FDA U.S. FOOD & DRUG ADMINISTRATION
CENTER FOR VETERINARY MEDICINE

Biotechnology Notification File No. 000193
CVM Note to the File

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From: Jing Ning, Ph.D.

To: Administrative Record, BNF No. 000193

Subject: Event MON 94313 Soybean

Keywords: Soybean, *Glycine max* (L.) Merr., *dmo*, *Stenotrophomonas maltophilia*, Dicamba mono-oxygenase, *pat*, *Streptomyces viridochromogenes*, Phosphinothricin N-acetyltransferase, modified version of R-2,4-dichlorophenoxypropionate dioxygenase (*RdpA*) gene, FT_T.1, *Sphingobium herbicidovorans*, Aryloxyphenoxypropionate (FOPs) and 2,4-dichlorophenoxyacetic acid (2,4-D) dioxygenase, *TDO*, *Oryza sativa*, Triketone dioxygenase, Tolerance to dicamba, glufosinate ammonium, 2,4-dichlorophenoxyacetic and mesotrione herbicides, OECD unique identifier MON-94313-8, 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 000193. Bayer CropScience LP (Bayer) submitted a safety and nutritional assessment for a genetically engineered (GE) soybean, transformation event MON 94313 (hereafter referred to as MON 94313 soybean), 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 94313 soybean have been resolved prior to commercial distribution. FDA's Center for Food Safety and Applied Nutrition summarizes its evaluation of uses of MON 94313 soybean 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 94313 soybean are to confer tolerance to several herbicides. Bayer states that the parental soybean variety was transformed

with the *demethylase* (*dmo*) gene from *Stenotrophomonas maltophilia*, which encodes the dicamba mono-oxygenase (DMO) protein that confers tolerance to dicamba herbicide. It also contains a modified version of the R-2,4-dichlorophenoxypropionate dioxygenase (*RdpA*) gene from *Sphingobium herbicidovorans*, which encodes the Aryloxyphenoxypropionate (FOPs) and 2,4-dichlorophenoxyacetic acid (2,4-D) dioxygenase protein (FT_T.1) that confers tolerance to 2,4-D herbicide. Additionally, MON 94313 soybean expresses a copy of the *phosphinothricin N-acetyltransferase* (*pat*) gene from *Streptomyces viridochromogenes*, which encodes the PAT protein that confers tolerance to glufosinate herbicide. Bayer also introduced the triketone dioxygenase (*TDO)* gene, derived from the *Oryza sativa HPPD INHIBITOR SENSITIVE 1* (*HIS1*) gene, that expresses the TDO protein to confer tolerance to mesotrione herbicide.

Regulatory Considerations

The purposes of this evaluation are (1) to assess whether Bayer has introduced into animal food a substance requiring premarket approval as a food additive and (2) to determine whether use of the new plant variety in animal food raises other regulatory issues with respect to the Federal Food, Drug, and Cosmetic Act (FD&C Act).

Genetic Modification and Characterization

Introduced DNA and Transformation Method

Bayer transformed meristem explants obtained from a non-genetically engineered soybean variety A3555 with vector PV-GMHT529103 using disarmed *Agrobacterium tumefaciens* mediated transformation. PV-GMHT529103 contains two separate transfer-DNA (T-DNA) regions, T-DNA I and T-DNA II. Bayer states that each of the T-DNA regions were delineated by left (LB) and right (RB) border sequences.

T-DNA I cassette includes:

- *dmo* gene from *S. maltophilia* strain DI-6 that was codon optimized for expression in soybean, which is preceded by the promoter region of the polyubiquitin gene (*ubq3*) from *Arabidopsis thaliana* and chloroplast targeting sequence of the *albino or pale green* 6 gene (*APG6*) from *A. thaliana*. Following the *dmo* gene is the 3´ untranslated region (UTR) sequence of the *sali3-2* gene from *Medicago truncatula*.
- *pat* gene from *S. viridochromogenes* that was codon optimized for expression in soybean, which is preceded by a synthetic *GSP579* promoter and *GSI102* intron developed based on sequences from *A. thaliana*[1] and followed by 3´UTR sequence of the *Hsp20* gene from *M. truncatula*.
- A modified version of the *RdpA* gene from *S. herbicidovorans*, which is preceded by the promoter region of the polyubiquitin gene (*ubq10*) from *A. thaliana* and followed by 3´UTR sequence of the *guf* gene from *M. truncatula*.

