Ice Cream Association (IICA). Members range from large multinational corporations to single plant operations, and represent more than 85% of the total volume of milk, cultured products, cheese, and ice cream and frozen desserts produced in the United States - an estimated \$70 billion a year industry.

NCA represents more than 700 companies that manufacture and market the vast majority of chocolate and non-chocolate confectionary in the United States.

NCCR, a division of the National Retail Federation ("NRF"), is a national trade association representing forty of the nation's largest multi-unit, multi-state chain restaurant companies. These forty companies own and operate in excess of 50,000 restaurant facilities. Additionally, through franchise and licensing agreements, another 70,000 facilities are operated under their trademarks. In the aggregate, NCCR's member companies and their franchisees employ in excess of 2.8 million individuals.

NRA is the leading business association for the restaurant industry. Together with the National Restaurant Association Educational Foundation, the Association's mission is to represent, educate and promote a rapidly growing industry that is comprised of 870,000 restaurant and foodservice outlets employing 11.7 million people. Founded in 1919, the National Restaurant Association's 60,000 member companies represent more than 300,000 restaurant establishments. NRA's membership base consists of many different facets of the industry.

NSDA is the trade association representing the broad spectrum of companies that manufacture and distribute non-alcoholic beverages in the United States.

I. Introduction

Several messages about plant-based drugs need to be conveyed unequivocally to industry and to the public. These points apply with equal force to plant-based industrial chemicals and other non-food products.

First, biotechnology holds immense promise -- not just because it offers food and feed producers and consumers the potential for improved crop yields, increased insect resistance, reduced pesticide use, and enhanced nutritional value -- but also because of its

potential medical, environmental, and industrial applications. All these uses need to be pursued. And all these uses can be and need to be carefully regulated to extract maximum benefit without sacrificing hard-won progress in other areas, particularly food safety. We encourage broader use of biotechnology, provided that these broader uses are subject to thoughtful, stringent, science-based regulation with equally stringent U.S. Government oversight and enforcement.

Second, growing drug crops is not commodity agriculture -- it is open-air drug manufacturing. Regulators must acknowledge that they are not simply regulating a new kind of crop, but they are now charged with regulating something that has until now been outside the purview of the USDA permitting process -- the regulation of drug manufacturing facilities. "Pharming" is not "farming"; It cannot be undertaken nor regulated in the same way as conventional crop agriculture.

Third, the proposed guidance glosses over the severe regulatory and liability consequences if non-food products contaminate the food supply. The FDA has a zero tolerance for articles in food that are not approved for human consumption. This means that containment of plant-based drugs must be 100% effective; anything less could subject the violator to criminal prosecution. Anything less than 100% containment also will subject all participants in the drug development efforts -- from farmers to pharmaceutical companies -- to potential liability for bodily injury to consumers and for economic losses and damage to the brands names of affected businesses. Most importantly, anything less than 100% containment could expose the food industry, which plays no role in and has nothing to gain from the development and commercialization of drug and chemical crops, to regulatory and civil liability consequences.

Fourth, in light of these potential consequences, the U.S. Government should quickly institute mandatory, science-based regulations that effectively isolate these products and prevent the inadvertent or intentional contamination of the U.S. food supply and should not permit the use of crops used for food production or crops that are sexually compatible with food crops in such manufacturing until those regulations are in place. Put simply, existing regulations must be strengthened significantly to address the increased risk to the food supply that these products present. The current U.S. regulatory framework does not inspire confidence among our collective members that that these drug and chemical crops will remain isolated and confined and not contaminate the food supply. Many of these controls must be established and policed by USDA through the permitting process; however, FDA also must be satisfied that these controls not only ensure proper drug manufacturing but that they are 100% effective in preventing contamination of the food supply.

