

Biotechnology Notification File No. 000200

HFP Note to the File

Date: November 4, 2024

From: Matthew L. Fabian, Ph.D.

To: Administrative Record, BNF No. 000200

Subject: Soybean with transformation event COR23134 (COR23134 soybean)

Keywords: soybean, *Glycine max* (L.) merr., insect resistance, Lepidoptera, crystal protein, *cry1B.34.1* gene, *cry1B.61.1* gene, *ipdo83Cb* gene, *gm-hra_1* gene, Cry1B.34.1 protein, Cry1B.61.1 protein, IPDo83Cb protein, GM-HRA protein, ALS herbicide tolerance, acetolactate synthase herbicide tolerance, Bt, *Bacillus thuringiensis*, maidenhair fern, *Adiantum trapeziforme* var. *braziliense*, Pioneer Hi-Bred International, Inc., Corteva Agriscience, COR23134 soybean, OECD Unique Identifier COR-23134-4 soybean

Summary

Pioneer Hi-Bred International, Inc. (Pioneer) has completed a consultation with the Food and Drug Administration (FDA) on food derived from COR23134 soybean. COR23134 soybean expresses the Cry1B.34.1, Cry1B.61.1, and IPDo83Cb proteins, conferring enhanced resistance to certain lepidopteran insects, as well as the protein GM-HRA, which confers resistance to acetolactate synthase (ALS)-inhibiting herbicides and was used as a selection marker. This document summarizes Pioneer's conclusions and supporting data and information that FDA's Human Foods Program (HFP, we) evaluated pertaining to human food uses of COR23134 soybean. FDA's Center for Veterinary Medicine summarizes its evaluation pertaining to animal food uses in a separate document.

Based on the safety and nutritional assessment that Pioneer has conducted, it is our understanding that Pioneer concludes that:

- it has not introduced into human food a new protein or other substance that would require premarket approval as a food additive, and
- human food from COR23134 soybean is comparable to, and as safe as, human food from other soybean varieties.

HFP evaluated data and information supporting these conclusions and considered whether COR23134 soybean raises other regulatory issues involving human food within FDA's authority under the Federal Food, Drug, and Cosmetic Act (FD&C Act). At this time, we have no further

questions about the safety, nutrition, and regulatory compliance of human food from COR23134 soybean.

The U.S. Environmental Protection Agency (EPA) evaluates and authorizes the use of plant incorporated protectants (PIPs) under the FD&C Act and the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA). A PIP is defined in 40 CFR 174.3 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.” In COR23134 soybean, the Cry1B.34.1, Cry1B.61.1, and IPDo83Cb proteins constitute PIPs and the GM-HRA protein, which was used as a selectable marker, is a PIP inert ingredient. Pioneer notes that, per 40 CFR §174.533, EPA has exempted residues of GM-HRA in or on food and feed commodities of soybean from the requirement of a tolerance when used as a PIP inert ingredient. The safety of Cry1B.34.1, Cry1B.61.1, IPDo83Cb, and GM-HRA falls under EPA’s purview and is therefore not addressed in this document. Pioneer states that they intend to submit a registration application with EPA’s Biopesticides and Pollution Prevention Division.

Subject of the Consultation

Crop	Soybean
Designation	COR23134
Intended trait	Insect resistance
Intended trait	Herbicide tolerance
Developer	Pioneer Hi-Bred International, Inc.
Submission received	February 13, 2024
Amendment(s) received	April 12, 2024
Intended use	For general use in human food
Transformation plasmid	PHP90315
Expression cassette 1	Cry1B.34.1 from <i>Bacillus thuringiensis</i> , conferring resistance to certain Lepidopteran insects
Expression cassette 2	Cry1B.61.1 from <i>Bacillus thuringiensis</i> , conferring resistance to certain Lepidopteran insects
Expression cassette 3	IPDo83Cb from <i>Adiantum trapeziforme</i> var. <i>braziliense</i> , conferring resistance to certain Lepidopteran insects
Expression cassette 4	GM-HRA from <i>Glycine max</i> (L.) merr., conferring tolerance to acetolactate synthase (ALS)-inhibiting herbicides for transformant selection
Method for conferring genetic change	<i>Agrobacterium</i> -mediated transformation

Inheritance and stability

To generate COR23134 soybean, Pioneer transformed a proprietary elite soybean line with plasmid PHP90315 via *Agrobacterium*-mediated transformation. Using Southern-by-sequencing (SbS), Pioneer verified the transformation event by determining insert copy number, organization, and the absence of plasmid backbone sequences. Pioneer reported that COR23134 soybean contained two unique plasmid-genome junctions, one at each end of the insertion, and concluded that COR23134 soybean contains a single copy of the intended T-DNA insertion. Pioneer also concluded that the lack of additional junctions between the plasmid backbone sequence and the soybean genome demonstrated the absence of plasmid backbone sequences in COR23134 soybean.

