GRAIN QUALITY
Task Force

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Purdue University

Concerns over Pharmaceutical Traits in Grains and Oilseeds

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An April 10 Reuters press release (www.reuters.com) indicates that a biotechnology company, ProdiGene®, College Station, TX (www.prodigene.com), through a grant from the National Institutes of Health (NIH), has produced a transgenic corn variety that contains a protein found on the surface of HIV, the virus that causes AIDS. The company's intent is to utilize such corn in the future as an oral delivery system for an AIDS vaccine, through corn-based products such as breakfast cereals. This transgenic corn variety apparently has been grown on enough acres already to produce sufficient quantities of grain to begin animal studies during the summer of 2002, to determine whether ingestion of this corn elicits an immune response.

Five other transgenic corn hybrids from Prodigene® have been released commercially via Stauffer Seeds®, Omaha, NE (www.StaufferSeeds.com), and have been grown by a select group of farmers on a few hundred acres primarily in the western Corn Belt, much of it in western Iowa and on irrigated acres in Nebraska. These hybrids contain:

- Aprotinin - a protease inhibitor that is used in medical applications to control blood loss during surgery and in non-medical applications as a cell culture reagent.
- Avidin - a protein that binds with biotin to make useful products for the medical and biochemical diagnostics industry and has application in protein purification.
- Laccase - an industrial enzyme used for adhesives in the manufacturing of medium density fiberboard (MDF) as well as in the detergent industry as an environmentally friendly "bio-bleach,"
- Brazzein - a low calorie, intense natural sweetener 2000 times sweeter than sucrose.
- Trypsin - a protease enzyme that has many uses including as an intermediate in pharmaceutical manufacturing and in the leather tanning and detergent industries.

Additional protein-based drugs and industrial compounds produced from genetically modified (GM) field crops are currently under development by several companies and are expected to be ready for commercial release approval within a few years. Examples include:

- A topically-applied antibody from Epicyte Pharmaceutical Inc., San Diego, CA (www.epicyte.com), that prevents the transmission of herpes simplex virus (HSV) 1 and 2, topical contraceptive microbicides and preventives for pulmonary infection due to Respiratory Syncytial Virus (RSV) and *Clostridium difficile*-associated diarrhea.
- Antibodies for therapeutic blood products from Monsanto's Integrated Protein Technologies, St. Louis, MO (www.iptbio.com).
- Prodigene's oral vaccine products including hepatitis-B vaccine, Lt-B vaccine to treat E. coli in humans, TGEV vaccine to treat the transmissible gastroenteritis virus that kills thousands of piglets every year, and additional confidential animal vaccines and human health products under development with such partners as Eli Lilly and Avant Immunotherapeutics.

Various seed companies that are partnering with biotechnology firms are already recruiting farmers, and in some instances crop acres have been acquired by foreign biotechnolgy companies such as Meristem Therapeutics Inc., Clermont-Ferrand, France (www.meristem-therapeutics.com), for experimental testing on private farmland throughout the midwestern Corn Belt.

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Contamination Concern

Obviously, biotechnology is not a new topic for grain producers and the grain handling and processing industry – and this fact sheet is not targeted against the enormous benefits and economic value the technology holds for our future. However, the fact that transgenic grains and oilseeds for use as pharmaceutical drug carriers and industrial chemicals may be making their way into a field near your farm, grain elevator, feed mill or processing plant should be a concern, especially in light of the grain industry's most recent contamination experiences with Aventis' StarLink™ corn, which contains a protein approved for feed but not food consumption, and Monstanto's GT200-containing canola seed, which contains a protein not approved for any end use. Both of these crops were grown on relatively few acres, yet containment protocols to channel or identity-preserve (IP) them at the seed plant, on the farm, and/or at the elevator failed to prevent trace amounts above detectable limits in commercial feed and food bulk grain samples taken from domestic and export market channels. Experience and science-based research tell us that no identity preservation system will ever be able to contain 100% of every seed kernel, plant pollen and grain kernel generated from crops grown in agricultural fields. The very definition of a quality-management-system approach to segregated and traceable production, harvesting, handling and transport of IP grains and oilseeds is based on defining, meeting and monitoring statistically-based threshold limits that are reasonable and practically achievable with respect to containment, purity and contamination.

Concern over Lack of Federally Regulated Tolerance Levels

Successful identity preservation has been the backbone of the seed industry for years. Most of us would consider seed producers among the most educated, dedicated and best equipped with respect to maintaining the identity of a crop and preventing that crop from contaminating or being contaminated by another crop during planting, growing, harvesting, post-harvest handling and transporting. Yet the seed industry cannot achieve 100% pure IP seed during production, handling, cleaning and bagging. Instead, a contamination level of 1% is the strictest limit the industry states can be achieved reasonably and practically, with respect to seed purity (www.amseed.com/intl_network.asp). The principle challenge for IP systems is that whenever new genetic material is introduced into the agricultural crop mix, trace contamination of non-target crops is unavoidable. This fact is common knowledge in the seed industry. Trace amounts, above detectable limits, of a newly commercialized genetic event are often detected whenever stored seed samples of three- to five-year old pre-commercialization varieties are tested, following the release of a new test kit. Thus, if containment of undesired or unapproved genetic events is not 100% effective, for the purpose of seed purity, it will also not be effective for the purpose of crop purity, especially as more GM traits for pharmaceutical and industrial compounds in grains and oilseeds are commercialized.