Fifth, to be effective, stronger regulations must be accompanied by stringent oversight and enforcement. For this reason, the guidance must address not only the drug manufacturing aspects of the new technology but also how the adverse impacts on the food supply will be handled. For example, it should discuss how food recalls will be classified and how information about contamination incidents will be communicated promptly and effectively to industry and consumers – both by the developer and by FDA. The regulators and the regulated community both need to be prepared to respond when -- as is inevitable -- preventive measures fail. This preparation must take place before there is a failure of containment. This stepped-up oversight and enforcement will require more hands-on involvement and resources by FDA and USDA to accomplish.

I. Discussion

The undersigned organizations support the development of new technologies that promise therapeutic and economic benefits to the public, but not at the expense of food safety. The flaw in the proposed guidance is that it addresses only the first of these two goals. Although no plant-based drugs have reached the market, there are many such products in the pipeline. Over 200 permits for field trials of pharmaceutical plants have been issued to date and many of the resulting drug products are expected to be commercialized within three to five years. Corn is the food crop most frequently used for the development of these products. Barley, rapeseed, rice, safflower, soybean, sugarcane, tomato, and wheat also have been used.

Prior experience with transgenic crops provides very limited data on which to predict the potential environmental impacts from non-food substances manufactured with food crops. This is so for at least two reasons. First, production of drug or non-food chemicals by transgenic methods involves the transfer of different types of transgenic traits. The National Resource Council, in its 2002 report titled *Environmental Effects of Transgenic Plants: The Scope and Adequacy of Regulation*, observed:

The significance of biotechnology for environmental risk resides primarily in the fact that a much broader array of phenotypic traits can be incorporated in crop plants than was possible about a decade ago. As such, our experience with the few herbicide-tolerant and insect- and disease-resistant varieties that have been commercialized to date

provides a very limited basis for predicting the questions needed to be asked when future plants with very different phenotypic traits are assessed for environmental risks.¹

Second, a change in the scale of production of transgenic crops also could have a dramatic impact on the risks to the environment and the food supply. The existence and nature of post-commercialization environmental impacts from manufacturing cannot be reliably predicted based on pre-commercialization testing that is conducted on a different spatial and temporal scale.² As a practical matter, an increase in the scale of field-testing also will increase the likelihood of cross contamination.

The likelihood of contamination is exacerbated further by growing food and non-food varieties of the same crops in close proximity, as is currently permitted by the Animal Plant Health Inspection Service (APHIS). For example, pharmaceutical barley can be planted as close as 500 feet from food barley; pharmaceutical corn can be planted a mile away from food corn, and pharmaceutical rice must have border rows of food rice to "dilute" pollen and an isolation distance of 100 feet from food rice.³ APHIS describes these restrictions as "risk mitigation" measures but does not suggest that these physical controls can provide 100% assurance that there will be no cross contamination of food

¹ National Research Council, Board on Agriculture and Natural Resources, Division on Earth and Life Studies, Committee on Environmental Impacts Associated with Commercialization of Transgenic plants, *Environmental Effects of Transgenic Plants: The Scope and Adequacy of Regulation*, at 220 (National Academy Press 2002) ("NRC Report").

² NRC Report, at 13.

³ APHIS, *Summary of Confinement Measures for Organisms Being Field Tested in 2002* (May 21, 2002) available at <http://www.aphis.usda.gov/ppq/biotech/pdf/pharm-2002.pdf>.

crops. In fact, the use of food crops for drug development presents a significant probability of some type of cross-pollination or gene flow.

At present, drugs are manufactured in highly controlled "brick and mortar" manufacturing facilities. Plants are grown in fields exposed to wind and other elements. When fields become drug-manufacturing plants, the manufacture of drugs takes place in an environment that is virtually impossible to control, as the Prodigene episode illustrates. In November 2002, a shipment of conventional soybeans delivered to a Nebraska grain elevator was found to contain stalks and corn containing a pharmaceutical protein developed by Prodigene at two test sites in Nebraska and Iowa. The company was fined \$250,000 and required to locate, purchase, and destroy 500,000 bushels of contaminated soybeans, at a cost of approximately \$3 million. This is a small but telling example of the potential consequences of inadequate containment.