To verify the generational stability of the transformation event, Pioneer employed Southern blots, utilizing probes complementary to regions of *cry1B.34.1*, *cry1B.61.1*, *ipdo83Cb*, and *gm-hra_1*, on plants selected across five generations. From the observed probe-specific hybridization band patterns, Pioneer concluded that the single T-DNA insertional event in COR23134 soybean is generationally stable.

To evaluate the inheritance of the T-DNA insertion, Pioneer utilized qualitative endpoint PCR assays with segregating individuals selected across three generations, as well as a Chi-squared test for statistical analysis of segregation ratios. Pioneer concluded that the T-DNA insert in COR23134 soybean exhibits a Mendelian inheritance pattern corresponding to an insertional event at a single locus.

Human Food Nutritional Assessment

The intended traits in COR23134 soybean are not expected to alter levels of key nutrients or anti-nutrients. To assess potential unintended changes in composition relevant to safety or nutrition, Pioneer analyzed seed tissue from COR23134 soybean, a near-isogenic, non-genetically engineered (non-GE) control line, and a group of conventional, non-GE commercial reference lines grown in eight locations in the U.S. and Canada during the 2022 growing season. At each site, COR23134 soybean, the control line, and four reference lines were planted in four randomized complete blocks, and for each line, pooled tissue samples were selected from each site and block. Seed samples were surveyed for analytes detailed in the Organisation for Economic Co-operation and Development (OECD) Consensus Document for soybean¹, including proximates, fiber, carbohydrates (by calculation), fatty acids, amino acids, minerals, vitamins, isoflavones, and antinutrients. Comparative statistical analyses were performed on analyte measurements from COR23134 soybean and the control line, wherein statistically significant differences between the two lines were assessed using false discovery rate (FDR)-adjusted p-values. Reference ranges for each analyte were sourced from the in-study reference lines, historical tolerance intervals derived from proprietary data accumulated from a population of 81

¹ OECD (2012) Revised Consensus Document on Compositional Considerations for New Varieties of Soybean [*Glycine max* (L.) merr.]: Key Food and Feed Nutrients, Antinutrients, Toxicants and Allergens, [https://one.oecd.org/document/ENV/JM/MONO\(2012\)24/en/pdf](https://one.oecd.org/document/ENV/JM/MONO(2012)24/en/pdf)

non-GE commercial soybean lines, and published literature, including the Agriculture and Food Systems Institute Crop Composition Database².

For four of the surveyed fatty acids (lauric acid, pentadecanoic acid, pentadecenoic acid, and nonadecanoic acid), Pioneer observed that all measurements fell below the lower limit of quantification, therefore no statistical analyses or comparisons to reference values were performed for these analytes. Considering FDR-adjusted p-values, statistically significant differences between COR23134 soybean and control soybean were identified for ten analytes (crude protein, myristic acid, palmitic acid, heptadecanoic acid, heptadecenoic acid, glutamic acid, isoleucine, leucine, calcium, and total genistein equivalent), however the values reported were within the ranges for soybean in the reference lines, tolerance intervals, and/or scientific literature. Overall, Pioneer concluded that food derived from COR23134 soybean is compositionally comparable to that of non-GE conventional soybean with a history of safe use in food.

Conclusion

Based on the information provided by Pioneer and other information available to HFP, we have no further questions at this time about the safety, nutrition, and regulatory compliance of human food from COR23134 soybean. We consider the consultation with Pioneer on COR23134 soybean to be complete.

Matthew
Fabian -S

Digitally signed by
Matthew Fabian -S
Date: 2024.11.04
11:46:47 -05'00'

Matthew L. Fabian, Ph.D.

²AFSI (2021) Crop Composition Database, Version 8.0. Agriculture & Food Systems Institute, <https://www.cropcomposition.org>