



## Biotechnology Notification File No. 000168 CVM Note to the File

**Date:** October 14, 2021

**From:** Jing Ning, Ph.D.

**To:** Administrative Record, BNF No. 000168

**Subject:** Event DBN9858 Corn

**Keywords:** Corn, Maize, *Zea mays*, modified 5-enolpyruvylshikimate-3-phosphate synthase, EPSPS, *Agrobacterium* sp. CP4, phosphinothricin acetyltransferase, PAT, *Streptomyces viridochromogenes*, herbicide tolerance, glyphosate, glufosinate ammonium, DBN9858, OECD Unique Identifier: DBN-Ø9858-5, Beijing DaBeiNong Biotechnology Co., Ltd.

### Purpose

This document summarizes the Food and Drug Administration (FDA) Center for Veterinary Medicine's (CVM, we) evaluation of biotechnology notification file (BNF) number 000168. Beijing DaBeiNong Biotechnology Co., Ltd. (DBNBC) submitted a safety and nutritional assessment of grain from a genetically engineered (GE) corn variety, transformation event DBN9858 (DBN9858 corn), and additional information afterwards.

DBNBC states the majority of DBN9858 corn grain will be used domestically in China, and some will end up in Chinese-produced human food products that may be exported to the United States. DBNBC also anticipates that a small amount of DBN9858 corn grain may be used in animal food products that might be exported to the United States. DBNBC expects that the majority of its GE corn will be used in human food products intended for domestic and export use.

CVM evaluated the information in DBNBC's submissions to ensure that regulatory and safety issues regarding the intermittent low levels of DBN9858 corn grain in animal food in the United States have been resolved prior to commercial distribution. FDA's Center for Food Safety and Applied Nutrition summarizes its evaluation of DBN9858 corn grain in human food in a separate document.

In CVM's evaluation, we considered all of the information provided by DBNBC as well as publicly available information and information in the agency's files.

### Intended Effects

The intended effects of the modifications in DBN9858 corn are to confer tolerance to specific herbicides. DBNBC introduced an *Agrobacterium* CP4 *epsps* gene, which encodes a modified 5-enolpyruvylshikimate-3-phosphate synthase (EPSPS) protein that confers tolerance to the herbicide glyphosate. EPSPS also served as a selectable marker. In addition, DBNBC introduced the *Streptomyces viridochromogenes pat* gene, which encodes for the phosphinothricin acetyltransferase (PAT) protein that confers tolerance to the herbicide glufosinate ammonium.

### Regulatory Considerations

The purpose of this evaluation is to determine whether intermittent low levels of the new plant variety in animal food raises safety or regulatory issues under the Federal Food, Drug, and Cosmetic Act (FD&C Act).

The Environmental Protection Agency (EPA) regulates herbicides under the FD&C Act and the Federal Insecticide, Fungicide, and Rodenticide Act. Under EPA regulations, the herbicide residues in DBN9858 corn are considered pesticidal residues.

### Animal Food Use

In its submissions, DBNBC states that it does not intend to grow DBN9858 corn in the United States or to import viable seed. As a consequence, DBNBC states it is not requesting regulatory action related to DBN9858 corn from EPA or from the United States Department of Agriculture.

Currently, corn intended for use in animal food is not typically imported into the United States from China. Under these conditions, DBN9858 corn from China may only be present in animal food in intermittent low levels. The primary food safety considerations under these conditions are the safety of any new substances introduced into the food.<sup>1</sup>

Corn (*Zea mays* L.) is a commodity crop grown worldwide for various uses, including human and animal food. In the United States, the world's leading producer of corn, several different types of corn are cultivated, including field corn (e.g., yellow dent, white dent), sweet corn, and popping corn. Corn is an important crop for animal food. Corn grain and byproducts of corn processing may be included in diets for most animal species. Corn silage is a readily digestible, high energy, fermented forage product. It is fed primarily to ruminants (e.g., cattle, sheep and goats). For animal nutrition, corn is considered to be an important source of energy, essential fatty acids and some of the essential amino acids.

<sup>1</sup> Guidance for Industry: Recommendations for the Early Food Safety Evaluation of New Non-Pesticidal Proteins Produced by New Plant Varieties Intended for Food Use, available at <https://www.fda.gov/regulatory-information/search-fda-guidance-documents/guidance-industry-recommendations-early-food-safety-evaluation-new-non-pesticidal-proteins-produced>.

## Protein Safety

DBN9858 corn was genetically engineered to express an EPSPS protein derived from *Agrobacterium sp.* strain CP4. DBNBC states the EPSPS protein in DBN9858 corn is similar to plant EPSPS enzymes and identical to other EPSPS proteins expressed in several plant varieties that have completed FDA's consultation program.

DBN9858 corn was also genetically engineered to express the PAT protein, which confers tolerance to the herbicide glufosinate ammonium. DBNBC states the PAT protein in DBN9858 corn is encoded by the *pat* gene isolated from *Streptomyces viridochromogenes*. The firm also summarizes scientific literature<sup>2</sup> to support the safety of the PAT protein in DBN9858 corn. DBNBC states the PAT protein has been previously evaluated in FDA's consultation program.

To assess the safety of the introduced proteins<sup>3</sup>, DBNBC conducted bioinformatics analyses of the EPSPS and PAT amino acid sequences as well as an acute oral toxicity study in mice.<sup>4</sup> DBNBC states that the EPSPS and PAT proteins in DBN9858 corn have no significant amino acid similarity to known toxins or other proteins known to cause adverse effects. DBNBC also reports that there was no evidence of acute toxicity for the EPSPS and PAT proteins when administered to mice.

Based on the history of safe use of the introduced proteins in other plant varieties and the information discussed above, DBNBC concludes that the safety of the EPSPS and PAT proteins in DBN9858 corn has been demonstrated.

## Conclusion

CVM has evaluated potential safety and regulatory issues associated with intermittent low levels of DBN9858 corn grain in animal food; CVM has not evaluated DBN9858 corn grain for general use in animal food. It is DBNBC's responsibility to ensure that any expressed proteins present in DBN9858 corn are safe and legal when present in animal food in the United States. Based on the information DBNBC has provided to FDA, CVM has no questions concerning the safety of intermittent low levels of DBN9858 corn grain in animal food. CVM recommends that should DBNBC or distributors of DBN9858 corn intend to market the corn or its byproducts as animal food in the United States, they should contact CVM's Director for the Division of Animal Feeds, David Edwards at [David.Edwards@fda.hhs.gov](mailto:David.Edwards@fda.hhs.gov).

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**Jing Ning -S**  
Jing Ning, Ph.D.  
Molecular Biology Staff Fellow

<sup>2</sup> Hérouet, C., D.J. Esdaile, B.A. Mallyon, E. Debruyne, A. Schulz, T. Currier, K. Hendrickx, R.J. van der Klis and D. Rouan. 2005. Safety evaluation of the phosphinothricin acetyltransferase proteins encoded by the *pat* and *bar* sequences that confer tolerance to glufosinate ammonium herbicide in transgenic plants. *Regul. Toxicol. Pharmacol.* 41: 134-149.

<sup>3</sup> DBNBC performed thermal degradation, stability in simulated gastric fluid, and glycosylation analyses for its allergenicity assessment.

<sup>4</sup> DBNBC conducted the acute oral toxicity study in mice using microbially-expressed EPSPS and PAT proteins. DBNBC demonstrated the equivalence of the plant-expressed and microbially-expressed proteins using SDS-PAGE, western blot, mass spectrometry, and N-terminal sequence analyses.