

**Corn Refiners Association
National Grain and Feed Association
National Oilseed Processors Association
North American Export Grain Association
North American Millers' Association**

Submitted Electronically

June 19, 2017

Division of Dockets Management
(HFA-305)
U.S. Food and Drug Administration
5630 Fishers Lane
Room 1061
Rockville, MD 20852

***RE: Docket No. FDA-2016-N-4389; Genome Editing in New Plant Varieties
Used for Foods; Request for Comments***

The undersigned national organizations¹ consisting of member companies involved in the grain and oilseed storage, handling, processing, feed manufacturing and export industries respectfully

¹ **Corn Refiners Association (CRA)** is the national trade association representing the corn refining industry of the United States. CRA and its predecessors have served this important segment of American agribusiness since 1913. Corn refiners manufacture sweeteners, ethanol, starch, bioproducts, corn oil and feed products from corn components such as starch, oil, protein and fiber.

National Grain and Feed Association (NGFA), established in 1896, is a U.S.-based nonprofit trade association that consists of approximately 1,050 grain, feed, grain processing, export and other grain-related firms that operate more than 7,000 facilities and handle more than 70 percent of the U.S. grain and oilseed crop. Affiliated with NGFA are 26 state and regional grain, feed and agribusiness associations. Given the diversity of NGFA's membership, which includes biotechnology owners and providers, the views expressed in this statement may not necessarily reflect the views of every NGFA associate or affiliate member.

National Oilseed Processors Association (NOPA), represents the U.S. soybean, sunflower seed, canola, flaxseed and safflower seed crushing industries. NOPA's 13 member companies crush approximately 95% of all soybeans processed in the United States. NOPA member companies process more than 1.8 billion bushels of soybeans annually at 64 plants located throughout the country, including 58 plants that process soybeans.

North American Export Grain Association (NAEGA), a not-for-profit trade association established in 1912, consists of private and publicly owned companies and farmer-owned cooperatives that are involved in and provide services

submit this joint statement in response to the Food and Drug Administration's (FDA) request for comments on the use of genome-editing techniques to produce new plant varieties intended for use in human and/or animal food.

Our organizations' member companies are engaged daily in storing, handling, processing, marketing and exporting the vast majority of America's grain and oilseed production to domestic and world consumers. As such, our organizations strongly support the utilization of biotechnology and plant breeding innovation, including genome editing, as well as other safe cropping technologies and practices that enhance the production of safe, affordable and sustainable food and energy for U.S. and world consumers.

In addition, as we have expressed previously to FDA, the U.S. Department of Agriculture and Environmental Protection Agency, our industry and the domestic and global consumers we serve depend upon the competence and objectivity of the science-based U.S. regulatory system that ensures the safety of genome-edited products for humans, animals and the environment. For this and other reasons, we commend FDA for seeking public input to inform the agency's thinking regarding the impact of the emergence of new breeding techniques intended to alter the genomes of plants.

Our top-line recommendation in this regard is to urge FDA, for the reasons explained subsequently herein, to require premarket notification of the agency by plant breeders and others intending to develop and commercialize plant gene-editing techniques – regardless of the technique used. Our organizations do not believe that this notification should necessarily trigger a full-fledged FDA safety review or risk assessment of these traits, as we recognize that plant-breeding techniques span a continuum, ranging from traditional crossing of two varieties to using molecular methods to introduce “foreign” genes from other species into a plant. As explained later, we believe FDA's determination regarding the level of safety consultation and risk-assessment that may be appropriate for a given biotech-enhanced trait should be based upon the characteristics of the resulting product, rather than on the technique used to develop the plant.

We do, however, believe mandatory premarket notification is essential if FDA is to fulfill its statutory obligation to protect and ensure consumer confidence in the safety of the human and animal food supply. Further, doing so is consistent with the prevention-based regulatory philosophy mandated under the Food Safety Modernization Act of 2011 (FSMA) and FDA's implementing regulations thereunder. Having an awareness of the types of new plant-breeding technology being deployed in human and animal food crops also will be invaluable in facilitating the domestic and international marketability of crops utilizing these new techniques, thereby benefiting agricultural producers, the value chain, consumers and ultimately plant breeders.

to the bulk grain and oilseed exporting industry. NAEGA-member companies ship and support the vast majority of the highly competitive, sustainable and fungible U.S. grain export supply.