Therefore, federally-regulated tolerance levels based on detectable thresholds similar to the Environmental Protection Agency's (EPA) pesticide residue limits and the Food and Drug Administrations' (FDA) mycotoxin limits are urgently needed to define the allowable residue limits of pharmaceutical and industrial compounds in grains and oilseeds for food and feed use. Additionally, availability of reliable and inexpensive testing technology such as strip test kits for grain elevator use must become mandatory with the commercial release of every new genetic event in order to give the U.S. grain production, handling, exporting and processing industry the competitive advantage to meet customer demands with respect to the presence of approved but undesired GM-crop traits below established tolerance levels.

Federal Oversight and Food Safety Requirement Concerns

Companies involved in the development and commercialization of plant-made pharmaceuticals are required to have the appropriate experimental licenses from USDA's Animal Plant & Health Inspection Service (APHIS) to grow sufficient quantities of transgenic grains and oilseeds for their research purposes under strict experimental protocols (see www.aphis.usda.gov/ppq/biotech/7cfr340.html). Additionally, these companies have stated that they "are committed to ensuring the

safety of these products during all stages of development and production … [and] to full compliance with all applicable laws, regulations and guidances" (see http://www.bio.org/pmp/PMPConfinementPaper.pdf). Nonetheless, grain producers and the grain handling and processing industry should be concerned about these recent developments, because the appropriate federal oversight has not yet been established that would ensure that once commercialized, transgenic crops for pharmaceutical and industrial purposes will not contaminate grains and oilseeds for food and feed use in the future market place. A recent report by the National Academy of Sciences (http://pewagbiotech.org/buzz/display.php3?StoryID=52) states that "the current APHIS review process will need to improve to deal with the risks of future modified crops … engineered to produce substances for non-food uses, such as pharmaceutical products, industrial chemicals, or fuel."

Although APHIS reserves the right to regulate and oversee commercial production of such transgenic crops, and the biotechnology industry recommends "that the appropriate government agencies oversee the application of science-based confinement procedures" (see http://www.bio.org/pmp/PMPConfinementPaper.pdf), the federal government currently does not require it. A voluntary industry commitment to keep crops intended for drug or industrial use out of the conventional food and feed stream channels using containment protocols without federal oversight and external auditing imposed to assure compliance, is a flawed approach. Another current oversight is the lack of a requirement that such GM grains and oilseeds need to meet FDA's food safety requirements. It cannot be assumed that trace contamination of non-target crops is avoidable and the possibility cannot be ignored that an active ingredient could be expressed so highly concentrated that a single kernel might exceed food safe exposure limits. Therefore, the major world food and feed staple crops should not be used for transgenic modifications for the purpose of expressing pharmaceutical ingredients and industrial chemicals, unless they can meet food safety requirements.

Grain Quality Workshop Recommendations

During its most recent meeting in Washington D.C. on April 16-17, the Grain Quality Workshop adopted a resolution concerning federal oversight of biotechnology. The Workshop is comprised of national associations representing all segments of the grain industry including producers, handlers, processors, exporters and others with interest in grain quality, to provide a forum for discussion of grain quality issues of importance to the market, to promote broad agreement where appropriate, and to represent workshop conclusions to all interested parties.

- To urge the FDA that when future commercialization approvals of genetically modified grains and oilseeds for non-food and feed purposes are considered, these approvals also meet food safety requirements because inadvertently traces of these genetically modified grains and oilseeds will be detected in food and feed.
- To request that appropriate federal agencies (USDA, FDA, EPA) specify how federal oversight will be established and imposed, to ensure that genetically modified grains and oilseeds for non-food and feed purposes – *if* approved for commercialization in the future – will not contaminate commercial grains and oilseeds for food and feed use in the domestic and export market channels.

This is an excellent starting point for the grain industry to initiate additional debate on this issue, given that so few in the grain production, handling and processing industries are aware of how rapidly these new-generation transgenic grains and oilseeds are approaching commercialization. If the federal government does not intervene with threshold limits and stricter regulation and oversight soon, it will be just a matter of time before trace amounts of unapproved and non-food/feed-safe pharmaceutical and industrial proteins will be detected in our domestic and export food and feed market channels. This potential scenario will likely cause a far greater public outcry than did the StarLink™ discovery in taco shells. The future use of the world's major food and feed staple crops for the development of edible

vaccines and other protein-based drugs and industrial chemicals on a few thousand acres far outweigh the risk of jeopardizing the United States' domestic and export markets due to contamination of grains and oilseeds produced on millions of acres for the purpose of satisfying the world's food and feed demand.

Grain Quality Fact Sheets can be accessed on-line through the World Wide Web at: http://www.agcom.purdue.edu/AgCom/Pubs/grain.htm

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