[1] To, J.P.C., I.W. Davis, M.S. Marengo, A. Shariff, C. Baublite, K. Decker, R.M. Galvao, Z. Gao, O. Haragutchi, J.W. Jung, H. Li, B. O'Brien, A. Sant, and T.D. Elich. 2021. Expression elements derived from plant sequences provide effective gene expression regulation and new opportunities for plant biotechnology traits. Front Plant Sci 12: 712179.

- *TDO* gene, derived from the *Oryza sativa HIS1* gene, that was codon optimized for expression in soybean, which is preceded by a synthetic *GSP576* promoter and *GSI17* intron and followed by a synthetic 3´UTR (*GST7*) developed based on sequences from *Zea mays*.

T-DNA II cassette includes:

- *splA* gene from *A. tumefaciens* strain C58, which is preceded by 5´UTR, promoter, and enhancer sequences of a putative seed protein gene from *Vicia faba* and followed by 3´UTR sequence of the nopaline synthase gene (*nos*) from *A. tumefaciens*.
- *aadA* gene under the control of enhancer from figwort mosaic virus 35S RNA, promoter, leader, and intron sequences of the *EF-1 alpha* gene and chloroplast-targeting sequence of the *ShkG* gene from *A. thaliana*, followed by 3´UTR sequence of the *rbcS* gene family from *Pisum sativum*. This confers spectinomycin and streptomycin resistance which was used as a selectable marker for transformed hypocotyls.

Following transformation, explants were grown in selection medium[2], and developed plants with normal phenotype were selected as the R0 generation. These plants were self-pollinated and Bayer subsequently selected R1 plants containing only T-DNA I, but not T-DNA II by polymerase chain reaction (PCR). R1 plants homozygous for T-DNA I were self-pollinated to obtain further generations. Additional breeding steps (up to five generations) were conducted to generate plants used in the characterization of the T-DNA insertion, genetic stability analyses, inheritance studies, and absence of vector backbone.

Bayer characterized the number of T-DNA inserts, the number of insert junctions, the absence of vector backbone sequences, and organization and intactness of each insert in MON 94313 soybean using whole genome sequencing (WGS). The parental cultivar, A3555, was used as the comparator in these analyses. Bayer reports a minimum average read depth of 75-fold. Bayer reports that a single copy of the T-DNA I sequence was inserted into the soybean genome and that MON 94313 soybean does not contain sequences from T-DNA II nor the vector backbone. Sanger sequencing and locus-specific overlapping PCR products demonstrated that the genetic elements within the inserted T-DNA I were intact and that only T-DNA I elements were present within the inserted DNA when compared to vector PV-GMHT529103. The sequencing analyses also determined the nucleotide sequence for 1,000 base pairs (bp) upstream and downstream of the site of insertion sequence. A sequence comparison between the PCR product generated from the control and the sequence generated from the 5´ and 3´ flanking sequence of MON 94313 soybean indicated that the T-DNA insert replaced 40 bp of soybean genomic DNA, with minor truncations at the right and left border regions. Bayer states that these types of changes are probably the result of double stranded break repair during the *Agrobacterium*-mediated transformation process.

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[2] The selection media contained spectinomycin for selection of transformants, and carbenicillin, cefotaxime and timentin for inhibition of *A. tumefaciens* growth.

The stability of the inserted T-DNA sequences in MON 94313 soybean across multiple breeding generations and the comparator A3555 were evaluated by WGS followed by bioinformatics analyses. Bayer reports that the single locus of integration that was characterized in the R3 generation of MON 94313 soybean is present in all five breeding generations of the MON 94313 soybean. Within each self-crossed generation, Bayer collected genotypic segregation data to assess inheritance pattern and these data were analyzed using Chi square analysis. Bayer concludes that the inserted DNA segregated as a single locus in accordance with the principles of Mendelian inheritance.

Bayer performed bioinformatics analyses using the nucleotide sequences obtained for the T-DNA insert and junction sequences to determine whether insertion of the introduced DNA created any potential open reading frames (ORF) that could encode for putative polypeptides. This analysis included nucleotide sequences for each of the six reading frames. Bayer evaluated the putative polypeptides against the TOX_2021 database[3] to determine the similarity of these putative polypeptides to known toxins. Analysis of the sequences spanning the junctions between the soybean genome and inserted DNA revealed 14 putative polypeptides (eight amino acids or greater in length), and there were no unintended polypeptides within the insert. Bayer reports that none of these putative polypeptides share significant similarity or identity to known toxins or biologically active proteins.