The NRC Report counsels particular caution about the use of food crops for non-food purposes and recommends a stringent scientific case-by-case analysis: "the production of non-edible and potentially harmful compounds in crops such as cereals and legumes that have traditionally been used for food creates serious regulatory issues. **With few exceptions, the environmental risks that will accompany future novel plants cannot be predicted. Therefore they should be evaluated on a case-by-case basis.**"⁴ This evaluation should take account of the potential risks associated with such plants, some of which were highlighted by the NRC:

Some of the coming applications of biotechnology may involve the use of plants to produce pharmaceutical products, biologics, fuels, and other

⁴ NRC Report, at 15 (emphasis in original).

substances not intended for human food use. The introduction of such transgenes poses the potential for environmentally associated risks of a wholly different order than those associated with existing transgenic crops. If such a transgene moves into food crops, either through pollen transfer or physical contamination, there could be serious human safety risks [emphasis added]. If such a transgene moves into a wild relative, there could be widespread environmental dissemination of the pharmaceutical substance or other non-food substances that could have impacts on wildlife as well as microbial populations.⁵

This case-by-case analysis must address the containment measures necessary to protect the food supply, as well as the potential consequences of a failure of such containment. Both points are addressed below.

A. Liability Issues

The proposed guidance notes correctly that the presence of an unapproved bioengineered material would render food or feed adulterated under the federal Food, Drug, and Cosmetic Act. For example FDA states, "The presence of [non-food or non-feed] material in food or feed could render such products adulterated under the FD&C Act. (21 U.S.C. 342)." However, the subject of potential civil and criminal liability resulting from drug contamination of the food supply warrants a clearer and more prominent discussion in Section III ("Environmental Controls") of the proposed guidance. It should follow the "General Considerations" (section III.A) and "National Environmental Policy Act" (sections III.B,) and should precede the discussion of "Confinement Measures" (section III.C).

First, FDA needs to make it absolutely unequivocal that drugs do not belong in food and that FDA will use the full arsenal of its civil and criminal enforcement powers if such

⁵ NRC Report, at 246 (emphasis added). See also *id.* at 235-36.

non-food or non-feed products appear in the food supply. Potential enforcement actions may include placing a clinical hold on an Investigational New Drug Application (IND), withholding approval of a New Drug Application (NDA), or initiating a criminal prosecution. Second, FDA should emphasize that the consequences of failed containment are not limited to regulatory violations and are not limited to those directly involved in drug development. Any failure of containment could expose large and small businesses involved at every stage of food manufacture and handling -- from farmers, to transporters, grain handlers, commodity processors, grocery manufacturers, and retail grocery establishments -- to liability. These entities would in turn look to those responsible for the containment failure for redress.⁶

For these reasons, the guidance needs to send a much stronger message to drug developers about the nature and magnitude of the risk they face and to which they expose the food industry in the event that drug crops contaminate the food supply.

B. Containment Controls

Where there are failures of containment for any reason, enforcement must be swift and severe. But clearly the focus of regulators and drug developers must be on preventing contamination. We outline below some of the necessary elements of a stringent system of containment controls designed to ensure that drugs do not get into the food supply in the first instance.

⁶ The NRC Report provides an example of the new types of liabilities and claims that could be triggered by inadequate containment of transgenic crops: "Farmers may incur legal liability for technology fees as a consequence of neighboring fields inadvertently pollinating a crop, leading to transgenic seed production. This, in turn, may create new forms of environmental nuisance lawsuits, as farmers attempt to protect themselves from complaints lodged by the owners of transgenic technology." NRC Report, at 237.

Quickly Finalize Mandatory, Science-based Regulations. The U.S. Government should quickly institute mandatory science-based regulations that effectively isolate these products and prevent the inadvertent or intentional contamination of the U.S. food supply. Moreover, the Government should not permit the use of crops used for food production or crops that are sexually compatible with food crops in such manufacturing until those regulations are in place. No new permits should be issued for the development of drug crops beyond the 200 field test permits that already have been issued until an effective containment regime like that outlined below has been developed and implemented. A similar approach should be pursued regarding USDA permits for commercial production of such products. We already have seen the risks that non-food drug crops present to the food supply. It would be irresponsible to allow drug development to proceed in open fields using food crops without a comprehensive system in place to control these risks.

