

Biotechnology Notification File No. 000166 CFSAN Note to the File

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From: Jianmei Zhu

To: Administrative Record, BNF No. 000166

Subject: Insect resistant and herbicide-tolerant DBN9936 Corn

Keywords: Corn, Maize, *Zea mays*, insect resistance, herbicide tolerance, Cry1Ab, *Bacillus thuringiensis*, 5-enolpyruvylshikimate-3-phosphate synthase, EPSPS, glyphosate, Beijing DaBeiNong Biotechnology Co. Ltd., DBNBC, OECD Unique Identifier DBN-Ø9936-2

Summary

Beijing DaBeiNong Biotechnology Co. Ltd. (DBNBC) has completed a consultation with the Food and Drug Administration (FDA) on food derived from DBN9936 corn genetically engineered to express Cry1Ab protein derived from *Bacillus thuringiensis* for insect resistance and EPSPS protein derived from *Agrobacterium* sp. strain CP4 for selection of the transfer DNA and to provide tolerance to glyphosate herbicides. This document summarizes DBNBC's conclusions and supporting data and information that FDA's Center for Food Safety and Applied Nutrition (CFSAN, we) evaluated pertaining to human food uses. FDA's Center for Veterinary Medicine summarizes its evaluation pertaining to animal food in a separate document.

DBNBC concludes that:

- it has not introduced into food a new protein or other substance that would require premarket approval as a food additive
- human food from insect and herbicide-resistant DBN9936 corn is comparable to and as safe as human food from other corn
- the majority of the insect resistant and herbicide tolerant DBN9936 corn will be used in China for domestic use and a small amount may be present in Chinese-produced food products that may be exported

We evaluated data and information supporting these conclusions and considered whether DBN9936 corn raises other regulatory issues involving human food under the Federal Food, Drug, and Cosmetic Act. We have no further questions at this time about the safety, nutrition, and regulatory compliance of food from DBN9936 corn.

The United States Environmental Protection Agency (EPA) defines a plant-incorporated protectant (PIP) as "a pesticidal substance that is intended to be produced and used in a living plant, or the produce thereof, and the genetic material necessary for the production of such a

pesticidal substance,” including “any inert ingredient contained in the plant, or produce thereof” (40 CFR 174.3). EPA regulates PIPs under the FD&C Act and the Federal Insecticide, Fungicide, and Rodenticide Act. Under EPA regulations, the *cry1Ab* gene and *epsps* gene in DBN9936 corn and the resulting expression products are considered PIPs. DBNBC consulted with EPA on the regulatory status of the Cry1Ab and EPSPS proteins. EPA confirmed that Cry1Ab and EPSPS proteins fall under current tolerance exemptions (40 CFR 174.511 and 40 CFR 174.523, respectively). Consequently, the safety of Cry1Ab and EPSPS in DBN9936 corn is under EPA’s purview and is not addressed in this document. DBNBC notes that viable seed is not intended for distribution or planting in the United States.

Subject of the Consultation

Crop:	Corn
Designation:	DBN9936
Trait:	Insect resistance and herbicide tolerance
Developer:	Beijing DaBeiNong Biotechnology Co. Ltd. (DBNBC)
Original submission received:	May 4, 2018
Amendments received:	March 5, 2019; March 26, 2019; September 26, 2019
Intended use:	Corn and its by-products
Transformation vector:	pDBN0030
Expression cassette 1:	<i>cry1Ab</i> cassette consisting of (1) the 35S promoter from the 35S RNA of cauliflower mosaic virus (CaMV), (2) the heat shock protein (<i>Hsp70</i>) intron from <i>Zea mays</i> as an enhancer, (3) <i>cry1Ab</i> from <i>Bacillus thuringiensis</i> , (4) the <i>Agrobacterium tumefaciens</i> nopaline synthase gene (<i>nos</i>) terminator.
Expression cassette 2:	<i>epsps</i> cassette consisting of (1) the rice <i>Actin1</i> promoter (<i>OsAct1</i> promoter), (2) the chloroplast transit peptide region of <i>shkG</i> gene (<i>AtCTP2</i>), (3) <i>epsps</i> gene from <i>Agrobacterium</i> sp. Strain CP4, and (4) the 35S terminator from the 35S RNA of CaMV.
Transformation method:	<i>Agrobacterium</i> -mediated transformation

Molecular Characterization

DBNBC used Southern blot analyses, PCR analysis, and DNA sequencing to confirm the integrity and determine the copy number of the inserted DNA. Donor gene-specific PCR confirmed that *cry1Ab* and *epsps* genes were stably integrated into the DBN9936 corn genome and were inherited across five generations in a Mendelian fashion. Southern blot analyses showed that only a single copy of T-DNA was inserted and that no plasmid backbone sequences were inserted.

Uses in Human Food

Corn is a commodity crop grown worldwide for various uses including food and feed. In the United States, several different types of corn are cultivated, including field corn (e.g., yellow dent, white dent), sweet corn, and popping corn. For human use, corn may be consumed as whole grain but is primarily used in foods mostly as an ingredient in the form of processed products such as high fructose corn syrup, cereals, oil, meal, flour, starch, and grits. Corn grain can be processed either by wet milling, dry milling or alkali treatment. Corn oil is rich in polyunsaturated fatty acids and is used as a salad oil, as cooking oil, and in margarine.

Human Food Nutritional Assessment

The intended traits in DBN9936 corn are not expected to alter levels of key nutrients, anti-nutrients, or toxicants. To ensure the absence of unintended changes in components relevant to safety or nutrition, DBNBC analyzed the seeds of corn and the non-genetically engineered parental variety (control line DBN318) for key components. DBNBC measured levels of proximates (moisture, ash, carbohydrates, fat, protein, coarse fiber), anti-nutrients (phytic acid and trypsin inhibitor), amino acids, fatty acids, minerals, and vitamins. DBNBC determined that the levels of most components in DBN9936 and the control line DBN318 were similar and were within ranges of variation reported in the literature (ILSI crop database¹ and OECD²). DBNBC noted that the levels of several components, such as Vitamin E, Vitamin B1, methionine, and phenylalanine from DBN9936 corn from different locations were outside of literature-reported ranges and concluded that the differences were relatively small and unlikely to have biological significance. DBNBC concludes that DBN9936 corn is compositionally and nutritionally comparable to conventional corn varieties.

Conclusion

Based on the information provided by DBNBC and other information available to CFSAN, we have no further questions at this time about the safety, nutrition, and regulatory compliance of human food from DBN9936 corn. We consider the consultation with DBNBC on DBN9936 corn to be complete.

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¹ International Life Sciences Institute Crop Composition Database (2018). On May 1, 2020, the International Life Sciences Institute Crop Composition Database became known as the Agriculture and Food Systems Institute Crop Composition Database.

² OECD. 2002. Consensus Document on Compositional Considerations for New Varieties of Maize (*Zea mays*): Key Food and Feed Nutrients, Anti-nutrients and Secondary Plant Metabolites. ENV/JM/MONO(2002)25. Organisation for Economic Co-operation and Development, Paris, France.