



Biotechnology Notification File No. 000179 CVM Note to the File

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From: Jing Ning, Ph.D.

To: Administrative Record, BNF No. 000179

Subject: Event MON 95379 Corn

Keywords: Corn, Maize, *Zea mays* L, Cry1B.868, modified Cry1Da_7, *Bacillus thuringiensis*, insect resistance, lepidopteran pests, OECD Unique Identifier: MON-95379-3, Bayer CropScience LP.

Purpose

This document summarizes the Food and Drug Administration (FDA) Center for Veterinary Medicine's (CVM, we) evaluation of biotechnology notification file (BNF) number 000179. Bayer CropScience LP (Bayer) submitted a safety and nutritional assessment for a genetically engineered (GE) corn, transformation event MON 95379 (hereafter referred to as MON 95379 corn) and additional information afterwards. CVM evaluated the information in Bayer's submissions to ensure that regulatory and safety issues regarding animal food derived from MON 95379 corn have been resolved prior to commercial distribution. FDA's Center for Food Safety and Applied Nutrition summarizes its evaluation of MON 95379 corn in human food in a separate document.

In CVM's evaluation, we considered all of the information provided by Bayer as well as publicly available information and information in the agency's files. Here we discuss the outcome of the consultation for animal food use, but do not intend to restate the information provided in the final consultation in its entirety.

Intended Effects

The intended effects of the modifications in MON 95379 corn are to confer resistance to certain lepidopteran pests including fall armyworm, sugarcane borer, and corn earworm. To confer insect resistance, Bayer introduced two genes, both derived from *Bacillus thuringiensis* (*Bt*): (1) a chimeric *cry1B.868* gene¹ that encodes for the Cry1B.868 protein and (2) a modified *cry1Da_7* gene that encodes for the Cry1Da_7 protein.

¹ Bayer states that the chimeric *cry1B.868* gene is composed of domains I and II from *cry1Be*, domain III from *cry1Ca* and C-terminal protoxin domain from *cry1Ab* from various subspecies of *Bt*.

Regulatory Considerations

The purpose of this evaluation is to determine whether use 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) 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 Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA) and the FD&C Act. Under EPA regulations, the Cry1B.868 and Cry1Da_7 proteins are considered pesticidal substances. Therefore, the safety assessment of these products falls under the regulatory purview of EPA.²

Bayer states that MON 95379 corn was developed for corn growers in South America. Bayer states that it has submitted a petition to the U.S. Department of Agriculture for a determination of nonregulated status for MON 95379 and an application to EPA requesting a FIFRA Section 3 seed increase registration of Cry1B.868 and Cry1Da_7 proteins in MON 95379 corn.

Inheritance and Stability

Bayer characterized the insertion event and genomic stability of the insert in the MON 95379 corn genome using bioinformatics techniques based on data obtained from whole genome sequencing (WGS), junction sequence analysis (JSA), and directed sequencing. Bayer estimated that it collected sufficient data for WGS to cover the corn genome at least 82-fold in each MON 95379 corn plant obtained from five different generations and the corresponding conventional controls. Bayer performed WGS and JSA on a total of two self-pollinated and three outcross generations to confirm the genomic stability. Bayer detected identical junction sequences in all five generations tested. In addition, Bayer evaluated the inheritance pattern in three self-pollinated generations using polymerase chain reaction. The results of Chi-square analysis of the phenotypic and genotypic segregation data from the three outcrossed generations show that the inserted nucleotide sequence was stably integrated at a single locus and segregated according to expected Mendelian principles. Bayer concludes that the insert in MON 95379 corn was integrated at one locus and is stably transmitted across multiple generations.

Animal Food Use

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

² Bayer states that it submitted a petition to EPA proposing the establishment of a tolerance exemption for residues of Cry1B.868 and Cry1Da_7 in or on the food and feed commodities of corn in 2020.

considered to be an important source of energy, essential fatty acids and some of the essential amino acids.