Presumption Against the Use of Food/Feed Crops for Pharmaceuticals. In the permitting and drug development process, there needs to be a presumption against the use of food or feed crops for drug development and manufacture. To overcome this presumption to obtain a permit from USDA, a drug developer who wishes to use such crops should be required to demonstrate that it has tested the suitability of non-food crops and has determined that the use of such crops is not feasible from either an economic or a technological standpoint.

In making the threshold determination as to whether a specific food crop may be used for a specific drug development purpose, certain features of the protein or the crop in question will warrant stricter scrutiny or a determination that the protein or crop is not appropriate for the use in question. For example, a novel or toxic protein in a food crop

should prompt stringent examination and regulation by both USDA and FDA. Similarly, USDA and FDA may question the suitability of crops that are inherently susceptible to containment problems; USDA also has noted that "plants that have a lengthy seed dormancy period and out cross to weed species (e.g., *Brassica species*), or that are bee pollinated (e.g., alfalfa) are not appropriate plants to produce these [pharmaceutical] products in the field."⁷

In the event that agricultural crops are used for drug development, there are two types of controls -- biological and physical -- that can and must be used in tandem to prevent contamination of the food supply. These correspond to containment risks that arise from both biological and physical factors. As the NRC Report observes, "[t]he probability of environmental damage from the next generation of transgenic crops will be determined by the specific phenotypic traits of each crop as well as by agronomic practices and land uses specific to each particular crop that is commercialized."⁸ Iterative biological and physical controls are essential to ensure isolation of drug crops.

Biological Containment. Biological containment measures go far to ensure that minimal to no cross-pollination or gene flow between the host plants will occur. The most stringent of these controls would be not to use food crops for drug development at all. Failing that, other biological methods should be used, such as rendering the drug plant

⁷ Letter from Hon. Bobby R. Accord, Administrator, Animal Plant Health Inspection Services, USDA, to C. Manly Molpus, President and Chief Executive Officer, GMA, at 3 (March 21, 2002).

⁸ NRC Report, at 245-46.

sexually sterile (often referred to as “terminator technology”) so that it cannot reproduce or transmit genetic material.⁹

Other biological mechanisms also can be used to prevent or minimize the risk of contamination. We strongly support the suggestion that biological markers be used to distinguish drug plants from their conventional counterparts used for food or feed. As the guidance indicates, these biological indicators include “genetic markers that alter the physical appearance of the plant (e.g., a novel color or leaf pattern), or change the conditions under which a plant will grow (e.g., “the use of an auxotrophic marker gene”) as well as “restricting the expression of the bioengineered pharmaceutical product to a few specific plant tissues (e.g., the use of tissue specific promoters) or . . . restricting the conditions under which the product will be expressed (e.g., those of an inducible promoter).”¹⁰

Physical Containment. As noted above, biological containment should be used in tandem with physical containment to isolate and contain these products from the food supply. The most stringent of these mechanisms would be to prohibit the growing of drug crops in the same areas of the country in which their counterpart food crops are grown. The Biotechnology Industry Organization (BIO) took a major step in this direction when it indicated that its members would manufacture non-food materials using food and feed crops only in areas of the country in which the crop in question is not a major production

⁹ The NRC Report observes that “[t]o restrict the transfer of transgenic traits to wild forest and orchard tree populations, it is generally considered essential to simultaneously genetically engineer reproductive sterility.” NRC Report, at 223.

¹⁰ Proposed Guidance, at 9.

area for that food crop.¹¹ GMA believes this is a constructive initiative but lacks sufficient information about the geographical crop production areas and proposed separation distances contemplated by BIO to determine its effectiveness.