North American Millers' Association (NAMA) represents millers of wheat, corn, oats and rye in the United States and Canada. NAMA members take the raw grain and, through grinding and crushing, create flour and other products that are used to make such favorite foods as bread, pasta, cookies, cakes, and snack foods. NAMA member companies represent more than 90 percent of total industry production capacity.

Simply put, from our perspective – and we suspect from the viewpoint of U.S. and global consumers – the worst possible outcome would be one in which FDA has only cursory or hearsay awareness, at best, about the types of plant gene-editing techniques being developed and the specific human and animal food products in which those techniques are being utilized.

Responses to Specific FDA Questions

In this section, we respond to questions posed by FDA in its notice.

1. In what ways are the food safety risks associated with human and animal foods from genome-edited plants the same as or different from those associated with other plant-development methods?

Our organizations are not aware of research or scientific evidence indicating that the food safety risks associated with human and animal foods from genome-edited plants are any different from those associated with other genetic engineering (e.g., rDNA/transgenics) or plant-breeding methods. We believe the level of FDA’s safety risk-assessment and regulation of gene-editing techniques should be proportional to the degree of risk, if any, posed by the characteristics of the end-product rather than based upon the technology used to create it.

2. Are there categories of genome-edited plant varieties for which there are scientific bases to conclude that foods from such categories are unlikely to present food safety risks different from or greater than those for traditional plant breeding?

Our organizations generally are not aware of research or scientific evidence indicating that the human or animal food safety risks associated with genome-edited plants differ from those associated with other plant-breeding methods. New plant varieties developed using applications of genome editing, to our knowledge, generally constitute a more precise way of cross-breeding or inducing mutagenesis, and generally should be considered in the same way as those new plant varieties developed through more traditional breeding methods. Examples of such categories of gene-edited plants are those that involve deletions or substitutions that could be achieved otherwise through traditional plant breeding; and introduction of only naturally occurring nucleic acid sequences from sexually compatible plants from the same plant genome that could cross otherwise with the recipient organism and produce viable progeny through traditional breeding.

Thus, we believe that plants developed using gene-editing techniques that could be achieved through traditional plant-breeding methods – ***provided*** they do not contain added foreign genetic material or involve alterations of the gene sequence in a way that would affect the nutritional, compositional or functional properties of the product or introduce pharmaceutical or industrial compounds – should not be regulated as though they present any different or greater food safety risks than those resulting from traditional plant breeding.

In this regard, it is important to stress that plant varieties produced through rDNA techniques and transgenic varieties produced through genome editing may result in novel functional gene(s) that could not be introduced through more traditional breeding methods. An example of such a trait requiring appropriate government oversight is Enogen® corn, which contains alpha amylase protein that can affect the nutritional, compositional and functional end-use properties of food, making its presence in the food or feed system inappropriate above certain threshold levels. However, because gene-editing is a relatively new technology, FDA needs to be nimble and flexible in its regulatory approach so it can adapt to future developments. That said, to our knowledge no unintended effects have been observed thus far with random insertion of transgenes through genetic engineering.

3. *Are there categories of genome-edited plant varieties for which there are scientific bases to conclude that foods from these categories are more likely than traditionally bred plants to present food safety risks?*

Our organizations strongly support utilizing the FDA voluntary consultation process for developers utilizing new plant-breeding techniques to help ensure any safety or legal questions regarding such traits are considered and resolved prior to commercialization. Indeed, our strong recommendation that FDA require mandatory pre-market notification by plant breeders of traits developed using new plant-breeding techniques (including gene-editing) before commercialization would better equip the agency to develop specific parameters and criteria that would inform a determination as to whether pre-market food safety and legal consultation between the plant breeder and the agency is warranted. These parameters and criteria, and the information and data required, should be transparent and accessible to plant breeders, value-chain stakeholders and the public.

In this regard, we recommend that FDA develop an updated version of the Safety Assessment Summary “decision-tree” it published as part of its “***Statement of Policy: Foods Derived from New Plant Varieties***” issued on May 29, 1992. In effect, FDA could list various factors (e.g., whether the trait involves simple gene deletions that produce phenotypes or genotypes found in nature versus the introduction of a foreign gene, or rearranging of the gene sequence, in a manner that alters the nutritional, compositional or functional characteristics of the resulting human or animal food product or results in production of a pharmaceutical or industrial compound) that would involve very different consultation and regulatory oversight scenarios.

