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Dockets Management Branch (HFA-305)
Food & Drug Administration
5600 Fishers Lane, Room 1061
Rockville, MD 20852

RE: Comments on Draft Guidance for Industry: Drugs, Biologics, and Medical Devices Derived from Bioengineered Plants for Use in Humans and Animals

Maintaining public confidence in the quality and safety of the food supply is of paramount importance to Iowa. Agriculture and related industries generate almost a quarter of Iowa's total industrial output with even greater potential through the evolving technology being conducted at the University of Iowa and Iowa State University. Our state is committed to developing the scientific safeguards, and the educational response, needed to ensure public confidence in the quality and safety of the food supply while introducing genetically engineered pharmaceutical crops that will be the basis for a new "bioeconomy."

The State of Iowa has actively pursued the potential of pharmaceutical crops in a pioneering way to spur new economic opportunity in agriculture. We believe great opportunity exists, and we believe certain pharmaceutical crops can be grown in Iowa whereas others should be grown in other parts of the country, and yet some others should not be grown in open field environments at all. Geography is not the main issue. The main issue should be the adoption of effective, science-based methods that ensure that pharmaceutical crops can be produced in a safe, responsible, well-managed and environmentally friendly manner that safeguards valuable agricultural resources.

The proposed FDA/USDA guidance, in its present form, are well intentioned but may unnecessarily impede the development of pharmaceutical crops in Iowa and other places around the country. Sections of the guidelines also adversely affect the perception of all biotechnology products with our international customers. However, with appropriate revisions, the guidelines can lead to improved operational procedures for producing plant-made pharmaceutical products. We propose such revisions to the FDA/USDA guidance document in the following sections:

Containment , traceability and certification

The effective, combined use of different containment strategies — both physical and biological — will help reduce the risk of contamination. Strategies may include methods of site preparation, planting, use of equipment, harvesting, product handling and distribution, and appropriate handling of fields in years following the planting of pharmaceutical crops. However,

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a certification system is the key to ensure that effective containment strategies are being implemented. Standard operating procedures, verification practices and identity-preservation programs can be implemented through process management and certification programs developed through the demonstrated expertise of institutions like Iowa State University, Iowa Crop Improvement Association, and various commodity groups. In addition, State and Federal regulatory agencies need sufficient personnel and resources to provide effective inspection and enforcement. Public confidence will rely on a combination of private sector initiatives and strong regulatory agency actions when problems arise.

Science-based Risk Analysis

Approval for production of plant-made pharmaceuticals should be based on science-based risk analysis. FDA needs to conduct, or request from the applicant, studies to define and evaluate the benefits and risks associated with production of each pharmaceutical crop. The National Research Council has established procedures for accomplishing science-based risk analysis. In fact, FDA has proposed such risk analysis studies in other guidance documents (Guidance for Industry on Evaluating the Safety of Antimicrobial New Animal Drugs with Regard to Their Microbiological Effects on Bacteria of Human Health Concern, September, 2002).

Hazards to human health and the environment need to be identified through examination of the probability of risks in every step of the process, from seed production to end-use. Once identified, the significance of risks must be assessed and plans developed to manage them. Communicating the risks to decision-makers and the public is a crucial step because public perception of risk often is much more significant than the technical possibility of risk. The overall risk, a statistical sum of each individual risk from the planting of seed to the processing by end user, should be the measure used by the FDA, along with other relevant data and information submitted in support of the product, to determine whether approval is granted.

Zero Tolerance and Setting of Thresholds

Contamination of food and feed crops by pharmaceutical crops appears to be held to a zero-tolerance standard. The need for zero tolerance should be evaluated on a protein-by-protein and a product-by-product basis. Thresholds should be defined for each protein grown in a crop so that the potential impacts of each can be examined. It should not be assumed that all proteins have similar effects on human or animal health or the environment. It should be recognized that certain proteins may be potentially harmful while others may be relatively benign, or even beneficial.

Public-supported research and education

The role of publicly funded research programs conducted by universities and government laboratories should be strengthened so that scientific knowledge can be applied to addressing issues surrounding plant-made pharmaceuticals. An independent, publicly funded institute is needed to coordinate the research and education activities on genetically modified agricultural products. Congress has called for authorization of such an institute in the new Farm Bill. At Iowa State University, a new program, the Biosafety Institute for Genetically Modified Agricultural Products (BIGMAP), has been initiated to provide unbiased, science-based and socially justifiable evaluation of the risks and benefits of these products. The program already has begun

a risk analysis of plant-made pharmaceuticals. The institute aspires to fulfill a role for genetically engineered products similar to the Underwriters Laboratory, conducting its work in a transparent manner that builds public trust in the technology and the evaluation process.

Currently, the only public research program in the nation working in the area of plant-based vaccines is based in Iowa, at Iowa State University — a program that has worked closely with USDA-APHIS on containment and biosecurity measures. Iowa State University has expertise in several critical research areas, including plant molecular biology, plant breeding, gene expression, plant transformation, immunology, and plant and animal health. Iowa also has made new investments to establish a biologics manufacturing pilot facility at the Iowa State University Research Park that would further explore the potential for processing drugs for humans from transgenic plants.

A well-informed public makes better choices about food, nutrition and health. Public dialog about issues surrounding the growing of pharmaceutical crops and the rules that will guide their production will lead to more informed public policy decisions. The recent (Nov. 21, 2002) open forum held at Iowa State University on the proposed FDA/USDA guidelines is an example of the kind of education and discussion needed. The FDA and USDA should encourage additional input on the guidelines from experts at the FDA's Center for Food Safety and Applied Nutrition and from farmers, grain elevators and other agribusinesses, and public and private scientists working in molecular biology, food safety, agronomy, medicine, and related disciplines.

Thank you for the opportunity to provide input on an issue important to Iowa's future and the future of people around the world.

Sincerely,

Thomas J. Vilsack
Governor

Sally J. Pederson
Lt. Governor