Protein Safety

Bayer used a weight of evidence approach to assess the safety of the four proteins expressed in MON 94313 soybean. This approach included:

1.) documentation of the history of safe consumption of the expressed protein or its structural and functional homology to proteins that lack adverse effects on human and animal health;
2.) characterization of the physicochemical and functional properties of each expressed protein;
3.) examination of the similarity of each expressed protein to known allergens, toxins or other biologically active proteins known to have adverse effects on humans and animals;
4.) evaluation of the susceptibility of each expressed protein to the digestive enzymes, pepsin and pancreatin;
5.) evaluation of the stability of each expressed protein after heat treatment;
6.) quantification of the expression of each of these proteins in plant tissues; and, if justified,
7.) investigation of potential animal toxicity through an animal assay.

DMO is an enzyme that catalyzes the demethylation of dicamba (3,6-dichloro-2-methoxybenzoic acid) to the non-herbicidal compounds, thereby conferring dicamba tolerance to MON 94313 soybean. Bayer highlights that the DMO protein has been expressed in several commodity crops and includes by reference information on safety

[3] TOX_2021 database contains 7,870 sequences and was selected using a keyword search of Swiss-Prot database (https://www.uniprot.org/) and filtered to remove likely non-toxin proteins.

of DMO protein isoforms in these crops.[4] In addition, the multistep approach to address the safety of these proteins is provided in the scientific literature.[5] Bayer notes that there were minor amino acid differences between the DMO proteins expressed in these crops, but these modifications are not anticipated to have any effects on the structure of the catalytic site, functional activity, immunoreactivity, or specificity of the protein. Because of these slight differences, Bayer assessed the specificity of the DMO protein that are expressed in MON 94313 soybean using dicamba and a structurally related compound, *o*-anisic acid, as substrates in an *in vitro* assay[6]. Bayer reports that dicamba was demethylated, whereas *o*-anisic acid was not catabolized by *Escherichia coli*-produced MON 94313 DMO protein[7], thus Bayer concludes that MON 94313 DMO protein has high specificity for dicamba as a substrate. Bayer also concludes that previous safety assessments are applicable to DMO protein expressed in MON 94313 soybean and that these data support the conclusion that animal food products containing MON 94313 soybean DMO protein pose no meaningful risk to animal health.

The PAT protein from *S. viridochromogenes* is an acetyltransferase composed of 182 amino acids. PAT protein confers tolerance to the herbicide glufosinate ammonium by acetylating the active ingredient, L-phosphinothricin, inactivating it. Bayer highlights that the PAT protein expressed in MON 94313 soybean is identical to proteins that have been expressed in several commodity crops[8]. Bayer states that the conclusions of these safety assessments are applicable to the PAT protein expressed in MON 94313 soybean. In addition, Bayer states that specificity of PAT protein for glufosinate has been reported in the scientific literature.[9] Based on the results obtained from the protein safety assessments, Bayer concludes that the PAT protein expressed in MON 94313 soybean does not pose a meaningful risk to animal health if it is presents in animal food

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[4] Bayer states completed consultations for DMO proteins that are highly similar (identical in structure of the catalytic site, function, immunoreactivity, and substrate specificity) to those produced in MON 94313 soybean include BNF No. 000125 (soybean), BNF No. 000135 (cotton), BNF No. 000148 (corn), and BNF No. 000173 (corn). Bayer also demonstrated that the amino acid sequence of DMO in MON 94313 soybean is identical to the mature DMO proteins that were expressed in BNF No. 000135 (cotton), BNF No. 000148 (corn), and BNF No. 000173 (corn). Detailed safety assessments on the DMO proteins were provided in BNF No. 000125 and BNF No. 000135, such as rapid digestion of protein in the presence of pepsin and pancreatin, loss of function after heating and oral acute toxicity evaluation.

[5] Wang, C., K.C. Glenn, C. Kessenich, E. Bell, L.A. Burzio, M.S. Koch, B. Li and A. Silvanovich. 2016. Safety assessment of dicamba mono-oxygenases that confer dicamba tolerance to various crops. Regul. Toxicol. Pharmacol. 81:171-182.

[6] Bayer reported in BNF No. 000125 that endogenous plant compounds, including ferulic acid, sinapic acid, syringic acid, and vanillic acid, were not catabolized by DMO protein, even though they were structurally similar to dicamba.