4. *What steps can we (FDA) take to help small firms, including those (that) may be considering using genome editing to produce new plant varieties for use in human or animal food, to engage with FDA about any questions related to food safety or the regulatory status of foods from their new plant varieties?*

We believe the proactive and extremely effective information and education outreach that FDA has conducted, and continues to conduct, with stakeholders during its development and implementation of FSMA good manufacturing practice and preventive control regulations for human and animal food represent a successful model the agency could consider deploying to inform and educate small firms and public and academic research institutions engaged in

plant breeding about their responsibilities under the Federal Food, Drug and Cosmetic Act related to human and animal food safety.

FDA also could consider designating a qualified individual within the agency to serve as a principal point-of-contact for small firms, as well as others using genome editing to produce new plant varieties for use in human or animal food.

Requiring Plant Breeders to Notify FDA of Intent to Commercialize Gene-Editing Techniques in Plants Intended for Human and/or Animal Food

As noted at the outset of this statement, our most important recommendation is that FDA require plant breeders utilizing new plant-breeding technology intended for use in human or animal food to provide pre-market notification to the agency prior to commercialization, and that FDA subsequently determine, based upon such notification, whether to encourage the notifying party to engage in voluntary pre-market safety and risk-assessment consultation with the agency. We believe that such a notification process can be done electronically in a way that is not burdensome to plant breeders, including smaller developers and public researchers, or to the agency itself.

As stated previously, we recognize that plant-breeding techniques represent a continuum of increasingly sophisticated techniques, and that the potential safety risk or labeling requirements depend upon the nature of the genetic modification and the resulting characteristics of the human or animal food product itself. For this reason, we believe, as with other risk-assessments, FDA should employ a scientific, risk-based approach that results in products being subjected solely to a notification requirement, with no further regulatory consultation or requirements imposed, if they are deemed unlikely to pose toxicity; allergenic; nutritional, functional or compositional affects; or other food safety risks. However, a notification requirement also would give the agency a better opportunity to be aware of the latest plant-breeding technologies being employed in the production of human and animal food. Having access to such information, in turn, would enable the agency to encourage the plant breeder to engage in whatever safety consultation and risk-assessment may be appropriate for those (admittedly likely few) products that may warrant such review prior to commercialization.

In this regard, we believe *FDA's Statement of Policy on Foods Derived from New Plant Varieties* remains relevant, where it states that, "*FDA has long regarded it to be a prudent practice for producers of foods using new technologies to work cooperatively with the agency to ensure that the new products are safe and comply with applicable legal requirements. It has been the general practice of the food industry to seek informal consultations and cooperation, and this practice should continue with respect to foods produced using the newer techniques of genetic modification.*" The less-desirable alternative would be for FDA to revert to its post-market authorities under the adulteration provisions of the Federal Food, Drug and Cosmetic Act – such as product recalls – exactly the kind of “after-the-fact” actions the agency rightfully is trying to minimize given its FSMA-based approach to preventing food safety hazards in the first place.

In the context of this recommendation, it is appropriate to cite FDA's proposed rule on "**Premarket Notice Concerning Bioengineered Foods**" published on January 18, 2001, which would have required the submission of data prior to the commercial distribution of plant-derived bioengineered foods. FDA noted in its proposal that there was a "*...substantial basis to conclude, however, that there is greater potential for breeders, using rDNA technology, to develop and commercialize foods that are more likely to present legal status issues and thus require greater FDA scrutiny than those developed using traditional or other breeding techniques.*" In the same proposed rule, the agency stated that it "*recognize(d) that unintended changes associated with other non-rDNA breeding methods may pose regulatory questions similar to those posed by rDNA methods. For example, wide crosses, especially between a food plant variety and an undomesticated nonfood plant variety, have much greater potential than do narrow crosses for introducing unintended traits that may alter the safety of food; undomesticated plants frequently produce toxins at levels unsafe for human consumption, and may also produce substances not found in food....*" Further, we believe it was correct for the agency to observe in its 2001 proposed rule that, "*...rDNA technology continues to evolve and...it is not possible for the agency to anticipate all of the novel scientific and regulatory issues that may arise as the number and types of foods developed using this technology expands.*"

While the agency did not proceed to issue a final rule, we believe these and other statements make it prudent for FDA now to consider issuing an updated version of its 2001 proposed rule reflecting the wider scope of technologies now used in plant breeding, including genome editing techniques. This particularly is appropriate given that these new plant-breeding techniques increasingly are intended to alter the food itself, rather than solely the seed's agronomic properties. Clearly, a safety risk-assessment, special labeling and/or risk-management measures to keep the product from entering the commingled commodity stream and food supply may be needed if a given gene-editing technique: 1) causes a material change in plant; 2) is intended to enable the plant to produce a pharmaceutical or industrial compound; or 3) alters the nutritional, compositional or functional properties of a human or animal food.

