

Biotechnology Notification File No. 000201 CVM Note to the File

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To: Administrative Record, BNF No. 000201

Subject: Event MZIR260 Corn

Keywords: Corn, Maize, *Zea mays* L., *eCry1Gb.1Ig-03* gene, eCry1Gb.1Ig protein, *Bacillus thuringiensis*, insect resistance, fall armyworm, *pmi-15* gene, Phosphomannose isomerase (PMI) protein, *Escherichia coli*, OECD identifier SYN-ØØ26Ø-3, Syngenta Seeds, LLC.

Purpose

This document summarizes the Food and Drug Administration (FDA) Center for Veterinary Medicine's (CVM, we) evaluation of biotechnology notification file (BNF) number 000201. Syngenta Seeds, LLC. (Syngenta) submitted a safety and nutritional assessment for a genetically engineered (GE) corn, transformation event MZIR260 (hereafter referred to as MZIR260 corn). We evaluated the information in Syngenta's submission to ensure that regulatory and safety issues regarding animal food derived from MZIR260 corn have been resolved prior to commercial distribution. FDA's Human Foods Program summarizes its evaluation of uses of MZIR260 corn in human food in a separate document.

In CVM's evaluation, we considered all of the information provided by Syngenta 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 effect of the modifications in MZIR260 corn is to provide resistance to fall armyworm (*Spodoptera frugiperda*). To confer the insect resistance trait, Syngenta introduced the *eCry1Gb.1Ig-03* gene¹ from *Bacillus thuringiensis*, that encodes for the eCry1Gb.1Ig protein. Syngenta also introduced the *pmi-15* gene from *Escherichia coli* that encodes phosphomannose isomerase (PMI) that serves as a selectable marker.

¹ The *eCry1Gb.1Ig-03* gene, a chimeric gene comprised of sequences from *Cry1Gb* and *Cry1Ig*, all derived from strains of *Bacillus thuringiensis*.

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’s regulations, the eCry1Gb.1Ig protein and the genetic material used to express it in MZIR260 corn are considered pesticidal substances, and the PMI protein and the genetic material used to express it in MZIR260 corn are considered inert ingredients. Therefore, the safety assessment of these products falls under the regulatory purview of EPA.

Stability and Inheritance

Syngenta characterized the insertion event and stability of the inserted DNA in MZIR260 corn using Whole Genome Sequencing (WGS) and junction sequence analysis. To confirm genomic stability, Syngenta performed WGS using genomic DNA obtained from multiple breeding generations of MZIR260 corn. Syngenta states that there was a single site insertion of the transfer-DNA (T-DNA) and that the inserted DNA was stably integrated into the genome across multiple generations of MZIR260 corn that were analyzed.

In addition, Syngenta assessed segregation of the T-DNA using real-time quantitative polymerase chain reaction (qPCR). The results of Chi-square analysis of the segregation data from multiple generations show that the segregation pattern of the T-DNA is consistent with Mendelian principles of inheritance for a single locus. Syngenta concludes that the T-DNA in MZIR260 corn was integrated at one locus and is stably transmitted across multiple generations in accordance with the principles of Mendelian inheritance.

Animal Food Use

Syngenta states that MZIR260 corn is expected to be grown for the similar uses as currently commercialized corn. The typical uses of corn-derived food and feed are well documented in Organisation for Economic Co-operation and Development (OECD) maize composition consensus document², including food use of the kernels for oil, starch, grits, meal, flour, and use of the kernels or whole plant silage for animal food. By-products that result from the processing of kernels are also used in animal food. Production and different methods of processing are also described in detail in the OECD maize composition consensus document.

² 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.

Composition

Scope of Analysis

Syngenta analyzed the nutrient composition of forage and grain obtained from MZIR260 corn, a non-GE near-isogenic corn variety (control), and six non-GE commercial corn varieties (reference varieties). The components selected for analyses were based on the OECD maize composition consensus document.

Study Design

Syngenta conducted field trials in 2022 at eight locations in the United States. A randomized complete block design with four replicate plots at each field site was used. Syngenta harvested grain and forage from each replicate within each site for composition analysis. Forage samples were harvested at R4 growth stage and grain samples were harvested at R6 growth stage. A subsample for compositional analysis was obtained from grain and forage samples from each replicate at each site and stored at approximately -20°C prior to nutrient analyses.

Syngenta conducted statistical analyses on composition data for each component from MZIR260 corn and the control across locations using mixed model analysis of variance. T-test analyses were used to assess statistical significance of the comparisons. Syngenta identified statistically significant differences based on an alpha level of 0.05. Syngenta also compared mean values for each component in MZIR260 corn to the range of values observed for the reference varieties and the range of values reported in the Agriculture and Food Systems Institute Crop Composition Database (AFSI-CCDB)³.

Results of Analyses

For forage, Syngenta reports values for proximates (moisture, crude protein, crude fat, carbohydrates by calculation, and ash), fiber (acid detergent fiber (ADF) and neutral detergent fiber (NDF)), calcium, and phosphorus. Syngenta found statistically significant differences between MZIR260 corn and the control in the mean values for moisture, crude protein, crude fat, and total carbohydrates. However, Syngenta notes that for all of these components, the mean values were within the ranges measured for the reference varieties and the ranges obtained from the AFSI-CCDB.

For grain, Syngenta measured proximates, fiber (total dietary fiber, ADF and NDF), starch, 18 amino acids, nine minerals, 10 fatty acids, seven vitamins, six secondary metabolite and antinutrients (ferulic acid, inositol, *p*-coumaric acid, phytic acid, raffinose and trypsin inhibitor). Syngenta reports that there were no statistically significant differences between MZIR260 corn and control for most of the analyzed components. Statistically significant differences between MZIR260 corn and the control were reported for 11 components⁴. The mean values for these components fell within the reference variety ranges, with the exception of 20:1 eicosenoic acid. Additionally, Syngenta notes that the mean values for all of the measured components fell within the ranges reported in the AFSI-CCDB.

³ Agriculture and Food Systems Institute (AFSI) Crop Composition Database:
<https://www.cropcomposition.org>.

⁴ These included alpha-tocopherol, beta-carotene, pyridoxine, thiamin, copper, manganese, 16:1 palmitoleic, 17:0 heptadecanoic, 20:1 eicosenoic acids, *p*-coumaric acid and raffinose.

Summary of Compositional Analyses

Syngenta highlights that the genetic modification does not meaningfully affect nutrient composition and nutritional value of forage and grain derived from MZIR260 corn.

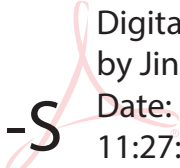
Syngenta concludes that MZIR260 corn is comparable to corn varieties that are currently used in animal food in the United States.

Conclusion

CVM evaluated Syngenta's submission to determine whether MZIR260 corn raises any safety or regulatory issues with respect to its use in animal food. Based on the information provided by Syngenta 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.

Syngenta concludes that MZIR260 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 Syngenta's data and information, CVM considers Syngenta's consultation on MZIR260 corn for use in animal food to be complete.

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