Composition

Scope of Analysis

Bayer analyzed the nutrient composition of MON 95379 corn and a genetically comparable conventional corn hybrid variety (control) that were grown and harvested under similar conditions. Compositional analyses of grain and forage samples were reported for components listed in the Organisation for Economic Co-operation and Development (OECD) corn composition consensus document.³

Study Design

Bayer conducted field trials in 2018 at five locations in the United States. A randomized complete block design with four replicate plots was used at each field site. Forage samples were harvested at R5 growth stage and were shipped on dry ice from the field sites to Bayer. A subsample for compositional analysis was obtained from forage and grain samples and stored at not less than -20°C prior to nutrient analyses. Bayer harvested grain and forage from each replicate within each site for composition analysis.

Bayer statistically compared each component for MON 95379 corn with the control across locations using a linear mixed model with site and replicate as random factors. Components were expressed on a dry matter basis prior to statistical analysis and moisture was not included in the statistical analysis. Bayer excluded components from statistical analysis if more than 50% of the observed values were at or below the limit of quantitation (LOQ). T-test analyses were used to test at the level of $P \leq 0.05$ for differences between MON 95379 corn and control. When a statistically significant difference in a component was detected between MON 95379 corn and control, Bayer assessed whether the difference was biologically meaningful including comparisons of the MON 95379 corn means with ranges in the published literature and in the International Life Sciences Institute Crop Composition Database (ILSI-CCDB), version 7.⁴

Results of analyses

In forage, Bayer reports values for crude protein, crude fat, ash, carbohydrates by calculation, fiber (acid detergent fiber (ADF) and neutral detergent fiber (NDF)), calcium, and phosphorus. Bayer found no statistically significant differences between MON 95379 corn and the control in these components.

In grain, Bayer measured the above mentioned components plus 18 amino acids, 22 fatty acids, nine minerals, seven vitamins, phytic acid, raffinose, ferulic acid, furfural and *p*-coumaric acid. Bayer notes that 15 components were not statistically analyzed as

³ Organisation for Economic Co-operation and Development. 2002. Consensus document on compositional considerations for new varieties of maize (*Zea mays*): Key food and feed nutrients, anti-nutrients, and secondary plant metabolites. OECD ENV/JM/MONO 25. OECD, Paris, France.

⁴ The ILSI Crop Composition Database has become the Agriculture and Food Systems Institute Crop Composition Database and is available at www.cropcomposition.org.

⁵ Percent carbohydrates = 100% - (% protein + % fat + % moisture + % ash).

more than 50% of the samples had levels that fell below the analytical LOQ in both MON 95379 corn and control. Bayer reports statistically significant differences between MON 95379 corn and the control in the levels of 18 components.⁶ However, Bayer notes that for these components, the mean difference between MON 95379 corn and the control were less than the range of values for the control. The mean values for these components were also within the range of values observed in the ILSI-CCDB and scientific literature. Bayer concludes that the differences in these components between MON 95379 corn and the control are not biologically meaningful from an animal food safety perspective.

Summary of Compositional Analyses

Bayer states that the observed statistically significant differences between MON 95379 corn and the control are not biologically meaningful because the mean values for all measured components in MON 95379 corn fell within the range of values observed in the literature and the ILSI-CCDB. Bayer concludes that these results support the conclusion that forage and grain obtained from MON 95379 corn are compositionally comparable to the control in the levels of nutrients and anti-nutrients.

Conclusion

CVM evaluated Bayer's submissions to determine whether MON 95379 corn raises any safety or regulatory issues with respect to its uses in animal food. Based on the information provided by Bayer and other information available to the agency, CVM did not identify any safety or regulatory issues under the FD&C Act that would require further evaluation at this time.

Bayer concludes that MON 95379 corn and the animal foods derived from it are as safe as and are not materially different in composition or any other relevant parameter from other corn varieties now grown, marketed, and consumed. At this time, based on Bayer's data and information, CVM considers Bayer's consultation on MON 95379 corn for use in animal food to be complete.

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⁶ The 18 components are crude protein, alanine, glutamic acid, isoleucine, leucine, methionine, phenylalanine, serine, threonine, valine, linolenic acid, carbohydrates by calculation, copper, iron, manganese, phosphorus, zinc, and vitamin A.