[7] Bayer states that it designed an *E. coli* expression vector to produce a DMO protein with an identical amino acid sequence as the MON 94313 DMO protein.

[8] Bayer notes that PAT protein produced in MON 94313 soybean is identical to the PAT protein expressed in MON 88701 cotton (BNF No. 000135), MON 87419 corn (BNF No. 000148) and MON 87429 corn (BNF No. 000173).

[9] Wehrmann, A., A. V. Vliet, C. Opsomer, J. Botterman and A. Schulz. 1996. The similarities of *bar* and *pat* gene products make them equally applicable for plant engineers. Nature Biotechnology 14(10):1274-1278; Christ, B., R. Hochstrasser, L. Guyer, R. Francisco, S. Aubry, S. Hortensteiner and J. K. Weng. 2017. Non-specific activities of the major herbicide-resistance gene BAR. Nature Plants 3(12):937-945

products.

Bayer notes that MON 94313 soybean expresses a modified version of the RdpA protein (FT_T.1). Bayer states that the amino acid sequence of FT_T.1 protein is identical, with the exception of three amino acids that were designed to improve enzymatic activity of the FT_T protein[10] towards its substrate 2,4-D.[11] Bayer notes that these changes would have no impact on the structure, immunoreactivity or specificity of the protein thus concludes that previous safety assessments of FT_T are applicable to FT_T.1 expressed in MON 94313 soybean. Bayer also notes that no sequence similarity exists between MON 94313 FT_T.1 and any known protein toxins. Bayer cites data in the scientific literature for FT_T.1 to demonstrate that the three amino acids changes do not impact the herbicide substrate specificity, integrity, and temperature stability of FT_T.1.[12] In addition, Bayer performed *in vitro* assays using 32 endogenous plant compounds[13] to confirm that the three amino acids differences in FT_T.1 do not change the substrate specificity. Bayer concludes that these data collectively support the conclusion that expression of the FT_T.1 protein in MON 94313 soybean poses no meaningful risk to animal health.

Mesotrione, a beta-triketone herbicide, is an inhibitor of the 4-hydroxyphenylpyruvate dioxygenase (HPPD). Bayer states that TDO oxidizes mesotrione sequentially into non-inhibitory metabolites, thereby conferring mesotrione tolerance in MON 94313 soybean.[14] Bayer highlights that TDO is a Fe (II)/alpha-ketoglutarate-dependent dioxygenase. This class of enzymes are produced by diverse groups of organisms ranging from bacteria to plants. Bayer states that these dioxygenases have been consumed by animals without any known adverse safety effects. Bayer further states that TDO-like proteins exhibit high homology to their corresponding proteins from various crop plants, including rice, wheat and corn, which are widely utilized as animal food. Bayer highlights that MON 94313 TDO protein is identical to the native rice HIS1 protein, except for the N-terminal methionine at position 1 which in the TDO protein is cleaved during protein processing in the cytosol in MON 94313 soybean. Bayer used *in silico* analyses and *in vitro* assays to verify that 32 endogenous plant compounds are not substrates for the TDO protein. For the assays, Bayer also included mesotrione as a positive control and five other HPPD inhibitor herbicidal substrates. Bayer concludes that the TDO protein was optimized for beta-triketone class of HPPD inhibitor

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[10] Bayer notes that FT_T protein is expressed in MON 87429 corn, which was previously evaluated in BNF No. 000173.

[11] Bayer states that the three amino acids changes are necessary due to the high sensitivity of dicots, such as soybeans, to 2,4-D herbicide.

[12] Larue, C. T., M. Goley, L. Shi, A. G. Evdokimov, O. C. Sparks, C. Ellis, A. M. Wollacott, T. J. Rydel, C. E. Halls, B. Van Scoyoc, X. Fu, J. R. Nageotte, A. M. Adio, M. Zheng, E. J. Sturman, G. S. Garvey and M. J. Varagona. 2019. Development of enzymes for robust aryloxyphenoxypropionate and synthetic auxin herbicide tolerance traits in maize and soybean crops. Pest Management Science 75(8):2086-2094

[13] The 32 endogenous plant small molecules compounds were the same compounds tested with FT_T protein in BNF No. 000173.