If drug crops are grown in areas of the country where the corresponding food crop is grown, it will be essential for regulators to require very stringent physical containment measures in order to achieve 100% containment. These measures should include mandated use of large-scale greenhouses, walls, fences, screens, isolation distances, bagging plants before flowering, guard and border rows of plants, and staggered flowering times. At all stages (from planting through processing and transport) drug and chemical crop material should be kept in separate labeled containers and, where appropriate, destroyed. At all times, drug crops or intermediate products should be physically distinguishable (e.g., colored, use of confetti mix) and bear a label indicating that the material is not to be used for food or feed and that such use is a violation of federal law.

This physical separation must extend even to the facilities used to grow and process the crops; they need to be grown on dedicated land and processed using dedicated labor and equipment. If the same land is to be used for pharmaceutical and agricultural products in different growing seasons, it needs to be subject to a fallow period

¹¹ In its *Statement Regarding Plants That Produce Pharmaceutical and Industrial Products*, BIO says, "BIO member companies working in this area previously agreed to voluntarily limit growing these articles except under conditions of substantial spatial isolation from major areas of crop production intended for animal or human consumption until such time as a scientifically proven track record of safe handling is established and demonstrated." Available at <http://www.bio.org/pmp/statement.asp>. In a similar vein, the NRC Report suggests that geographical separation is advisable: "it would be essential to grow these plants [engineered to produce monoclonal antibodies now produced in mammalian tissue cultures] in restricted locations, but the value of the products would easily be sufficient to offset the cost of growing the crop in isolation." NRC Report, at 228.

following the harvest of the transgenic crop to prevent the appearance of volunteer pharmaceutical plants in an agricultural commodity.

Training. The distinction between drug development and commodity agriculture systems must extend not only to the crops but also should include the individuals involved in handling such crops. "Pharmers" should be carefully selected, trained, licensed, and bonded in order to handle pharmaceutical crops and dedicated solely to the production and harvesting of drug crops.

Identity Preservation/Chain of Custody. As the StarLink and Prodigene episodes illustrate, our agricultural system is not designed to prevent commingling of crops. Yet that is precisely what must be done when crops are used to develop drug active ingredients and it is therefore what regulation of drug crops must be designed to achieve. The U.S. Government must build upon the regulatory foundation for "brick and mortar" drug manufacturing facilities in establishing the measures to regulate these new open air drug manufacturing sites and take account of the unique hazards posed by drug manufacturing in new and heretofore far less controllable environments.

FDA and USDA also should look to other regulatory approaches that are designed to eliminate the risk that potentially hazardous substances might be found in food or released into the environment. One model is the Hazard Analysis and Critical Control Point (HACCP) approach that is designed to reduce food safety hazards -- whether biological, chemical, or physical -- for seafood and low-acid canned foods under FDA's jurisdiction and for meat and poultry plants under USDA's jurisdiction. HACCP is based on seven steps: (1) identification of the hazards, (2) identification of the critical control points at each stage in the food's production -- from its raw state through processing and shipping to

consumption by consumers -- at which the potential hazard can be controlled or eliminated, (3) establishment of critical limits for preventive measures at each control point, (4) monitoring of the values of the critical limits at each control point, (5) establishment of corrective measures when the critical limits at each control point are not met, (6) verification that the system is working properly, and (7) recordkeeping to document each of the foregoing steps.¹²

United States environmental laws also are instructive. For certain materials, manifests requiring signatures by a trained and responsible individual must be obtained at each step in the handling and transport of certain materials. As applied to drug crops, this should include transport of seeds and plants, planting, growing, harvesting, processing, purifying, packaging, storage, and disposal. The level of individual responsibility in such an identity preservation system underscores the need for individuals handling drug crops to be trained, licensed, and bonded.

Security. Once again, where a field or greenhouse serves the same purpose as a brick-and-mortar drug manufacturing facility, it should be subject to exactly the same security requirements, seven days a week, twenty-four hours per day.

Monitoring and Auditing. All drug development facilities should be subject to continuous self-auditing requirements and regular reporting requirements, and validated by third-party auditors trained in the regulations and complexities of plant-made drug production. In addition, continuous field inspections by USDA should be required.

¹² See generally *HACCP: A State-of-the-Art Approach to Food Safety (FDA Backgrounder)*, available at <http://www/cfsan/fda/gov/~lrd/bghaccp.html> (October 2001).

