Biotechnology Notification File No. 000167
CFSAN Note to the File

Date: December 18, 2020

From: Jianmei Zhu

To: Administrative Record, BNF No. 000167

Subject: PY203 corn

Keywords: Corn, Maize, *Zea mays*, PY203, Phy02 phytase, Agrivida, OECD Unique Identifier AGV-PY203-4, AGRN 21, NPC 000015

Summary

Agrivida, Inc. (Agrivida) has completed a consultation with the Food and Drug Administration (FDA) on food derived from PY203 corn, which is genetically engineered to express the phytase enzyme Phy02 derived from *Escherichia coli* strain K-12. This document summarizes Agrivida'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 of PY203 corn. FDA's Center for Veterinary Medicine (CVM) summarizes its evaluation pertaining to animal food in a separate document.

Agrivida concludes:

- it has not introduced into human food a new protein or other substance that would require premarket approval as a food additive
- human food from PY203 corn is comparable to and as safe as human food from other corn varieties
- ground grain from PY203 corn is intended for use as a source of the Phy02 phytase enzyme when added to animal food; however, Agrivida considers that some PY203 grain may inadvertently enter the human food supply

We evaluated data and information supporting these conclusions and considered whether PY203 corn raises other regulatory issues involving human food within FDA's authority under the Federal Food, Drug, and Cosmetic Act. We have no further questions at this time about the safety, nutrition, and regulatory compliance of human food from PY203 corn.

Subject of the Consultation

Crop:	Corn
Designation:	PY203
Trait:	Corn containing the phytase enzyme Phy02
Developer:	Agrivida, Inc.

Original submission received:	June 13, 2018
Amendments received	October 5, 2020
Intended use:	General use in human and animal food

In BNF 000167, Agrivida relies on incorporating information from previous submissions to FDA to establish several aspects of its evaluation of the safety of PY203 corn.

In 2015, Agrivida submitted a New Protein Consultation (NPC 000015) to FDA to address the safety of low levels of the Phy02 protein in food. In NPC 000015, Agrivida provided data and information to support that Phy02 protein is unlikely to be allergenic or toxic. On August 7, 2015, FDA responded that it had no questions about Agrivida's conclusions regarding the safety of low levels of the Phy02 protein in food. In BNF 000167, Agrivida incorporated the data and information from NPC 000015 to support its safety assessment of PY203 corn (for presence in human food).

In 2016, Agrivida submitted a GRAS notice (Animal Food GRAS Notice (AGRN) 21) to CVM regarding the use of ground grain from PY203 corn in food for poultry. In AGRN 21, Agrivida provided data and information to support the integrity and stability of the intended genetic changes in PY203 corn. On May 23, 2017, CVM responded to Agrivida with a letter stating that it had no questions regarding Agrivida's conclusion that ground corn containing Phy02 protein from PY203 corn is safe for its intended use in poultry feed.[1] In BNF 000167, Agrivida incorporated and summarized the data and information on the genetic changes and molecular characterization and stability in PY203 corn described in AGRN 21.

Agrivida used phosphomannose isomerase (PMI) protein as a selectable marker in the development of PY203 corn. In BNF 000167, Agrivida states that the *manA* gene from *Escherichia coli* K-12, which encodes PMI, and associated regulatory sequences introduced to PY203 corn are identical to the genetic sequences submitted to FDA in NPC 000002 by Syngenta.[2]

Human Food Nutritional Assessment

The intended traits in PY203 corn are not expected to alter levels of key nutrients, anti-nutrients (except the intended effect), or toxicants. To ensure the absence of unintended changes in components relevant to human food safety or nutrition, Agrivida analyzed the grain of PY203 corn and a related control (a null segregant, the control) for key components. Agrivida measured

[1] CVM responded with a letter stating that it had no questions to a second notice (AGRN 27) from Agrivida on use of the ground corn from PY203 corn in swine feed on July 8, 2019.

[2] In 2005, Syngenta Seeds, Inc., submitted an NPC (NPC 000002) to FDA to address the safety of low levels of phosphomannose isomerase (PMI) in food. In NPC 000002, Syngenta provided data and information to support that PMI protein is unlikely to be allergenic or toxic. On February 10, 2009, FDA responded that it had no questions about Syngenta's conclusions regarding the safety of low levels of PMI in food.

levels of proximates (protein, moisture, crude fat, crude fiber, ash and carbohydrates), amino acids, fatty acids, minerals, vitamins, and anti-nutrients (phytic acid, trypsin inhibitor, inositol, p-coumaric acid, raffinose, and ferulic acid). Agrivida observed that the levels of most components in PY203 corn and the control were similar and were within ranges of variation reported in the literature (ILSI-CCDB[3]). Agrivida noted that levels of several components, including crude fat, β-carotene, and phytic acid[4] in PY203 corn differ from levels in the control but were still within the ranges reported in the literature. Agrivida concludes that human food derived from PY203 corn is as safe and nutritious as human food from conventional corn.

Jianmei Zhu -S

Digitally signed by Jianmei Zhu -S
Date: 2020.12.18 11:00:33 -05'00'

Jianmei Zhu, Ph.D.

[3] ILSI-CCDB (2016). International Life Sciences Institute Crop Composition Database, Version 6.0, www.cropcomposition.org. On May 1, 2020, the International Life Sciences Institute Crop Composition Database became known as the Agriculture and Food Systems Institute Crop Composition Database.

[4] Agrivida reported a mean value of phytic acid for PY203 corn at approximately half the value of the means of both the control and the literature data; this is expected as the Phy02 phytase hydrolyzes phosphates from phytic acid.