In this same vein, also warranting consideration is that the development and use of new plant-breeding technology will not be confined to the United States. Indeed, it will encompass plant developers in other countries from which human or animal food and ingredients will be exported to the United States. In the absence of a notification requirement, FDA's awareness about the presence of foods developed through various plant-breeding techniques in other countries or regions of the world would be limited severely.

We believe the transparency made possible by plant-breeder notification of the agency also is essential to maintaining and further enhancing consumer confidence in FDA's science-based approach for determining food safety, as well as beginning to build consumer confidence in these new plant-breeding technologies and their benefits. Such an outcome would benefit all sectors of the value chain.

Consultation with Food Safety Regulatory Agencies in Other Countries

One of the abysmal failures of the approach to regulating transgenic biotechnology by the United States and other countries has been the inability or unwillingness of government authorities around the globe to develop comparable and compatible regulatory approaches that avert the risk of major, costly market and trade disruptions.

The U.S. regulatory system has never operated in a vacuum. And the marketability of crops matters – for U.S. producers and agribusinesses, the U.S. agricultural economy and ultimately to world food security, the latter of which is linked directly to the bounty of U.S. agriculture. Marketability considerations have become of paramount importance given the increasing lack of coherence in various nations’ regulatory systems regarding safety reviews and approval of new transgenic biotech-enhanced events. As our organizations have pointed out repeatedly, there are no shortages of documented cases in which U.S. export customers’ access to U.S. crops has been disrupted or halted entirely – leading to significant downward pressure on farmgate prices, severe economic damage to U.S. exporters and reduced economic value of U.S. agricultural production – as a result of commercialization of biotech-enhanced crops prior to commensurate approval by competent government authorities in significant U.S. export markets.

We raise these issues because commerce in grains and oilseeds is tied inextricably to global sourcing, and because of the irrefutable fact that achieving a sustainable supply of these basic commodities depends upon fungibility – the principle that the supply of a given crop has a degree of substitutability and relatively comparable value, regardless of the geographic production area from which it originates. Grain and oilseed supplies that can be comingled without concern over regulatory status can be accessed in a timely, cost-effective and efficient manner in response to buyer demands, providing time-and-space utility that is essential to achieving supply integrity and food security. Production and logistics systems that benefit from a fungible supply of grains and oilseeds are critical to the efficient movement of these essential commodities to global consumers.

Importantly, these marketability-related and global regulatory coherence concerns promise to become even more crucial given the advent of plant-breeding innovation, such as genome editing, that is much more precise, less expensive and more adaptable to other plants than rDNA and transgenic engineering techniques. Those inherent advantages of genome editing are expected to expand the number of plant breeders and products involved exponentially, raising the potentially alarming prospect of even greater and more severe market and trade disruptions in the future unless the United States and its international counterparts can adopt a less-divergent international regulatory model going forward. There needs to be a sense of urgency on this matter, as the advent of genome-editing technology for commercialization in grain and other crops may be only two to five years away.


As such, we join our colleagues in the biotechnology, seed and agricultural producer and commodity value chain in stressing the absolute criticality of the U.S. government doing everything it can to interact with and provide the necessary leadership to achieve alignment with significant U.S. trading partners on a sound, science-based mutual-recognition approach for

determining which, if any, of these new plant-breeding techniques warrant safety assessments and regulatory review.

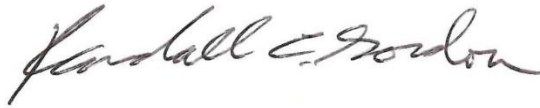
Conclusion

The undersigned national organizations again appreciate the opportunity to provide our views, and would be pleased to respond to any questions FDA may have.

Sincerely,



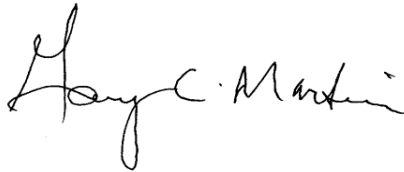
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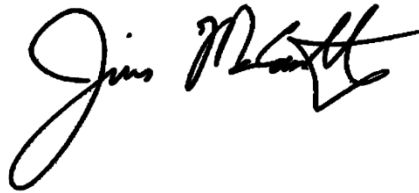
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