Waste. The controls outlined above also should encompass the waste products from drug crops. Once the drug active ingredient has been extracted, the entire plant should be destroyed and records of the destruction maintained.

Accident Prevention and Response. Measures must be in place to prevent the release of such materials into the environment and to mitigate and remediate a release if one occurs. This requires, at a minimum, a readily available, qualified, and rapid test that can be used on agricultural commodities to detect trace amounts of (or markers for) the active drug ingredient. In addition, individuals involved in the handling of drug crops must be required to give prompt notice to appropriate authorities of any releases of such material into the environment and must be required to develop an appropriate communication plan in conjunction with those authorities to communicate promptly and clearly with the public about the incident. Such accident prevention and communication requirements must be outlined in FDA's final guidance, but also in individual USDA permits for the development and commercialization of these crops.

Enforcement. Violations of any permit provision should result in immediate and severe enforcement, given the high risks involved. Further, all harvesting of drug crops should be prohibited unless and until an infraction of the permit conditions is remedied and verified by USDA and/or FDA. If FDA concludes that the method of drug manufacturing is unsafe -- taking into account both the drug product and the risks to the food supply -- it should impose a clinical hold on any Investigational New Drug (IND) application or should withhold approval of a pending New Drug Application (NDA) for a new drug containing an active ingredient produced in a food crop. When the manufacture of therapeutic products is conducted by plant-based technology, FDA approval of an NDA, a Biologics License

Application (BLA) for a biological product, or Pre-Market Approval Application (PMA) for a medical device, should be expressly conditioned on full compliance with all APHIS permit conditions.

CFSAN. Protection of the food supply is a responsibility entrusted to FDA's Center for Food Safety and Applied Nutrition (CFSAN). Given that the use of food crops for the manufacture of drugs poses an undeniable risk to the integrity and safety of the food supply, FDA cannot oversee such drug development efforts effectively without involving its own food safety experts. CFSAN should play a pivotal role in evaluating whether the proposed containment controls will be 100% effective in protecting the food supply. We strongly urge that FDA revise the proposed guidance to specify the role of CFSAN in the oversight of plant-based pharmaceuticals. In addition, CFSAN should play a parallel role in the oversight of food crops for non-food uses other than drug development. Accordingly, USDA should issue a guidance document that provides a role for CFSAN in the permitting and oversight of industrial crops.

FDA and USDA Resources. Collectively, we recognize that the stringent controls outlined above -- which are needed to police the drug development process and to protect the food supply -- will tax FDA's and USDA's already limited resources. For example, the NRC report notes that "because of the large number of applications for field testing, more resources are needed in order to maintain a suitable number of well-trained APHIS officers for field inspection."¹³ We believe that securing sufficient resources should be a priority for FDA and USDA.

¹³ NRC Report, at 12.

III. Summary

The undersigned U.S. trade associations support technological advances that can bring safer, more effective, and less expensive therapies to market. But these tremendous potential benefits must be balanced against serious risks. Consumers need new drugs but they also need to know that the food they eat every day is safe. GMA believes that FDA and USDA are making a good faith effort to impose appropriate controls on this new technology, as the issuance of the proposed guidance demonstrates. However, the risks we now face must be addressed in a far more stringent and unequivocal manner. The time to develop appropriate safeguards is before use of this technology becomes widespread -- not after larger and more severe contamination episodes.

FDA and USDA need to draw a bright line between commodity agriculture and drug manufacturing, between food/feed and drugs and chemicals. They need to provide precise, detailed, stringent regulations to govern the responsible use of this new technology. They need to put their full enforcement powers behind these regulations, and they need to alert both the biotechnology, pharmaceutical, agricultural and food industries to the spectrum of regulatory and civil liability risks that this technology presents.

Sincerely,

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FAX COVER SHEET

DATE: February 6, 2003
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FROM: **KARIL L. KOCHENDERFER**

PAGES: 22 (INCLUDING COVER SHEET)

RE: Please see attached comments on: Guidance
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