[14] Dai, S., N. Georgelis, M. Bedair, Y.-J. Hong, Q. Qi, C. T. Larue, B. Sitoula, W. Huang, B. Krebel, M. Shepard, W. Su, K. Kretzmer, J. Dong, T. Slewinski, S. Berger, C. Ellis, A. Jerga and M. Varagona. 2022. Ectopic expression of a rice triketone dioxygenase gene confers mesotrione tolerance in soybean. Pest Management Science 78:2816-2827

herbicides, such as mesotrione, tembotrione, and sulcotrione.

To obtain sufficient quantities of the TDO protein for conducting safety assessment, Bayer produced the TDO protein in *E. coli*. Bayer confirmed the identity and biochemical equivalence of the TDO proteins expressed in *E. coli* and MON 94313 soybean, using several analytical techniques.[15] Bayer demonstrated that TDO protein was cleaved within 0.5 minutes in simulated gastric fluid and 5 minutes in simulated intestinal fluid, and TDO protein was denatured when exposed to high temperatures (≥ 55°C) for 15 minutes. Bayer also demonstrated that MON 94313 soybean and *E. coli* expressed TDO proteins were not glycosylated. Bayer used the FASTA algorithm against the TOX_2021 database to determine the similarity of MON 94313 TDO amino acid sequence to known toxins. Bayer concludes that no sequence similarity exists between MON 94313 TDO and proteins in its toxin database. Bayer states that there was no evidence of acute toxicity in mice that were given a single oral dose of 2000 milligrams of TDO protein/kilogram of body weight (mg/kg BW/d). In a separate study, mice were given up to 1000 mg/kg BW/d as an oral gavage for 28 days. Bayer concludes that the acute exposure No Observed Adverse Effect Level (NOAEL) for TDO protein was 2,000 mg/kg BW/d and the chronic exposure NOAEL for TDO protein was 1,000 mg/kg BW/d. Bayer concludes that these data collectively support the conclusion that expression of the TDO protein in MON 94313 soybean poses no meaningful risk to animal health.

Expression Levels of Proteins in MON 94313 Soybean

Bayer quantified DMO, PAT, FT_T.1 and TDO protein levels in various tissues of MON 94313 soybean. The study included five field trial sites with four replicate plots at each site. Forage, leaves, grain, and root tissue samples were collected from MON 94313 soybean plants from each replicated plot at all field sites treated with dicamba, glufosinate ammonium, 2,4-D, and mesotrione herbicides. Samples were analyzed using multiplexed immunoassay or enzyme linked immunosorbent assay. Bayer reports that mean DMO protein level in MON 94313 soybean across all sites was highest in over-season leaf (OSL) 4 at 410 micrograms/gram of tissue dry weight (DW), lowest in root at 20 micrograms/gram DW and at 40 micrograms/gram DW for grain. Mean PAT protein level in MON 94313 soybean across all sites was highest in OSL3 at 25 micrograms/gram DW, lowest in root at 3.7 micrograms/gram DW and at 3.8 micrograms/gram DW for grain. Mean FT_T.1 protein level in MON 94313 soybean across all sites was highest in OSL4 at 28 micrograms/gram DW, lowest in root at 4.1 micrograms/gram DW and at 6.1 micrograms/gram DW for grain. Mean TDO protein level in MON 94313 soybean across all sites was highest in OSL1 at 41 micrograms/gram DW, lowest in root, which was below the limits of quantitation and at 5.0 micrograms/gram DW for grain.

Bayer concludes that the safety of the newly expressed proteins has been demonstrated through a weight of the evidence approach and these proteins in MON 94313 soybean

[15] The analytical techniques discussed in the notice include sodium dodecyl sulfate polyacrylamide gel electrophoresis (SDS-PAGE), Western blot analysis, TDO enzymatic activity, N-terminal amino acid sequence analysis using nano liquid chromatography mass spectrometry/mass spectrometry (nano LC-MS/MS), and peptide mass fingerprint analysis (nano LC-MS/MS analysis of trypsin digested peptides).

are safe when used in animal food.

Animal Food Use

The developer states that MON 94313 soybean is expected to be grown for the same uses as currently commercialized soybean, and no new or specialty food or feed uses are anticipated. The typical uses of soybean-derived food and feed are well documented in Organisation for Economic Co-operation and Development (OECD) soybean composition consensus document[16] and scientific literature[17]. Most soybean seeds are processed into oil and meal. Soybean oil is commonly used as a human food ingredient. The preponderance of soybean meal is used in animal food, primarily in poultry, swine, and beef and dairy cattle diets. Soybean meal is processed in moist heat to inactivate trypsin inhibitors and lectins, which are anti-nutrients occurring in raw soybeans.

