Concerns over Pharmaceutical Traits in Grains and Oilseeds

Dirk E. Maier, Agricultural & Biological Engineering

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 biotechnology companies such as Meristem Therapeutics Inc., Clermont-Ferrand, France (www.meristem-therapeutics.com), for experimental testing on private farmland throughout the midwestern Corn Belt.
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 transporting 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/ppg/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.