Composition

Scope of Analysis

Bayer analyzed the nutrient composition of MON 94313 soybean and soybean variety A3555 (control) that were grown and harvested under similar conditions. Compositional analyses of grain and forage samples were reported for components listed in the OECD soybean composition consensus document.

Study Design

Bayer conducted field trials in 2020 at five locations in the United States. A randomized complete block design with four replicate plots was used at each field site. The MON 94313 soybean plots were treated with glufosinate, dicamba, 2,4-D, and mesotrione herbicides. Forage samples were harvested at R5 growth stage and were shipped on dry ice from the field sites to Bayer. Grain was harvested at physiological maturity and shipped at ambient temperature from the field sites to Bayer. A subsample for compositional analysis was obtained from forage and grain samples and stored at approximately -20°C prior to nutrient analyses.

Components that were analyzed in forage samples included crude protein, crude fat, ash, carbohydrates by calculation,[18] acid detergent fiber (ADF), and neutral detergent fiber (NDF). Nutrient analyses in grain included the above-mentioned components plus 18 amino acids, 22 fatty acids, two minerals, two vitamins, phytic acid, raffinose, lectin, stachyose and trypsin inhibitor, and three isoflavones. Bayer notes that nine of the fatty acids were not statistically analyzed because more that 50% of the observations fell below the lower limits of quantitation. Results were all expressed on a dry matter basis prior to statistical analyses. Moisture of forage and grain were not statistically analyzed.

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[16] Organisation for Economic Co-operation and Development. 2012. Revised consensus document on compositional considerations for new varieties soybean [*Glycine max* (L.) Merr.]: Key food and feed nutrients, anti-nutrients, toxicants and allergens. Series on the Safety of Novel Foods and Feeds No. 25. ENV/JM/MONO 24. OECD, Paris

[17] Stein, H., L.L. Berger, J.K. Drackley, G.C. Fahey, D.C. Hernot, and C.M. Parsons. 2008. Nutritional properties and feeding values of soybeans and their coproducts. Soybeans 613-660.

[18] Percent carbohydrates = 100% - (% protein + % fat + % moisture + % ash).

Bayer statistically compared each component for MON 94313 soybean with the control across-locations using a linear mixed model with site and replicate as random factors. T-test analyses were used to test at the level of $p \leq 0.05$ for differences between MON 94313 soybean and control. Differences between MON 94313 soybean and control were evaluated in context of variation within the control germplasm grown across multiple sites and of natural variability defined by values for soybean varieties in the Agriculture and Food Systems Institute Crop Composition Database (AFSI-CCDB)[19] and in the scientific literature.

Results of Analyses – Forage

Bayer reported that there were no statistically significant differences between MON 94313 soybean and control for any of the analyzed components. In addition, the mean value for each component in MON 94313 soybean forage fell within the range of values observed in the AFSI-CCDB and scientific literature.

Results of Analyses – Grain

Bayer reports that there were no statistically significant differences between MON 94313 soybean and control for most of the analyzed components. Statistically significant differences between MON 94313 soybean and the control were reported for cystine, tryptophan, palmitic acid, linolenic acid, carbohydrates by calculation, vitamin K1, and glycitein in the grain samples. However, Bayer notes that for all of these components, the mean differences between MON 94313 soybean and the control were less than the range of values for the control. The mean values for all of these components were also within the range of values observed in the AFSI-CCDB and scientific literature. Bayer concludes that the observed statistically significant differences between MON 94313 soybean and the control are not biologically meaningful from an animal food safety perspective.

Summary of Compositional Analyses

Bayer states that expression of the four proteins that impart tolerance to different herbicides does not meaningfully alter the nutrient composition of MON 94313 soybean. Bayer concludes that these results support the conclusion that forage and grain obtained from MON 94313 soybean are compositionally equivalent to the control in the levels of key nutrients and anti-nutrients.

Conclusion

CVM evaluated Bayer's submissions to determine whether MON 94313 soybean raises any safety or regulatory issues with respect to its use 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.

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[19] Agriculture and Food Systems Institute (AFSI) Crop Composition Database: https://www.cropcomposition.org.

Bayer concludes that MON 94313 soybean 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 soybean varieties now grown, marketed, and consumed. At this time, based on Bayer's data and information, CVM considers Bayer's consultation on MON 94313 soybean for use in animal food to be complete.

Jing Ning -S

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